MEASURING NUTRITION RELATED OUTCOMES IN A COHORT OF MULTI-TRAUMA PATIENTS FOLLOWING INTENSIVE CARE UNIT DISCHARGE

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Transparency Declaration:

The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported. The reporting of this work is compliant with STROBE[(1)] guidelines. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained. This project was approved by the Melbourne Health Human Research Ethics Committee (QA2018048).

Authorship declaration:

K. Wittholz, K. Fetterplace, A. M. Deane, equally contributed to the conception and design of the research; E. S. George, R. Judson and C M. MacIsaac contributed to the design of the research; K. Wittholz, M. Clode, K. Fetterplace contributed to the acquisition of the data; K. Wittholz, K. Fetterplace and J. J. Presneill contributed to the analysis and the interpretation of the data; K. Wittholz, K. Fetterplace and A. M. Deane drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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Conflicts of interest

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Abstract:

Background: Aims: Functional recovery is an important outcome for those that survive critical illness. The aim of this study was to assess nutrition provision and nutrition related outcomes in a multi-trauma cohort following intensive care unit (ICU) discharge.

Methods: A prospective cohort study of patients discharged from the ICU alive who had been admitted because of major trauma and required mechanical ventilation for at least 48 hours. Nutrition-related outcomes including body weight, quadriceps muscle layer thickness (QMLT), handgrip strength and subjective global assessment were recorded on ICU discharge, day 5-7 post ICU discharge and then weekly until hospital discharge. Nutrition intake was recorded for 5 days post ICU discharge. Unless otherwise stated, data are presented as mean (SD).

Results: Twenty-eight patients [75% males, 55 (22.5) years] were included. Intake met 64% (28%) of estimated energy and 72% (32%) of protein requirements over the 5 days post ICU discharge, which was similar to over the ICU admission. From ICU admission to hospital discharge the mean reduction in weight was 4.2 kg (95% CI 2.2 to 6.3, $p < 0.001$) and after

ICU discharge, the mean reduction in weight and QMLT were 2.6 kg (95% CI 1.0 to 4.2, p =0.004) and 0.23 cm (95% CI 0.06 to 0.4, p = 0.01) respectively.

Conclusion: Patients received less energy and protein than estimated requirements after ICU discharge. Weight loss and reduction in QMLT also occurred during this period.

Introduction:

Functional ability and health-related quality of life are important outcomes for those that survive critical illness [1-3]. An intensive care unit (ICU) admission can lead to rapid reductions in muscle mass and substantial muscle weakness [1, 4, 5] and changes in body composition have been associated with prolonged hospital admissions, reductions in post-hospital discharge functional recovery and diminished health-related quality of life (QOL) [1, 4-7].

Nutrition has been identified as a potential modifiable factor which may aid in the preservation of skeletal muscle during critical illness and help to restore muscle lost in the recovery phase [8-10]. However, the amount, type and phase of critical illness, or recovery which nutrition support will have greatest impact, remain unknown [8-10]. Various nutritional interventions have been administered within the ICU with the objective of attenuating muscle loss and functional weakness but the impact has been inconsistent [7, 11, 12]. This may be because the interventions chosen are of limited or no benefit, the period that the nutrition intervention is provide is not ideal for the substrate to be utilised, the period of the ICU admission is too brief to obtain benefit or that the studies to date have not been sufficiently powered to detect a difference[8]. It has been suggested that nutritional interventions administered after the acute phase of critical illness may have greater impact [8, 13-15]. However quantifying nutritional intake and nutrition-related outcomes after ICU discharge is likely to be more challenging due to a variety of factors including equipment and personnel availability, challenges in accurately quantifying volitional ingested nutrient intake, and less predictable timing of discharge from hospital [16-18].

One cohort of patients that may benefit from a nutritional intervention post-ICU discharge are those admitted because of severe traumatic injuries. After a traumatic injury, patients can have elevated energy expenditure and increased protein catabolism [19, 20], which is likely to continue post ICU and throughout recovery [20, 21]. Despite patients with traumatic injury frequently being prescribed more energy and protein than non-trauma patients in ICU [22], substantial cumulative nutritional deficits have been observed during ICU for this cohort [16, 22].

