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Tools to evaluate the impact of nutrition delivery on muscle and physical-related outcomes in critical care: a scoping review

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Abstract

Understanding the impact of nutrition delivery on critically ill patient-centered outcomes is crucial. Patient-centered outcomes should be physical-related due to the natural course of catabolism experienced during critical illness. This review aims to map the existing tools used in research to evaluate the impact of nutrition delivery on muscle and physical-related outcomes among intensive care unit (ICU) patients. A search was conducted in PubMed and Scopus, initially yielding 502 articles published since 2010 on the topic using search terms related to ICU patients, muscle and physical outcomes, and nutrition delivery. Articles were screened based on inclusion criteria, resulting in 45 articles included in the analysis. Findings indicated that the outcome domains used ranged from muscle strength, muscle mass, to function. Imaging techniques and performance-based measures were the most used type of tools, with varying comprehensiveness, precision, simplicity, and feasibility. Despite most studies using repeated measurements throughout ICU stays, challenges in performing comprehensive assessments were reported. This review provides an overview of the assessment tools utilized in ICU nutritional research, highlighting the variability of choice that can be suited with researcher's objectives and the availability of resources. To improve consistency and comparability across studies, future research should focus on developing standardized protocols for selecting appropriate tools to measure the effects of nutrition delivery on muscle and physical-related outcomes.

Keywords: *critical care, functional outcomes, nutrition therapy, scoping review*

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Introduction

A critically ill patient will often experience a shift towards hypercatabolism due to the metabolic changes triggered by high stress levels (Hsu *et al*., 2021). The state of critical illness leads to metabolic instability, where tissue breakdown fuels survival mechanisms in response to physiological stress (Preiser *et al*., 2016). This stress response triggers several metabolic consequences such as insulin resistance due to uncontrolled catabolism and blunted anabolic signalling. Energy production and cellular functions are also compromised, forcing reliance on alternative substrates. This hypercatabolic response can lead to rapid skeletal muscle loss, with up to 5% of lean body mass loss daily (Preiser *et al*., 2014). The muscle wasting often persists in longer duration after intensive care unit (ICU) discharge, negatively impacting survivors' quality of life and physical function for months or even years (de Carvalho *et al*., 2023; Hofhuis *et al*., 2015; Jubina *et al*., 2023; Latronico *et al*., 2017).

Adequate nutrition is essential for critically ill patients to counteract catabolism and promote muscle regeneration through medical nutrition therapy (Hill *et al*., 2021; Van Zanten *et al*., 2019). The revised European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend adjusting energy dosage based on the phases of critical illness and calculation methods, with a gradual delivery of 1.3g/kg protein equivalents per day in the ICU (Singer *et al*., 2023).

Consequently, a consensus statement recommends that research on nutritional interventions in critically ill patients focus on outcomes involving physical function, muscle mass, and muscle function, especially when guided by indirect calorimetry (Sundström-Rehal *et al*., 2023). Moreover, further evaluation of the impact of nutritional therapy on functional outcomes after ICU and hospital discharge is required (Wischmeyer *et al*., 2023; Wittholz *et al*., 2020). Other than that, patients' quality of life (QoL) is also a crucial outcome measure that requires further exploration, as data on QoL outcomes from dietary interventions remain scarce (Barth *et al*., 2023; Bear *et al*., 2017; Wischmeyer, 2016).

A previous systematic review by Taverny *et al*. (2019) found that critically ill nutrition randomized controlled trials (RCTs) rarely use patient-important outcomes, missing the opportunity to elucidate the positive effects of nutritional interventions. As suggested by Bear *et al*. (2018) in their review, compared to mortality, outcome measures related to function and muscle mass are potentially becoming more important. This is consistent with another statement by Taverny *et al*. (2019), highlighting that clinical outcomes such as mortality are decreasing in relevance compared to muscle strength or quality of life, due to the advancement in intensive care. Another review by L. S. Chapple *et al*. (2020) reported that out of 73 trials, only 2 utilized physical, cognitive, or mental health outcomes as primary endpoints. As secondary or tertiary outcomes, only 7 trials used physical function. Therefore, there is a need to understand the impact of nutrition on muscle and physical function and the tools available to measure them.

This scoping review was conducted to identify and classify the assessment tools used in nutrition delivery research evaluating the impact of nutrition delivery on patients' muscle and physical-related outcomes. Understanding the assessment tools utilized in nutrition research is essential for standardizing methodologies, enhancing the comparability of studies, and improving the quality of evidence in clinical nutrition research. This review may help to identify gaps in the current research, guiding future studies, and contributing to more robust and consistent evaluations of nutritional interventions in critical care settings. The following research question was formulated using the PCC (population-concept-context) model: What assessment tools have been used in research to evaluate the impact of nutrition delivery on muscle and physical-related outcomes among critically ill patients?

Materials and Methods

Protocol

The methodology of this scoping review was drafted and revised using the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) protocol (Tricco *et al*., 2018).

Eligibility criteria and search strategy

To be included in the review, articles need to report on energy and/or protein delivery research conducted among critically ill adult patients with at least one outcome related to muscle or physical function. The articles were searched in PubMed and Scopus databases, limited to English publications from 2010 to August 2024. Articles were excluded if muscle or physical-related outcomes were measured only after patients' discharge from the ICU. All types of study addressing the target topic except qualitative, review, and conference abstracts were eligible for inclusion to consider different aspects of outcome measurements.

The search strategy was built by selecting groups of keywords and subject headings for each part of the PCC model, covering the population (adult critically ill patients aged 18 years or older), concept (muscle and physical-related outcomes assessment tools in ICU), and context (nutrition delivery study). Afterwards, each group of keywords was combined using the Boolean operator AND (Table 1). The final search results were exported to Endnote where duplicates were removed.

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Table 1. Search strings.

