

Nutrition therapy in the older critically ill patients: A scoping review

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ABSTRACT

Introduction: There is a lack of guidelines or formal systematic synthesis of evidence for nutrition therapy in older critically ill patients. This study is a scoping review to explore the state of evidence in this population.

Method: MEDLINE and Embase were searched from inception until 9 February 2022 for studies that enrolled critically ill patients aged ≥ 60 years and investigated any area of nutrition therapy. No language or study design restrictions were applied.

Results: Thirty-two studies (5 randomised controlled trials) with 6 topics were identified: (1) nutrition screening and assessments, (2) muscle mass assessment, (3) route or timing of nutrition therapy, (4) determination of energy and protein requirements, (5) energy and protein intake, and (6) pharmaconutrition. Topics (1), (3) and (6) had similar findings among general adult intensive care unit (ICU) patients. Skeletal muscle mass at ICU admission was significantly lower in older versus young patients. Among older ICU patients, low muscularity at ICU admission increased the risk of adverse outcomes. Predicted energy requirements using weight-based equations significantly deviated from indirect calorimetry measurements in older vs younger patients. Older ICU patients required higher protein intake (>1.5 g/kg/day) than younger patients to achieve nitrogen balance. However, at similar protein intake, older patients had a higher risk of azotaemia.

Conclusion: Based on limited evidence, assessment of muscle mass, indirect calorimetry and careful monitoring of urea level may be important to guide nutrition therapy in older ICU patients. Other nutrition recommendations for general ICU patients may be used for older patients with sound clinical discretion.

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Keywords: Critical care nutrition, geriatric patients, intensive care medicine, older adults, scoping review

INTRODUCTION

The increasing levels of life expectancy and decreasing fertility are shifting the age structure of the world population towards older ages.¹ From year 2020 to 2050, population aged ≥ 65 years is expected to rise from 9.3% to 16%.¹ The number of older intensive care unit (ICU) patients are expected to rise correspondingly.

The growing number of older patients may warrant more specific nutrition recommendation. Ageing is associated with increased fat mass and decreased muscle mass.² These changes in body composition may have

important implications to nutritional requirements and metabolism. However, to date, no guidelines for nutrition therapy specifically for older ICU patients exist. This might be due to the lack of systematic summary of critical care nutrition studies on older patients. Nevertheless, several narrative reviews are available to provide recommendations based on expert opinion.^{3,4} Therefore, we aimed to systematically search the literature and explore the state of evidence of critical care nutrition in older ICU patients through a scoping review.

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CLINICAL IMPACT

What is New

- Results from this review suggest that the recommendations from the general adult critically ill population are also applicable to older patients, with some exceptions.

Clinical Implications

- Evaluation of nutrition risk and status should be done early upon intensive care unit admission to guide nutrition therapy.
- Objective assessment of muscle mass or muscularity status using imaging methods such as ultrasound may be considered to monitor the progress of nutrition therapy.
- Indirect calorimetry should be used to determine energy requirements if feasible.
- Older critically ill patients may require higher protein intake (~1.5kcal/kg/day) than younger patients, with careful monitoring of urea level to prevent azotaemia.

METHOD

This scoping review is conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) extension for scoping reviews checklist (online Supplementary Materials, Supplementary Appendix S1).⁵

We included original studies that enrolled critically ill patients aged ≥ 60 years, and investigated any area related to critical care nutrition. Conference abstracts and studies that did not enrol critically ill patients or investigate any nutrition-related topics were excluded. We searched MEDLINE and Embase from inception until 9 February 2022. The detailed search strategy is available in the online Supplementary Appendix S2. No language or study design restrictions were applied. The search was supplemented by screening the reference lists of published reviews.

We imported all references into Covidence (Veritas Health Innovation, Melbourne, Australia) to screen them and remove duplication. Two authors screened the titles and abstracts, and reviewed the full-text article of the potential studies to confirm their eligibility. Disagreements were resolved by consulting a third senior author.

Based on the authors' judgement, the included studies were grouped based on the topic investigated. The characteristics (e.g. first author name, year of publication, study design, sample size, mean/median age of patients) and main findings of the studies were summarised in separate tables for each topic identified in the included studies. Each co-author was assigned a topic to summarise, and accuracy of this was checked by the first author. A generic table was provided to each co-author, which can be adapted to suit the summary work of each assigned topic. Critical appraisal of the included studies was not performed.

Post hoc, since there were limited ICU studies that specifically recruited older adults, we decided to include studies that enrolled adult patients but had subgroup analyses of older versus younger patients. However, such analyses were not apparent in the title or abstract, which reduced identifiability. Hence, we only reported findings in the eligible studies and those that were known to the authors.