There are limited data reporting nutrition intake and nutrition-related outcomes after ICU discharge. The primary aim of this study was to determine the feasibility of repeatedly assessing nutrition intake and measuring nutrition-related outcomes (weight, nutritional status, muscle mass and strength) in a cohort of patients with traumatic injury following ICU discharge. Secondary aims were to i) compare nutrition intake post ICU discharge to nutrition intake whilst in the ICU, ii) to determine whether post ICU discharge there were any differences between those receiving only oral intake compared to any artificial nutrition support and iii) to explore the relationships between nutritional intake and nutrition-related outcomes.

METHODS:

This cohort study was conducted in one of the two trauma referral centres that receive all major adult trauma for the state of Victoria (population approximately 6.3 million). Between July to September 2018, all patients admitted to the ICU due to a traumatic injury who were ≥18 years old and mechanically ventilated for at least 48 hours were screened for eligibility. Recruitment occurred on the day of discharge from the ICU. Patients were excluded if on discharge to the ward they had impaired neurology (defined as best motor score of abnormal flexion or worse), bilateral upper arm injury, or the goal of treatment was altered to include a focus on palliative care. Reporting of this study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [23]. This project was approved by the Melbourne Health Human Research Ethics Committee (QA2018048). Eligible patients, or their person responsible (if they were unable to comprehend written information), were provided with written information regarding the study and they were given the opportunity to opt out from inclusion in the study.

Data were collected from ICU discharge and censored 26 days after ICU discharge or on hospital discharge, whichever came first (figure 1). Baseline demographic data and patient characteristics were collected from the ICU admission. Routine care in this ICU includes that all patients who are mechanically ventilated for ≥ 48 hours and are receiving nutritional therapy are assessed by an ICU dietitian. Protein and energy requirements were based on the dietitians' assessment in the ICU and post ICU discharge. Estimated nutritional requirements were calculated using actual body weight for patients below or within the ideal body weight (IBW) range (Body mass index (BMI) 18.5 - 25kg/m^2 and for those aged ≥65 years BMI 22 - 27kg/m^2) [24]. For overweight participants IBW was used and for obese participants with a BMI greater than 30 kg/m^2, an obesity adjusted weight was used (IBW + 25% (actual body weight - IBW) [24].

Figure 1. Outcome Measurement Procedure

Nutrition intake over the ICU admission was retrospectively determined from fluid balance charts, through daily analysis of enteral and parenteral nutrition delivery. Energy provided from other sources (e.g. intravenous propofol and glucose as part of fluid therapy) were not included and discarded gastric residual volumes were not subtracted from energy provision.

Ward nutrition intake was collected for five days post ICU discharge. Diet orders, nutrition consumed and mode of nutrition delivery were recorded daily. For patients receiving artificial nutrition, fluid balance charts were reviewed to determine protein and energy intakes. For patients with volitional intake, the proportion of each component of the meal consumed (using visual estimates of 0%, 25%, 50%, 75% or 100%) was recorded in the Mobile Intake™ data application in the hospitals electronic menu management system (CBORD™, The CBORD group, New York). If a meal period was not able to be assessed by a dietitian, food record charts, completed by nursing staff including visual estimates of meals consumed, or patient reported intake, were used to estimate the food intake. The hospital menu management system CBORD™ was used to analyse protein and energy intake using the 2011-2013 AUStralian Food and NUTrient (AUSNUT) database.

The ward (5 days) and ICU energy and protein adequacy was calculated in the same way, daily intake was compared to dietitian estimated requirements, and averaged over the study period; the ICU adequacy excluding the day of ICU admission and discharge if it was less than 12 hours.

Nutrition-related outcomes including weight and muscle mass and strength were recorded at baseline (within 48 hours of discharge from the ICU), day 5-7 post ICU discharge and then weekly thereafter.

Weight on admission to ICU was recorded using bed scales (Hill-Rom®, Indiana USA) for the majority of patients. If it was not physically possible to weigh the patient on admission, family reports were used for the admission weight. Post ICU weight was measured using standing scales (Seca 876, Hamburg, Germany), chair (Colonial BW1122, Melbourne, Australia) or hoist scales (Ajor Maxi Move L8038, Malmö, Sweden) depending on the patient's injury type and mobility. Weight change was calculated as the difference in weight from ICU admission to ICU discharge and to hospital discharge.