Strings	Database
((muscle* OR "muscle function*" OR "muscle mass" OR "muscle strength" OR "muscle weakness" OR "muscle wast*" OR "muscle loss" OR "functional outcome*" OR "physical rehab*" OR "physical function*") AND ("energy intake" OR "calor* intake" OR "protein intake" OR "nutrition therapy"[Mesh])) AND ("intensive care units"[Mesh] OR "critical Illness*"[Mesh] OR "critical care"[Mesh])	PubMed
(TITLE-ABS-KEY (muscle* OR "muscle function*" OR "muscle mass" OR "muscle strength" OR "muscle weakness" OR "muscle wast*" OR "muscle loss" OR "functional outcome*" OR "physical rehab*" OR "physical function*") AND TITLE-ABS-KEY ("energy intake" OR "calor* intake" OR "protein intake" OR "nutrition therapy") AND TITLE-ABS-KEY ("intensive care units" OR "critical Illness*" OR "critical care")) AND PUBYEAR > 2009 AND (EXCLUDE (DOCTYPE , "re")) AND (LIMIT-TO (LANGUAGE , "English"))	Scopus

Study selection and data collection

The initial articles underwent a title and abstract review, resulting in several articles selected for full-text evaluation. Disagreements on study selection and data extraction were resolved by consensus and discussion. Data were extracted using a customized data collection sheet to record the article characteristics (e.g., year published, study type), objectives, type of population, duration, assessment tools and frequency of measurement, other outcome measures, and findings (Table 2). Variables to extract were determined based on the research question and piloted on several articles with modifications made accordingly until a consensus was reached on the final format. No methodological quality criteria were considered.

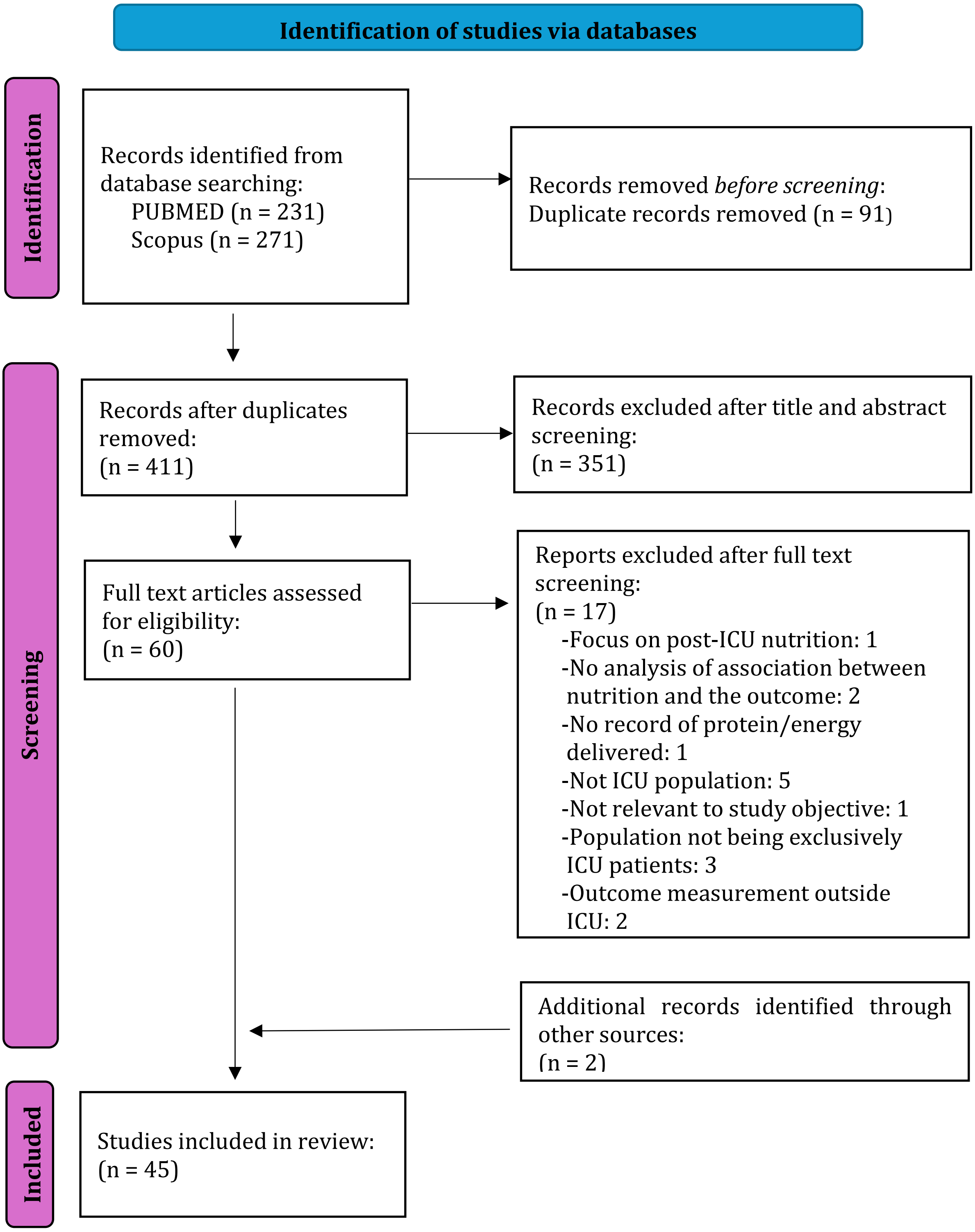

Figure 1. Flow chart of the article search and selection process (Tricco *et al.*, 2018).

Results

Search results, study selection, and data extraction

From the literature search, 502 articles were initially identified using the search terms from both databases. After removing duplicates, the articles underwent title and abstract screening, resulting in 60 articles eligible for full-text screening. Following full-text screening, 17 articles were excluded for reasons reported in Figure 1. Another 2 additional articles were identified from the reference lists of included studies. As a result, 45 articles were qualified to be included in the review (Figure 1).

Study characteristics

The 45 articles included primarily consist of randomized controlled trials (RCTs), with the rest being pilot RCTs, subanalysis of RCTs, observational, and comparative studies published between 2010 to 2024. The number of participants varied widely, ranging from 21 to 1,372. A summary of the key characteristics of the included studies is reported in Table 3.

Most studies (84%) repeatedly assessed muscle and physical-related outcomes while in ICU to capture the changes over time in relation to the nutrition delivered. In the studies with a single timepoint outcome assessment, the measurements were mostly conducted at ICU discharge. While most studies enrolled general ICU patients, certain studies focused on specific subpopulations, such as surgical patients, those with COVID-19, indicating targeted approaches to understanding the association between nutrition and outcomes in these groups.

Assessment of muscle and physical-related outcomes

Overall, the findings from this scoping review indicate that the outcomes assessed by researchers can be categorized into three major domains: muscle mass, muscle strength, and function. Table 4 categorizes the various assessment tools used across the included studies into their respective domain, reflecting different aspects of muscle and physical-related outcomes relevant to be examined concerning nutrition delivery. This categorization was performed to investigate which outcomes were used. The most commonly used domain was muscle mass, utilized in 78% of the studies. Conversely, the domain function was less frequently used, with only 16% of studies using the tests categorized under this domain.