Muscle mass was assessed using an ultrasound to measure quadriceps muscle layer thickness (QMLT). QMLT measurements were performed using a portable ultrasound machine (Sonosite S-ICU) with a multiple-frequency transducer (13-6 MHz, 6 cm) using the technique initially described by Tillquist and colleagues [7, 16, 25]. Measurements were taken with the patient lying supine with leg relaxed and in extension and the bedhead elevated at approximately 30 degrees. QMLT was measured unilaterally (on the right side unless contraindicated due to injury or impairment) at two points; the midpoint between the anterior superior iliac spine and the upper pole of the patella and at the point two thirds between the anterior superior iliac spine and the top of the patella. A still image was taken with minimal pressure and then again with maximal pressure applied. The measurements were taken twice for each point and then the four measurements were averaged to obtain the final QMLT measurement. A third measure was taken if there was a difference of >10% between the first two measurements, and the measurement with greater than a 10% difference was discarded.

A trained dietitian used handgrip dynamometry (JTECH Medical Commander Echo Dynamometer) to assess upper limb muscle strength bilaterally [26]. Patients were assessed in a seated position, in a chair where possible or sitting at least at 45 degrees in bed, with their forearm in flexion at 90 degrees and wrist in extension, supported by the arm of the chair or a pillow. Patients were asked to perform a maximal voluntary isometric contraction and maintain the contraction for 3–5 seconds. Three consecutive isometric contractions with 30-60 second of rest in between test were completed and the highest measurement was recorded. The Subjective Global Assessment (SGA), was used to assess nutritional status [27]. Patients were categorised as well nourished (Score A), mild to moderately malnutrition (Score B) or severely malnourished (Score C). As part of usual care at the study institution, the SGA is completed by ICU dietitians on initial assessment (within 48hrs of admission). This score was then retrospectively extracted from the notes of eligible patients. The SGA was subsequently repeated at hospital discharge by the trained research dietitian.

Feasibility was determined though retention of study participants for at least 5 days post ICU. Feasibility was predefined as >75% of eligible participants completing 5 days of intake data and having ≥ 1 repeat measure recorded.

Statistical analysis

Continuous and interval data were reported as means (standard deviations, SD) and/ or medians [inter-quartile ranges, IQR] as appropriate. Proportions were used to summarise ratios, and malnutrition was compared over time with McNemar's test accompanied by a 95% confidence interval. Initial univariable exploration of differences in continuous measures over time used the construction of trajectory plots, followed by paired t-tests. Changes in QMLT over time were explored using a population-averaged multivariable linear model with a generalised estimating equation (GEE) approach, an exchangeable working correlation structure and robust standard error estimates accounting for clustering within individual subjects. Independent variables included baseline QMLT, protein adequacy, BMI, presence of traumatic brain injury, age at or above 65 years, and the patient's ICU admission APACHE II severity of illness score. A two-sided p value of <0.05 was set for statistical significance for all tests, with no adjustment for multiple testing. Data analysis was carried out using the Statistical Package for the Social Sciences (IBM® SPSS® Statistics Premium Grad Pack Version 23.0) and Stata version 15.1 (StataCorp. 2017. Stata Statistical Software: Release 15.1. College Station, TX: StataCorp LP).

RESULTS:

During the 4-month study period 67 patients were screened for inclusion, 32 (47%) met all inclusion and no exclusion criteria, and 28 (42%) patients agreed to participate (figure 2). Study participant characteristics are described (table 1).

Figure 2. Consort diagram

Table 1. Patient characteristics

During ICU admission participants received 62 (17) % and 63 (19) % of estimated energy and protein requirements. At ICU discharge 19 (68%) of participants were receiving exclusive oral intake, five (18%) participants were on a combination of oral diet and enteral nutrition (EN) via a feeding tube, three (11%) participants were receiving exclusive EN via a feeding tube, and one (4%) patient was receiving a combination of EN and parenteral nutrition (PN).

Over the 5 days post ICU discharge that nutritional intake was observed, there were a total of 120 days (85% of all days) of data available, with all missing data due to patient discharge from hospital (table 2). Daily energy and protein intake was 1478 (651) kcal and 75 (37) grams which equated to 64 (28) % and 72 (32) % of estimated energy and protein requirements (Figure 3). There were no statistical group differences in either energy [-3 % (95%CI -15 to 10), p = 0.66] or protein adequacy [-10 % (95% CI -25 to 5), p = 0.19] between ICU admission and post ICU periods.