Additionally, the assessment tools employed can be further classified by types, as detailed in Table 5. This classification provides a more detailed look at how the outcomes were measured. Overall, the assessment tools were categorized into 7 types: performance-based test, imaging techniques, anthropometric assessment, physical examination, body composition, biochemical, and disability scale. Imaging techniques which include ultrasound and computed tomography (CT) scan, as well as performance-based measures, particularly the Medical Research Council (MRC) scale and handgrip/quadriceps strength, were predominant across the included studies. On the other hand, some types of tools, although less common, were utilized in specific subpopulations. For example, the disability scale, specifically the Modified Rankin Scale, was used in a study involving critically ill patients with subarachnoid haemorrhage.

Association between nutrition delivery and muscle/physical-related outcomes

In addition to identifying and categorizing the measurement tools employed in the studies, findings on the association between nutrition delivery and the outcomes were also charted. Various associations were identified, including positive, negative, mixed, and null. Several studies (n=14) reported significant positive associations, where higher energy and/or protein intake was associated with improved muscle and physical-related outcomes. Conversely, negative associations were reported in only a few studies (n=2) in which higher nutrition delivery resulted in poorer muscle and physical outcomes.

Table 2. Data collection sheet.

No.	Author (Year)	Objective	Population (n)	Study type	Duration	Physical-related measurement in ICU	Frequency of measurement	Other outcome measure	Finding

Table 3. Characteristics of the included studies (n = 45).

No.	Author (year)	Objective	Population (n)	Study type	Frequency of outcome measurement
1	Arabi *et al.* (2021)	To assess the feasibility of a large randomized controlled trial testing higher versus lower protein intake in critically ill patients.	Adult critically ill patients ≥18 years receiving enteral feeding and expected to stay ≥1 week in the ICU (704).	Pilot RCT	Repeated
2	Azevedo *et al.* (2019)	To evaluate differences in outcomes for an optimized calorie and high protein nutrition therapy versus standard nutrition care in critically ill adult patients.	Patients expected to stay in the ICU for at least 3 days (57 intervention; 63 control).	RCT	Once
3	Badjatia *et al.* (2020)	To study whether NMES and HPRO in the first 2 weeks after SAH could preserve neuromotor and cognitive function.	SAH subjects with a Hunt Hess grade>1, modifed Fisher score>1 and BMI<40 kg/m2 (12 intervention; 13 control).	RCT	Repeated
4	Berger *et al.* (2019)	To investigate the potential mechanisms underlying the reduction of infectious complications observed in the SPN group of the initial trial in a similarly selected study population, whose gut was not enabling feeding to measured energy target while requiring further ICU treatment.	Critically ill patients on day 3 of admission to the ICU who were fed less than 60% of their energy target by EN alone (23).	RCT	Repeated

5	Braunschweig *et al.* (2014)	To determine if CT scans completed for diagnostic purposes in a heterogenous population of ICU patients could be exploited to measure changes in abdominal skeletal muscle and fat depots; to assess the association between the amount of estimated energy and protein needs received and changes in these depots.	Patients admitted to the medical or surgical ICUs with respiratory failure requiring MV (33).	Retrospective observational	Repeated
6	Bury *et al.* (2020)	To determine the rate of LBM loss in critically ill SICU patients using bedside US compared with that of age-, gender-, and BMI–matched HCs; to correlate energy and protein delivery with the rate of muscle loss.	Surgical ICU patient fed solely via nutrition support for at least 3 consecutive days (52); Healthy control (15).	Observational	Repeated
7	Casaer *et al.* (2013)	To assess the effect of early administration of PN on muscle volume and composition by repeated quantitative CT.	EPaNIC study neurosurgical patients requiring prescheduled repeated follow-up CT scans (15); Healthy volunteers matched for age, gender, and BMI (6).	Substudy of RCT	Repeated
8	Chapple *et al.* (2020)	To quantify intake and nutrition-related outcomes of non-IMV critically ill patients; to establish feasibility of methods to measure nutrition-related outcomes in this population.	Non-IMV adult patients expected to remain in the ICU for ≥24 h (23).	Pilot observational	Repeated
9	Chapple *et al.* (2022)	To assess the effect of augmented calorie delivery on muscle mass, strength, and function.	Patients in TARGET randomised to 1.5 kcal/ml or 1.0 kcal/ml enteral formulae at a single centre (80).	Substudy of RCT	Repeated
10	de Azevedo *et al.* (2021)	To evaluate the efficacy of high protein intake and early exercise versus standard nutrition care and routine physiotherapy on the outcome of critically ill patients.	Mechanically ventilated patients expected to stay in the ICU for 4 days (87 in HPE group; 94 in control group).	RCT	Once

11	Deana *et al.* (2024)	To evaluate muscle mass changes with BIA during the first 7 days after ICU admission; to correlate between muscular loss and caloric and protein debt.	Patients with an expected ICU-stay ≥72h and the need for artificial nutritional support (72).	Secondary analysis of prospective observational	Repeated
12	Doig *et al.* (2013)	To determine whether providing early PN to critically ill adults with relative contraindications to early EN alters outcomes.	Critically ill adults with relative contraindications to early EN who were expected to remain in the ICU longer than 2 days (686 to standard care; 686 to early PN).	RCT	Repeated
13	Dresen *et al.* (2022)	To calculate the intake of individual amino acids and to evaluate the potential associations of amino acid patterns with muscle mass loss during the ICU stay.	Long-term immobilized, critically ill patients receiving medical nutrition therapy (21 intervention; 21 control).	Secondary analysis of RCT	Repeated
14	Dresen *et al.* (2021)	To evaluate the effect of two different quantities of protein as part of a standardized energetically controlled nutrition therapy for the preservation of muscle mass in the later phase of critical illness.	Mechanically ventilated critically ill patients (42).	RCT	Repeated
15	Dreydemy *et al.* (2021)	To determine the association between CLCR and urinary nitrogen loss to better determine the targeted daily protein intake in critically ill trauma patients with or without ARC; to explore the relationship between ARC and muscle wasting in critically ill trauma patients.	Critically ill trauma patient admitted in Surgical and Trauma (ICU), with length of stay ≥ 10 days, no history of CKD and no need for RRT (162).	Retrospective pilot study	Repeated
16	Elizabeth *et al.* (2024)	To test the hypothesis that with optimal nutrition and early physical therapy acting in synergism, muscle mass loss can be reduced, and functional outcomes can be improved.	Older ICU patients (10 intervention; 11 control).	Pilot RCT	Repeated
17	Ferrie *et al.* (2016)	To use a wide range of quantitative and qualitative measures to compare a	Patients requiring PN in ICU (60 intervention; 60 control).	RCT	Repeated