Patients receiving solely oral intake consumed less energy and protein compared to patients receiving any artificial nutrition support (oral diet plus EN, EN alone or EN plus PN); the mean energy and protein intakes were 1298 (640) kcal and 68 (39) grams and 1857 (524) kcal and 89 (30) grams respectively. The between group difference was statistically significant for daily energy [mean difference 558 kcal (95% CI 53 to 1062), p = 0.03)] but not protein [mean difference 22 g (95% CI -8 to 51), p = 0.15]. Compared with dietitian prescriptions, patients on any artificial nutrition received a mean adequacy of 87 (14) % of energy and 87 (17) % of protein compared to those on oral diets who consumed a mean adequacy of 54 (26) % of energy and 65 (36) % of protein.

Figure 3: Mean daily energy and protein adequacy for the ICU admission and the first 5 days post ICU discharge

Nutritional intake data and the measurement of nutritional status using the SGA were both found to be feasible outcomes measures, however the other nutrition-related outcome measures (weight, QMLT and handgrip strength) were not found to be feasible in this cohort (Table 2).

The proportion of participants observed to be malnourished increased from ICU admission to hospital discharge, however this was not found to be statistically significant [3/28 (11%) versus 7/28 (25%), change 14% (95%CI -2 to 31), $p = 0.13$]. Of the participants who had weight measured at ICU admission and ICU discharge ($n = 25$), there was a significant reduction in weight [mean reduction 2.3 kg (95% CI (0.5 to 4.2), $p = 0.02$], with the mean percentage loss of weight over this period of 3.9 (4.6) %. From ICU admission to hospital discharge the mean reduction in weight was 4.2 kg (95% CI (2.2 to 6.3, $p < 0.001$), with a significant loss of weight also observed over the first five days post ICU (table 3).

Quadriceps muscle layer thickness (QMLT) was measured on more than one occasion post ICU discharge in 18/28 patients (64%) (table 2). There was a significant reduction in mean QMLT (no pressure) over ward admission by 0.23 cm (95% CI (0.06 to 0.40), $p = 0.01$) (table 3) and the mean percentage reduction was 7.2 (13) %. Change in QMLT (no pressure) for individuals over time is shown in supplementary figure 1. Mean change in QMLT over time was associated with greater baseline QMLT and a greater number of days post ICU discharge (table 4).. There was no significant association found between change in QMLT and age, BMI, severity of illness on admission to the ICU, presence of a traumatic brain injury or ward protein adequacy. There was a significant improvement in handgrip strength from baseline to day five post ICU discharge in the group of participants ($n = 10$) who had two measurements completed (table 3).

Discussion:

In this single-centre cohort study of patients with a traumatic injury who were discharged from ICU, patients received less energy and protein than it was estimated that they required. Energy and protein provision and nutritional adequacy on the ward were similar to what was provided during the ICU admission; however patients receiving artificial nutrition support post ICU discharge had improvements in energy and protein provision. It was also observed that after ICU discharge a significant reduction in weight and QMLT occurred. According to the pre-defined criteria, missing data limited feasibility for several nutrition-related outcomes.

The results observed in the present study are similar to several studies conducted in the ICU, with patients receiving approximately 60% of their nutritional targets [28-31]. Whilst few studies have reported nutritional adequacy after ICU discharge, in a single-centre study of 37 patients with traumatic brain injury by Chapple and colleagues, patients received similar nutritional adequacy in ICU and after ICU discharge [18]. However, they observed greater energy and protein provision in both settings than the present study, with patients receiving 81% (35) of energy and 77 % (35) of protein requirements after ICU discharge. These differences could be related to the different patient cohorts and the proportion of patients with traumatic brain injury who require artificial nutrition after ICU discharge rather than consuming oral intake. In the present study it was observed that patients who received any artificial nutrition had significant increases in energy but not protein adequacy in the post ICU period compared to those receiving oral intake alone. These results are similar to that observed by Chapple and colleagues who described less intake in those reliant solely on oral diet [18]. Additionally, Peterson and colleagues examined oral nutrition intake via multi-pass 24 hour food recall for 7 days post extubation in a single centre cohort of 50 critically ill patients [32]; they observed that mean energy and protein intake never exceeded 55% of daily requirements [32]. These results highlight that nutritional inadequacy persists in the cohort of patients after traumatic injury, and patients receiving oral intake alone are possibly at greatest risk of nutritional inadequacy in ICU and the post ICU period. This may be due to early withdrawal of artificial nutrition support or that hospital systems do not support achieving nutritional adequacy during periods of volitional oral intake [33]. Further research is warranted to understand why nutritional inadequacy persists after ICU discharge and how to improve nutritional adequacy throughout the entire hospital admission [34].

In the present study nutrition-related outcome data for weight, QMLT and handgrip strength were not recorded in sufficient numbers to meet the pre-defined feasibility criteria. Patient factors, including delirium, agitation, and post-traumatic amnesia; hospital factors, including appropriate equipment availability, multiple procedures and scans; early discharge; and research resource allocation all contributed to missing data. It has been reported that the prevalence of cognitive impairment after a traumatic brain injury is up to 70% [35], and this may affect capacity to complete some of the outcome measures. Therefore, outcome measures, which do not require participation, volitional movements and cooperation such as QMLT are probably more feasible in this population, rather than handgrip strength and functional capacity and quality of life [36]. Although the frequency of QMLT measurements did not achieve the predefined feasibility criteria, it was successfully measured in 64% of participants and, of the missing data, five (14%) participants were discharged prior to the first repeat measure time point (day 5 post ICU). These results are similar to that reported by Chapple and colleagues, who measured QMLT weekly post ICU in 79% of their TBI cohort [16, 25]. Evidence from these two centres therefore supports the concept that QMLT is perhaps the most feasible variable to repeatedly measure in this population when attempting to evaluate the impact of nutritional therapies on body composition.

It remains unclear what, if any, impact energy and protein provision in the ICU or following ICU admission has on patient-centred and nutrition-related outcomes [8]. In the present study it was observed that there was a significant reduction in weight and QMLT over the study period, however there was no evidence found to suggest that greater protein provision was associated attenuation of QMLT loss. Similarly, in a previous multi-centre observational study (UK MUSCLE), they reported that greater loss of quadriceps muscle was associated with greater protein delivery in ICU [5]. However in contrast to this observed association, other cohort studies [37, 38], and a recent randomised control trial by our group, report that greater protein delivery is associated with attenuation of muscle loss in ICU [7]. These conflicting results highlight the issues with interpreting associations in observational studies of critically ill cohorts, particularly as severity of illness is a confounder that may not be adequately accounted for. Whilst muscle thickness and body composition outcomes are only surrogate physiological outcomes for outcomes that are important to patients, Chapple and colleagues reported that greater QMLT at hospital discharge was associated with significant improvements in self-related quality of life three months after hospital discharge [16]. Further research is required to evaluate the impact of nutritional therapies on functional outcomes post discharge from hospital [8, 34].

This is the first study to evaluate the feasibility of measuring nutrition-related outcomes and nutritional intake in patients with multiple injuries following trauma after ICU discharge. Nutritional intake was measured using meal observations and an electronic menu management system and nutritional outcomes such as muscle mass, muscle strength and nutritional status were recorded. However there are several limitations, including that this was a single centre study and a relatively small number of patients were studied. Moreover, the size of the cohort was not sufficient to determine whether nutrition-related outcomes were affected by nutritional adequacy, and due to the observational nature, causality cannot be established for any associations observed. Data collection was limited to weekdays and the acute hospital admission. Increasing the resource allocation and study timeframes in future interventional studies may increase sample size and data completeness and consideration should be given to include outcome data form admissions to rehabilitation facilities. It was also not within the scope of this study to examine the feasibility of measuring nutrition-related outcomes post hospital discharge. With recovery from acute illness, patient participation in outcome measures may increase and therefore increase their utility.

Conclusions:

Mean energy and protein intake were below the estimated requirements, and were similar during the ICU admission and after ICU discharge; however patients receiving artificial nutrition support received greater amounts of energy. Within the limitation of missing data, weight loss and reductions in QMLT were observed after ICU discharge. Greater change in QMLT was associated with greater baseline QMLT and the length of ward admission. The most appropriate outcome measures to investigate associations between nutrition provision and recovery remains unclear and warrants further investigation. Well-designed and adequately powered randomised clinical trials are required to determine the effect of greater nutrition provision on nutrition-related outcomes in patients discharged from ICU after major trauma.