		standard intake of amino acids (0.8 g/kg) with guideline recommendations (1.2 g/kg) in critically ill patients receiving PN while controlling for energy intake.				
18	Fetterplace *et al.* (2019)	To explore the associations between cumulative energy deficits (using indirect calorimetry and estimated requirements), nutritional and functional outcomes.	Mechanically ventilated for at least 48 h (60).	Prospective observational	Repeated	
19	Fetterplace *et al.* (2018)	To determine whether a high-protein volume-based enteral feeding protocol with additional protein supplementation delivered more protein and energy than a standard hourly-rate-based nutrition protocol without protein supplementation; to evaluate whether this intervention attenuated muscle or weight loss or the prevalence of malnutrition at ICU discharge.	Adult, mechanically ventilated, on EN feeding (30 intervention; 30 control).	Pilot RCT	Repeated	
20	Hermans *et al.* (2013)	To assess whether late PN and early PN differentially affect muscle weakness and autophagic quality control of myofibres.	EPaNIC study participants (305 late PN; 295 early PN).	Subanalysis of RCT	Repeated	
21	Kangalgil *et al.* (2024)	To determine the factors associated with acute skeletal muscle loss in critically ill patients.	Patients who were expected to stay in the ICU for at least a week (44).	Prospective observational	Repeated	
22	Kim *et al.* (2011)	To assess the nutritional status of patients receiving enteral tube feeding in the ICU at admission; to evaluate its effects on nutritional status over the 7 days after admission; to understand the contribution of energy intake during	Adult medical patients who had been admitted to the medical ICU, started EN after admission to the ICU, had not received preoperative or postoperative care, did not have do-not-resuscitate orders, had received NBM	Prospective descriptive	Repeated	

		hospitalisation to the changes in nutritional status during the ICU stay.	since admission, and had not received TPN (48).		
23	Lakenman *et al.* (2024)	To assess body composition during acute and late phase of illness in these patients in relation to clinical outcome and secondary to tailored nutrition support.	Adult critically ill patients with COVID-19 (70).	Prospective observational	Repeated
24	Lambell *et al.* (2021)	To describe changes in CT–derived SMA and SMD across different weeks of critical illness and investigate associations between changes in these parameters and energy and protein delivery.	Adults ICU patients who had ≥2 CT scans at the third lumbar area performed ≥7d apart, if the predominant nutrition route was enteral and/or parenteral (planned >70% requirements), due to oral intake not being routinely recorded in a quantifiable manner (32).	Retrospective observational	Repeated
25	Liu *et al.* (2020)	To explore the therapeutic effects of EEN on patients with sepsis on mechanical ventilation.	Patients with sepsis on mechanical ventilation in the medical ICU (35 EEN; 28 DEN).	RCT	Once
26	Matsushima *et al.* (2021)	To examine the effects of protein intake on physical performance in critically ill adult patients admitted to the ICU.	Adult patients mechanically ventilated over 48h in the ICU (20 pairs).	Retrospective cohort propensity-matched analysis	Once
27	McNelly *et al.* (2020)	To evaluate whether intermittent enteral feed decrease muscle wasting compared with continuous feed in critically ill patients.	Mechanically ventilated adult patients with multiorgan failure (121).	RCT	Repeated
28	Nakamura *et al.* (2020)	To evaluate the efficacy of HMB complex on muscle volume loss during critical care.	ICU patients for whom EN could be performed (43 control; 45 HMB).	RCT	Repeated
29	Nakamura *et al.* (2021)	To assess high-protein and medium-protein delivery under equal total energy delivery with and without active early rehabilitation.	Patients admitted to the ICU (25:31 without EMS, 35:26 with EMS).	RCT	Repeated

30	Nakano *et al.* (2021)	To verify the efficacy of the protocol to ameliorate muscle injury in ICU-AW.	Adult patients admitted to the ICU (45 control; 56 intervention).	Historical control	Repeated
31	Nickel *et al.* (2023)	To assist clinicians to identify critically ill patients at greatest risk of acute muscle loss; to analyse the associations between protein intake and exercise on acute muscle loss.	Adult patients expected to be mechanically ventilated for greater than 48 h and expected to remain in the ICU for more than 2 days after study enrolment (72).	Secondary analysis of RCT	Repeated
32	Pardo *et al.* (2018)	To assess the evolution of the quadriceps muscle during the first 3 weeks after ICU admission and its possible association with nutritional intake.	Patients expected to stay more than 7 days in the ICU (29).	Observational	Repeated
33	Ridley *et al.* (2018)	To determine if an individually titrated supplemental PN strategy commenced 48-72 hours following ICU admission and continued for up to 7 days would increase energy delivery to critically ill adults compared to usual care EN delivery.	Mechanically ventilated adults with at least one organ failure and EN delivery below 80% of estimated energy requirement in the previous 24 hours (100).	Pilot RCT	Repeated
34	Umbrello *et al.* (2021)	To compare the time course of the size and quality of both rectus femoris and diaphragm muscles between critically ill, COVID-19 survivors and non-survivors; to explore the correlation between the change in muscles size and quality with the amount of nutritional support delivered and the cumulative fluid balance.	Patients admitted to ICU for acute hypoxemic respiratory failure, undergoing invasive MV for ≤48 h and with confirmed SARS-CoV-2 infection (36).	Prospective observational	Repeated
35	Uyar *et al.* (2023)	To demonstrate the effect of high protein on diaphragm muscle thickness; to evaluate the correlation of diaphragm thickness fraction with rectus femoris muscle thickness in high protein patients.	Mechanically ventilated patients (49).	RCT	Repeated