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Figure 1: Outcome Measurement Procedure

HGS; handgrip strength, QMLT; Quadriceps muscle layer thickness, SGA; subjective global assessment

Figure 2: Consort Diagram

*Eligible patients, were those admitted to the ICU due to a traumatic injury

Table 1: Patient characteristics

Patient Characteristics (n = 28)	**Value**
Age – year, mean (SD)	50 (22.5)
Males – n (%)	21 (75)
Length of Stay, mean (SD)	
ICU	10.6 (6.7)
Ward	10.9 (9.2)
Total hospital	21.6 (11.8)
Mechanical Ventilation – days, median [IQR]	6.0 [3.0-9.5]
Injury – n (%)	
Multi-trauma	16 (57)
Multi-trauma with TBI	12 (43)
APACHE II score, mean (SD)	15 (6)
APACHE III score , mean (SD	111 (55)
Body Mass Index – kg/m^2, median [IQR]	26 [25-32]
Body weight ICU admission – kg, mean (SD)	86 (23)
Malnourished – SGA B/C, n (%)	3 (11)

Abbreviations: APACHE; acute physiology and chronic health evaluation, ICU; Intensive Care Unit, IQR; Inter Quartile Range, Kg; kilogram, SD; Standard deviation; TBI, Traumatic Brain Injury , SGA; Subjective global assessment.

Figure 3: Mean daily energy and protein adequacy for the ICU admission and the first 5 days post ICU discharge

*Error bars represent mean and standard deviation; (n) represents the number of participants included at each time point.

Table 2: Feasibility of outcome measures

	Baseline[+] n (%)	**Day 5 post ICU discharge n (%)**	**At least ≥ 1 time point**	**Met feasibility criteria (Y/N)**
Weight	25 (89)	13 (46)	15 (54)	N
QMLT	27 (97)	18 (64)	18 (64)	N
Handgrip Strength	17 (61)	12 (43)	14 (50)	N
Subjective Global Assessment	28 (100)	NA	28 (100)	Y
Intake -days[┼]	NA	120 (85)	NA	Y

[+]Baseline: within 48 hours of ICU discharge

[++]SGA completed at baseline and hospital discharge.

[┼]Intake days: number of days intake data was recorded for the first 5 days post ICU discharge.

Abbreviations: ICU; intensive care unit, QMLT; quadriceps muscle layer thickness,

Table 3: Change in nutrition related outcomes from ICU discharge to day 5 post ICU discharge

	n	**Baseline[+] Mean (SD)**	**Day 5 post ICU discharge, mean (SD)**	**Mean difference (95% CI)**	**P-Value**
Body weight – kg	13	83.6 (16.1)	81.0 (16.2)	-2.6 (-0.98 to -4.2)	0.004*
Handgrip strength – kg	10	27.9 (9.5)	30.1 (11.1)	2.3 (0.22 to 4.3)	0.034
QMLT no pressure – cm	18	2.8 (0.8)	2.6 (0.8)	-0.23 (-0.06 to -0.40)	0.01*

[+]Baseline: within 48 hours of ICU discharge

Abbreviations: Cm; centimetres, Kg; kilograms, ICU; intensive care unit, QMLT; quadriceps muscle layer thickness.

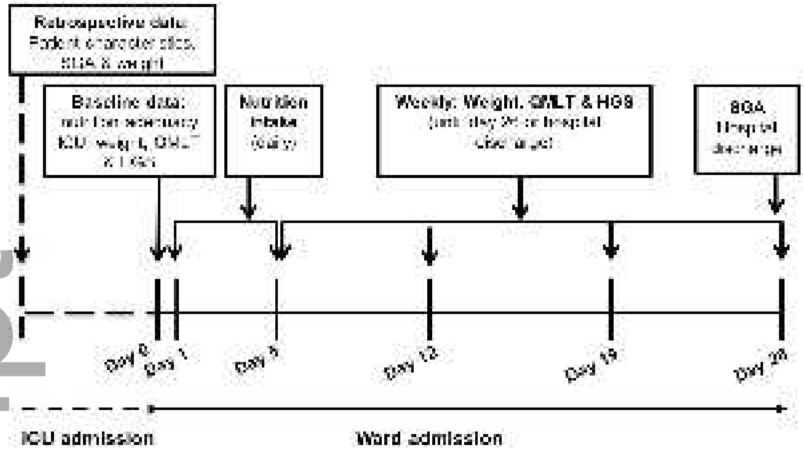
Table 4. Effect estimates from multivariable linear model assessing change in QMLT from baseline to hospital discharge

Variable	Coefficient of effect[+]	95% CI	P value
QMLT Baseline, cm	0.88	0.79 to 0.96	<0.001
ICU protein adequacy, per 10%	-0.04	-0.07 to 0.002	0.06
Number of days post ICU discharge	-0.04	-0.05 to -0.02	<0.001
BMI ≥ 30kg/m^2	0.07	-0.08 to 0.2	0.37
Presence of a traumatic brain injury	0.05	-0.05 to 0.15	0.31
Age ≥ 65 years	-0.02	-0.13 to 0.0.9	0.69
APACHE II score on admission, per 5 points	0.02	-0.04 to 0.07	0.59

[+]All reported effect estimates are adjusted for all other variables in the table within a multivariable linear model, using a generalised estimating equation approach (refer to statistical analysis methods for details)

Abbreviations: QMLT; quadriceps muscle layer thickness, ICU; Intensive Care Unit, BMI; Body Mass Index, APACHE; acute physiology and chronic health evaluation.

Supplementary Figure 1. Quadriceps muscle layer thickness measurements over time post ICU discharge



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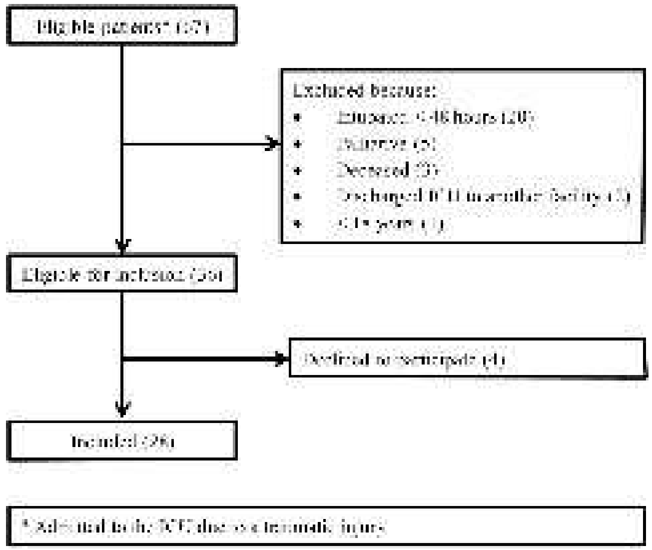

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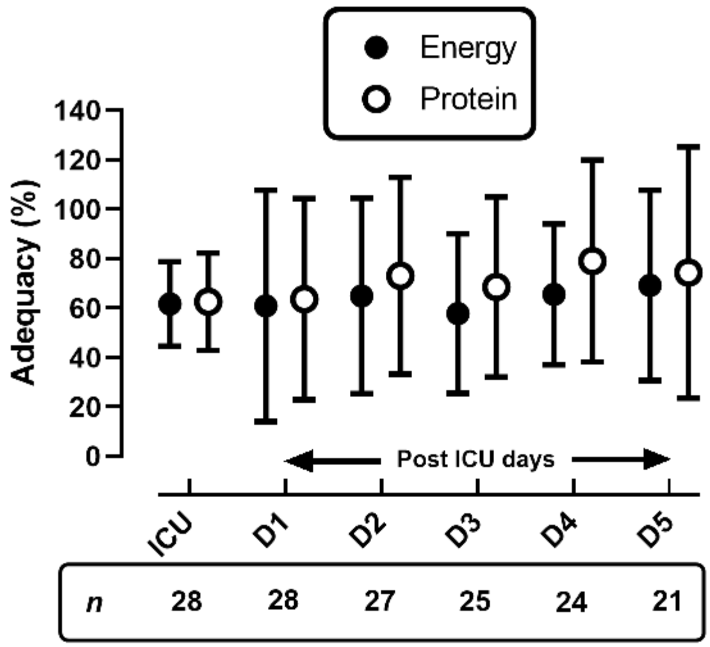

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