36	Verceles *et al.* (2023)	To assess the effectiveness of combined NMES+HPRO+PT in mitigating sarcopenia as evidenced by CT volume and cross-sectional area when compared to usual ICU care.	Older (>50-year-old), mechanically ventilated participants (≥24 hours) with pre-admission Barthel Index of ≥70, ability to follow commands and able to perform physical therapy testing prior to ICU admission (23 control; 16 intervention).	RCT	Repeated
37	Viana *et al.* (2021)	To determine whether HMB, a metabolite of leucine, can attenuate wasting process.	ICU patients depending on mechanical ventilation on day 3 having a functional gastrointestinal tract (30).	RCT	Repeated
38	Wang *et al.* (2024)	To assess the influence of higher early protein intake on the prognosis of critically ill patients.	Critically ill patients aged above 18 years admitted to ICU and EICU, with mNUTRIC score > 5 and an anticipated ICU stay ICU/EICU of more than 7 day (86 intervention: 87 control).	RCT	Repeated
39	Wischmeyer *et al.* (2017)	To test the hypothesis that increased nutrition delivery via SPN + EN to underweight and obese ICU patients would improve 60-day survival and QoL versus usual care (EN alone).	Adult ICU patients with acute respiratory failure expected to require mechanical ventilation for >72 hours and with a BMI of <25 or ≥35 (125).	Pilot RCT	Once
40	Wittholz *et al.* (2023)	To determine feasibility of administering a blinded nutrition supplement in the ICU and continuing it after ICU discharge.	Patient after traumatic injury necessitating admission to ICU (26 intervention; 24 control).	Pilot RCT	Repeated
41	Yatabe *et al.* (2019)	To investigate the impact of nutritional management and rehabilitation on physical outcome.	Patients who received mechanical ventilation for at least 24h and those admitted to the ICU for > 72 h (389).	Observational	Once
42	Yeh *et al.* (2018)	To explore whether psoas CSA and density (HU) are associated with nutritional adequacy and clinical outcomes in surgical intensive care unit patients.	Subjects with at least one CT scan within 72h of ICU admission (140).	Observational	Repeated
43	Yousseff *et al.* (2022)	To evaluate the effect of parenteral proteins on ICU outcome; to compare the	Acute critically ill patients who had PN during their ICU stay (60).	Prospective comparative	Repeated

		effect of two different protein concentrations on handgrip strength in critically ill patients.			
44	Zaragoza *et al.* (2023)	To assess the incidence and determinants of ICUAW in adult patients with EN during the first 7 days in the ICU and mechanical ventilation for at least 48 hours.	ICU patients receiving invasive mechanical ventilation for at least 48 hours and EN the first 7 days of their ICU stay (319).	Prospective cohort	Once
45	Zhang *et al.* (2022)	To evaluate the effect of high protein to the target of 2.0 g/kg/d on diaphragm atrophy and clinical prognosis of patients receiving prolonged MV.	Patients who were treated with ≥7 days' MV (41).	RCT	Repeated

RCT: randomized controlled trial, NMES: neuromuscular electrical stimulation, HPRO: high protein supplementation, SPN: supplemental parenteral nutrition, EN: enteral nutrition, SAH: subarachnoid hemorrhage, CT: computed tomography, LBM: lean body mass, SICU: surgical ICU, US: ultrasound, BMI: body mass index, HCs: healthy controls, CLCR: creatinine clearance, ARC: augmented renal clearance, CKD: chronic kidney disease, RRT: renal replacement therapy, EPaNIC: Early Parenteral Nutrition Completing Enteral Nutrition in Adult Critically Ill Patients, IMV: invasive mechanical ventilation, TARGET: The Augmented versus Routine approach to Giving Energy Trial, HPE: high protein and early exercise, BIA: bioimpedance analysis, PN: parenteral nutrition, NBM: nothing by mouth, TPN: total parenteral nutrition, SMA: skeletal muscle area, SMD: skeletal muscle density, EEN: early enteral nutrition, DEN: delayed enteral nutrition, HMB: β-Hydroxy-β-methylbutyrate, ICU-AW: ICU-acquired weakness, EMS: electrical muscle stimulation, SARS-CoV-2: Severe acute respiratory syndrome *coronavirus 2,* PT: mobility and strength rehabilitation, EICU: emergency ICU, mNUTRIC: modified Nutrition Risk in the Critically Ill, QoL: quality of life, CSA: cross sectional area, HU: Hounsfield units, MV: mechanical ventilation

Table 4. Domains of outcome assessment.

Domain	Specific tests	Author
Muscle mass	Ultrasound of muscle cross-sectional area/thickness	Berger *et al*. (2019) Bury *et al*. (2020) Chapple *et al*. (2020) Chapple *et al*. (2022) Dresen *et al*. (2022) Dresen *et al*. (2021) Elizabeth *et al*. (2024) Ferrie *et al*. (2016) Fetterplace *et al*. (2018) Kangalgil *et al*. (2024) McNelly *et al*. (2020) Nickel *et al*. (2023) Pardo *et al*. (2018) Umbrello *et al*. (2021) Uyar *et al*. (2023) Viana *et al*. (2021) Wang *et al*. (2024) Wittholz *et al*. (2023) Yousseff *et al*. (2022)
	Mid-upper arm circumference/calf circumference/triceps skinfold thickness	Chapple *et al*. (2020) Doig *et al*. (2023) Kim *et al*. (2011) Yousseff *et al*. (2022)
	CT imaging	Badjatia *et al*. (2020) Braunschweig *et al*. (2014) Casaer *et al*. (2013) Dreydemy *et al*. (2021) Lambell *et al*. (2021) Nakamura *et al*. (2020) Nakamura *et al*. (2021) Nakano *et al*. (2021) Verceles *et al*. (2023) Yeh *et al*. (2018) Zhang *et al*. (2022)
	Bioimpedance analysis	Chapple *et al*. (2020) Deana *et al*. (2024) Fetterplace *et al*. (2019) Lakenman *et al*. (2024)
	Subjective Global Assessment (SGA) item scoring muscle wasting	Doig *et al*. (2023)
	Level of butyrylcholinesterase (BChE)	Zhang *et al*. (2022)
Muscle strength	Medical Research Council (MRC) scale	Arabi *et al*. (2021) Elizabeth *et al*. (2024) Fetterplace *et al*. (2019) Fetterplace *et al*. (2018) Hermans *et al*. (2013) Liu *et al*. (2020) Matsushima *et al*. (2021) Nakano *et al*. (2021) Zaragoza *et al*. (2023)
	Handgrip/quadriceps strength	Chapple *et al*. (2022)

		de Azevedo *et al*. (2021) Elizabeth *et al*. (2024) Ferrie *et al*. (2016) Fetterplace *et al*. (2018) Matsushima *et al*. (2021) Nakano *et al*. (2021) Ridley *et al*. (2018) Wischmeyer *et al*. (2017) Yousseff *et al*. (2022) Azevedo *et al*. (2019)
	Sit to stand test & bed to chair transfer test	McNelly *et al*. (2020)
Function	Chelsea Critical Care Physical Assessment Tool (CPax)	Elizabeth *et al*. (2024)
	Physical Function in Intensive Care Test-scored	Fetterplace *et al*. (2019) Fetterplace *et al*. (2018)
	Functional Status Score for the Intensive Care Unit (FSS-ICU)	Nakamura *et al*. (2021) Nakano *et al*. (2021)
	ICU Mobility Scale	Nakano *et al*. (2021)
	Physical status (more than end sitting/bed rest and sitting)	Yatabe *et al*. (2019)
	Modified Rankin Scale (mRS)	Badjatia *et al*. (2020)
	Short Physical Performance Battery (SPPB)	Badjatia *et al*. (2020)

Table 5. Type of outcome assessment tool.

Type	Specific tests	Author
Performance-based	Medical Research Council (MRC scale)	Arabi *et al*. (2021) Elizabeth *et al*. (2024) Fetterplace *et al*. (2019) Fetterplace *et al*. (2018) Hermans *et al*. (2013) Liu *et al*. (2020) Matsushima *et al*. (2021) Nakano *et al*. (2021) Zaragoza *et al*. (2023)
	Handgrip/quadriceps strength	Chapple *et al*. (2022) de Azevedo *et al*. (2021) Elizabeth *et al*. (2024) Ferrie *et al*. (2016) Fetterplace *et al*. (2018) Matsushima *et al*. (2021) Nakano *et al*. (2021) Ridley *et al*. (2018) Wischmeyer *et al*. (2017) Yousseff *et al*. (2022) Azevedo *et al*. (2019)
	Sit to stand test & bed to chair transfer test	McNelly *et al*. (2020)
	Chelsea Critical Care Physical Assessment Tool (CPax)	Elizabeth *et al*. (2024)
	Short Physical Performance Battery (SPPB)	Badjatia *et al*. (2020)

	Physical Function in Intensive Care Test-scored	Fetterplace *et al*. (2019) Fetterplace *et al*. (2018)
	Functional Status Score for the Intensive Care Unit (FSS-ICU)	Nakamura *et al*. (2021) Nakano *et al*. (2021)
	ICU Mobility Scale	Nakano *et al*. (2021)
	Physical status (more than end sitting/bed rest and sitting)	Yatabe *et al*. (2019)
Imaging techniques	Ultrasound of muscle cross-sectional area/thickness	Berger *et al*. (2019) Bury *et al*. (2020) Chapple *et al*. (2020) Chapple *et al*. (2022) Dresen *et al*. (2022) Dresen *et al*. (2021) Elizabeth *et al*. (2024) Ferrie *et al*. (2016) Fetterplace *et al*. (2018) Kangalgil *et al*. (2024) McNelly *et al*. (2020) Nickel *et al*. (2023) Pardo *et al*. (2018) Umbrello *et al*. (2021) Uyar *et al*. (2023) Viana *et al*. (2021) Wang *et al*. (2024) Wittholz *et al*. (2023) Yousseff *et al*. (2022)
	CT imaging	Braunschweig *et al*. (2014) Casaer *et al*. (2013) Dreydemy *et al*. (2021) Lambell *et al*. (2021) Nakamura *et al*. (2020) Nakamura *et al*. (2021) Nakano *et al*. (2021) Verceles *et al*. (2023) Yeh *et al*. (2018) Zhang *et al*. (2022) Badjatia *et al*. (2020)
Anthropometric assessment	Mid-upper arm circumference/calf circumference/triceps skinfold thickness	Chapple *et al*. (2020) Doig *et al*. (2023) Kim *et al*. (2011) Yousseff *et al*. (2022)
Physical examination	Subjective Global Assessment (SGA) item scoring muscle wasting	Doig *et al*. (2023)
Body composition assessment	Bioimpedance analysis	Chapple *et al*. (2020) Deana *et al*. (2024) Fetterplace *et al*. (2019) Lakenman *et al*. (2024)
Biochemical assessment	Level of butyrylcholinesterase (BChE)	Zhang *et al*. (2022)
Disability scale	Modified Rankin Scale (mRS)	Badjatia *et al*. (2020)

Mixed associations were demonstrated in 6 studies with multiple outcomes related to muscle or physical function, where each outcome varied in their relationship with the amount of nutrition. On the other hand, most of the studies (n=22) reported the absence of a significant association between nutrition and the outcomes. Interestingly, in one study, the improvement in muscle outcomes due to higher protein delivery was reported to be substantial only if combined with active early rehabilitation, while another study reported no significant impact of such treatment combination. Details on the results of each included study are illustrated in Table 6.

Table 6. Findings on the association between nutrition delivery and muscle or physical-related outcomes.

	Author (year)	Findings	Type of association
1	Arabi *et al.* (2021)	No significant differences over time in MUAC and MRC sum-score.	0
2	Azevedo *et al.* (2019)	No significant difference in handgrip strength in the OCHPN group versus the Control group	0
3	Badjatia *et al.* (2020)	Reduction in quadriceps muscle atrophy by PBD 14 in NMES+HPRO as compared to SOC group.	+
4	Berger *et al.* (2019)	Total loss of muscle surface tended to be less in SPN compared to EN group with no significant difference.	0
5	Braunschweig *et al.* (2014)	Amount of energy received significantly reduced SKM loss.	+
6	Bury *et al.* (2020)	Changes in QMLT were not associated with nutrition support received.	0
7	Casaer *et al.* (2013)	Early parenteral nutrition did not prevent the pronounced wasting of skeletal muscle observed over the first week of critical illness.	0
8	Chapple *et al.* (2020)	Sample size and ICU LOS were not sufficient for analysis of changes in nutrition-related outcomes.	0[a]
9	Chapple *et al.* (2022)	No difference in QMLT and handgrip strength at any timepoint between intervention and control group.	0
10	de Azevedo *et al.* (2021)	A trend that ICUAW was higher in the control group compared to high protein intake group (borderline significance).	+
11	Deana *et al.* (2024)	Total amount of nutrition delivered does not correlate with changes in muscle mass and phase angle.	0
12	Doig *et al.* (2023)	Significantly greater muscle wasting in standard care compared to early PN group. MUAC differences did not remain significant over the entire ICU stay.	+-

13	Dresen *et al.* (2022)	No statistically significant association between quantitative intake and the skeletal muscle changes after terminating intervention phase.	0
14	Dresen *et al.* (2021)	No statistically significant impact on the loss of muscle mass between higher and standard protein group.	0
15	Dreydemy *et al.* (2021)	No statistically significant difference in changes of muscle psoas CSA and % changes of CSA in patients who received low vs. high protein intake.	0
16	Elizabeth *et al.* (2024)	A trend towards decreased muscle loss in higher protein compared to control group, but no significant difference.	0
17	Ferrie *et al.* (2016)	Handgrip strength was improved at day 7 and muscle thickness was greater in the group receiving the higher compared to lower level of amino acids. No significant difference between groups in handgrip strength at ICU discharge and leg circumference.	+-
18	Fetterplace *et al.* (2019)	Cumulative energy deficit from artificial nutrition support was associated with the development of ICUAW, reduced physical function at ICU discharge and greater loss of fat-free mass.	+
19	Fetterplace *et al.* (2018)	Higher protein was associated with less QMLT loss at discharge compared to standard nutrition, but both groups showed similar muscle strength and physical function.	+-
20	Hermans *et al.* (2013)	Tolerating a substantial macronutrient deficit early during critical illness did not affect muscle wasting, but reduced weakness.	-
21	Kangalgil *et al.* (2024)	The adequacy of energy and protein intake was not associated with the rate of change in RFCSA.	0
22	Kim *et al*. (2011)	Both adequately fed and underfed group had decreased TSF, MAC, and MAMC.	+-
23	Lakenman *et al.* (2024)	Increase in administrated protein intake resulted in <1% difference (40g) of FFM, of which 20g SMM.	+
24	Lambell *et al.* (2021)	Nutrition delivery and adequacy were not associated with muscle loss.	0
25	Liu *et al.* (2020)	Early enteral nutrition can reduce the incidence of ICUAW compared to delayed enteral nutrition.	+

26	Matsushima *et al.* (2021)	High-protein group had significantly higher muscle strength than low-protein group at the time of discharge from the ICU.	+
27	McNelly *et al.* (2020)	Intermittent feeding (higher achievement of nutritional target) in early critical illness is not shown to preserve muscle mass or affect the sit-to-stand or first transfer before ICU discharge, compared to continuous feeding.	0
28	Nakamura *et al.* (2020)	HMB complex supplementation from the acute phase of intensive care does not inhibit muscle volume loss.	0
29	Nakamura *et al.* (2021)	High protein delivery provided better muscle volume maintenance compared to medium protein delivery, but only with active early rehabilitation. FSS-ICU were not significantly different between groups.	+-
30	Nakano *et al.* (2021)	Early mobilization combined with high-protein nutrition prevented femoral muscle volume loss compared to standard protein. The number of days to achieve IMS 1, MRC scores and FSS-ICU at ICU discharge did not significantly differ between the two groups.	+-
31	Nickel *et al.* (2023)	No observed relationship between combined protein delivery and in-bed cycling and muscle loss.	0
32	Pardo *et al.* (2018)	No correlation was found between muscle loss and caloric or protein debt over the first week	0
33	Ridley *et al.* (2018)	Handgrip strengths were similar between the supplemental PN and usual care EN groups.	0
34	Umbrello *et al.* (2021)	The change in both RFCSA and diaphragm end-expiratory thickness was inversely related to the cumulative protein deficit.	+
35	Uyar *et al.* (2023)	Diaphragmatic muscle thicknesses were higher in patients who received protein supplement.	+
36	Verceles *et al.* (2023)	The addition of physical therapy, neuromuscular electric stimulation and high protein nutritional supplementation to standard critical care resulted in an increase in lower extremity muscle volume and cross-sectional area when compared to standard medical care.	+

37	Viana *et al.* (2021)	HMB treatment did not significantly reduce muscle wasting.	0
38	Wang *et al*. (2024)	The atrophy rates of RFMLT and RFCSA in the high early protein group were both significantly lower than the low early protein group.	+
39	Wischmeyer *et al.* (2017)	Potential non-significant tendency to improved handgrip strength at ICU discharge in the SPN + EN group compared to usual care (EN only) group.	0
40	Wittholz *et al.* (2023)	Marked loss of quadriceps muscle thickness occurred in both groups, with the point estimate favouring attenuated muscle loss in the intervention group, albeit with wide CIs.	0
41	Yatabe *et al.* (2019)	Patients might benefit from low caloric intake (less than 10 kcal/kg/day) until day 3 and rehabilitation during ICU stay.	-
42	Yeh *et al.* (2018)	Early nutritional deficits were correlated with muscle quality deterioration.	+
43	Yousseff *et al.* (2022)	High parenteral protein intake was associated with better handgrip strength and significant improvement of muscle thickness.	+
44	Zaragoza *et al.* (2023)	Energy intake during days 3–7 was similar among patients who did and did not develop ICUAW, no effect of energy or protein intake on the onset of ICUAW.	0
45	Zhang *et al.* (2022)	INT improved the diaphragm atrophy and muscle mass of critically ill patients receiving prolonged MV compared to SNT.	+

Abbreviations: MUAC: mid-upper arm circumference, MRC: Medical Research Council, OCHPN: optimized calorie-high protein nutrition, PBD: post bleed day, NMES: neuromuscular electrical stimulation, HPRO: high protein supplementation, SOC: standard of care, SPN: supplemental parenteral nutrition, EN: enteral nutrition, SKM: skeletal muscles, QMLT: quadriceps muscle layer thickness, LOS: length of stay, ICUAW: ICU-acquired weakness, PN: parenteral nutrition, CSA: cross sectional area, RFCSA: rectus femoris cross sectional area, TSF: triceps skinfold thickness, MAMC: mid-arm muscle circumference, MAC: mid-arm circumference, FFM: fat free mass, SMM: skeletal muscle mass, HMB: β-Hydroxy-β-methylbutyrate, FSS-ICU: Functional Status Score for The Intensive Care Unit, IMS: ICU Mobility Scale, RFMLT: rectus femoris muscle thickness, CI: confidence interval, INT: intensive nutrition treatment, SNT: standard nutrition treatment.
0: No association, +: Positive association, -: Negative association, +-: Mixed association
[a] Insufficient data for statistical analysis.

Discussion

The primary aim of this scoping review was to map the broad range of assessment tools used by researchers in examining the association between nutrition delivery with muscle and physical-related outcomes among critically ill adult patients. The identified domains and types of tools allow an overview of the current landscape of critical care nutrition research.

A notable trend was the frequent use of the muscle mass domain, suggesting its significance and a preference for an objective measure in assessing nutrition-related outcomes. Monitoring muscle mass to guide adequate nutritional support during the changing phases of critical illness is helpful (De Rosa *et al*., 2023), as patients were reported to experience muscle loss at a rate of 2% daily during their first week of ICU stay (Fazzini *et al*., 2023). Objective muscle quantifications are potentially sensitive to small changes over short periods, allowing evaluation of nutrition interventions (Umbrello *et al*., 2023). In addition, the assessment of muscle mass by imaging techniques demonstrated great intra- and inter-observer reliability (Pardo *et al*., 2018). This agreement may improve result validity, reproducibility, and bias reduction, both in research, and clinical settings.

On the contrary, the domain function was less frequently used among the included studies, which may suggest a lesser focus on functional ability or challenges to be implemented in the ICU setting. Possible explanation might be the limited feasibility of conducting these ability-to-function tests among the critically ill patients who may not be alert, conscious, or have enough strength. Patients' heterogeneity in their ability to conduct function assessment was reflected in a study by Nordon-Craft *et al*. (2014) where 14 patients could not perform the sit-to-stand and marching-in-place components of the PFIT-s (Physical Function in Intensive Care Test). Effort from the patients would be required to perform the tests for function (Parry *et al*., 2017). In addition, measurements are prone to subjectivity, as reported by Denehy *et al*. (2013), scoring the amount of assistance in the sit-to-stand test relied on researchers' subjective assessment. Nevertheless, measuring functional ability in the ICU is valid and may greatly contribute to informing further rehabilitation strategies.

Other than that, this review revealed that a few assessment tools such as performance-based tests and imaging techniques are commonly utilized and favoured by most of the included studies. For instance, the handgrip strength test, a performance-based, may be commonly employed due to its simplicity, apart from serving as an accurate substitute for other tests in diagnosing ICU-acquired weakness (ICUAW) (Bragança *et al*., 2019; Özyürek *et al*., 2017; Zhang *et al*., 2024). On the other hand, imaging techniques such as computed tomography (CT) scan and ultrasound allows accurate, reliable, and objective evaluation of the muscle cross sectional area, volume, and quality (Mourtzakis *et al*., 2017; Umbrello *et al*., 2023), given that sufficient and proper training is given to research personnel (Mourtzakis *et al*., 2017). These imaging technologies can be greatly useful to evaluate muscle in critically ill populations as they do not require patients' effort, cooperation, or compliance, compared to the tests which require patients to participate actively. Nonetheless, it comes with certain limitations, such as using resources and medical risks to transport patient for a CT scan (Rooyackers & Wernerman, 2014). Nevertheless, the variation in the assessment tool types portray the diverse strategies available for researchers to capture the outcomes of nutritional interventions, depending on study design, target population, and resources available.

It is also important to highlight that the association between nutrition delivery with muscle and physical-related outcomes was inconsistent among the included studies, with many of the included studies reported no significant association. Bels *et al*. (2023) stated that no significant effect of protein supplementation was observed on muscle strength or function in most of the previous trials, despite a few reports of reducing muscle volume loss particularly with muscle activation. The inconsistencies may be due to differences in sample size, study design, methodology, or assessment tools. The broad range of domain and types of assessment tools underscores the complexity of precisely capturing the influence of nutrition on muscle and physical in the critically ill setting. While certain tools are highly validated, reliable, or precise, their use in the ICU setting may be limited due to significant resource constraint, compared to other affordable measures, though subjective and prone to measurement bias.

Furthermore, challenges exist in the measurement of the muscle and physical-related outcomes for critically ill patients. Fetterplace *et al*. (2018) reported that the quadriceps muscle layer thickness (QMLT) readings were not measured at baseline and discharge in 23% of participants from the intervention group and 27% from the control group. This is due to participant unavailability, change of focus to comfort care, death, other medical issues, or participants being discharged from the ICU when the primary investigator was not available. Other circumstances hindering complete observations include participants being uncooperative with the voluntary strength assessment, patients being too debilitated or ill to perform tests, and difficulties in scheduling of measurements by research personnel (Arabi *et al*., 2021; Wischmeyer *et al*., 2017).

This review identified a significant gap which is the lack of a universally accepted standard to measure muscle and physical-related outcomes in the ICU, specifically concerning nutrition delivery. The broad range of tools used in previous studies, while allowing flexibility for researchers according to the available resources, might lead to contradictory findings on the association between nutrition and outcomes. This may indicate the need to develop guidelines or standardization in the field. In agreement with previous reviews, a broad range of outcomes are used in critical care nutrition trials, affecting the comparison of datasets across studies, and indicating the lack of consensus on where nutrition exerts its most significant benefit (L. S. Chapple *et al*., 2020; Taverny *et al*., 2019).

This review is limited by the scope of the included studies, which primarily focused only on assessing muscle and physical-related outcomes while patients are still in the ICU. Furthermore, categorizing tools into specific domains and types may have introduced subjectivity in interpretation. Nevertheless, this review uniquely categorizes the tools used in relation to nutritional delivery, providing a more focused analysis of their applicability and limitations.

Future research may focus on developing standardized protocols for selecting the tools to measure muscle and physical-related outcomes in critical illness nutrition studies. In addition, the tools currently available for measuring long-term effects of nutrition beyond ICU stay should be systematically mapped to allow a more comprehensive understanding of survivors' trajectories.

Conclusion

A diverse range of assessment tools has been identified for measuring muscle and physical-related outcomes in research evaluating the impact of nutrition delivery among critically ill patients. These tools vary significantly in their approaches, reflecting differences in researchers' objectives, resource availability, and the specific outcomes targeted. The variability in tool selection emphasizes the need for careful consideration when aligning methodologies with study goals. In order to improve consistency and comparability across studies, future research should focus on developing standardized protocols for selecting appropriate tools to measure the effects of nutrition delivery on muscle and physical-related outcomes. Standardization will ensure that findings are reliable and reproducible, contributing to improved patient outcomes in the ICU.

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