RESULTS

The databases identified 4,689 references, and 81 full-text articles were retrieved. About 1,148 citations were screened from previous review articles. Online Supplementary Appendix S3 shows the PRISMA flowchart and Appendix S4 lists the reason of exclusion of all retrieved studies that were excluded. We included 32 original studies, of which 5 were randomised controlled trials (RCTs). These studies were published from 1997 to 2021, with sample sizes ranging from 25–1,279. They were divided into 6 topics: nutrition screening and assessments ($n=10$), muscle mass assessment ($n=5$), route or timing of nutrition therapy ($n=3$, including 2 RCTs), determination of energy and protein requirements ($n=6$), energy and protein intake ($n=4$), and pharmaconutrition ($n=4$, including 3 RCTs).

Nutrition screening and assessments

Ten observational studies (5 prospective and 5 retrospective) were included, with sample sizes ranging from 87–1,250 (online Supplementary Materials, Supplementary Table S1).

Prevalence data

Studies that used validated nutrition assessment tools in critically ill patients⁶ (i.e. Subjective Global Assessment [SGA]^{7,8} and Mini Nutrition Assessment [MNA])⁸ showed that malnutrition prevalence in older patients ranged from 23.2–34.4%. Studies that used validated nutrition screening tools (i.e. MNA-short form [MNA-SF],⁸ Nutrition Risk Screening 2002 [NRS-2002],^{8–10}

and Malnutrition Universal Screening Tool [MUST])¹¹ found that malnutrition-risk prevalence ranged from 25.8–71.2%. Other studies used nutrition screening tools that mainly relied on biochemical indices such as serum albumin (i.e. controlling nutritional status index [CONUT]),¹² prognostic nutritional index [PNI],¹² geriatric nutritional risk index [GNRI],^{10,11,14} and Onodera's prognostic nutritional index [OPNI]).¹⁰ They reported 43.9–76.3% of older ICU patients had biochemical derangements. A study that used mid-arm circumference reported that 23.3% of older ICU patients had measurements below the 10th percentile of a population-specific database.¹⁵ One study that used an ICU-specific nutrition score (modified nutrition risk in critically ill [mNUTRIC])¹¹ reported nutrition risk in 91.1% of the older ICU patients.

Prognostic data

Malnutrition assessed by the SGA, but not MNA, was associated with hospital mortality/need for hospice care and lower risk of being discharged home.⁸ However, it was not associated with ICU and hospital length of stay (LOS).⁸

Malnutrition risk identified by NRS-2002 and MNA-SF was associated with a higher risk of hospital mortality/need for hospice care, but only NRS-2002 could prognose the risk of being discharged home.⁸ Malnutrition risk identified by NRS-2002 was also associated with an increased risk of infection, complications, ICU mortality and longer ICU LOS.⁹ Malnutrition risk defined by MUST was associated with higher mortality at 1-year post-discharge.¹¹

Biochemical derangement measured by GNRI was associated with mortality (hospital or 30-day) and hospital LOS,^{10,13,14} but not associated with ICU mortality and ICU LOS.¹⁵ Similarly, biochemical derangements measured by CONUT and PNI were not associated with ICU mortality.¹²

Low mid-arm circumference was associated with a higher risk of 6-month mortality.¹⁵ Older ICU patients with high mNUTRIC score had increased ICU, hospital or 30-day mortality, and ICU/hospital length of stay.^{10,16} However, patients with high mNUTRIC and achieved $\geq 80\%$ prescribed calories and protein had lower ICU and/or hospital mortality.¹⁶

Muscle mass assessment

Five observational studies were included (2 prospective, 2 retrospective and 1 case-control study) with sample sizes ranging from 50–150 patients. All studies used imaging methods to assess muscle mass (online Supplementary Table S2).

Three studies assessed muscle mass using computed tomography (CT) scan and enrolled ICU patients aged ≥ 60 ^{17,18} or ≥ 65 .¹⁹ Two studies measured skeletal muscle index¹⁹ or skeletal muscle area (SMA)¹⁷ at the third lumbar vertebral level (L3), and 1 study measured the dorsal muscle group area at the twelfth thoracic vertebral level.¹⁸ The definitions for low muscularity (LM) used were from cancer patients,²⁰ ICU patients,²¹ or derived internally.¹⁸ The prevalence of LM was 71% in 1 study.¹⁹ All studies found that muscularity status was associated with hospital mortality.^{17–19} Furthermore, LM was associated with lower ventilation-free days and ICU-free days.¹⁹

Two studies enrolled adult ICU patients and demonstrated that older patients had significantly lower SMA at L3^{22,23} and a higher prevalence of low muscularity,²² compared to younger patients. Using ultrasound, 1 study found that mid-upper arm, forearm, abdomen and thighs muscularity was significantly lower in older than younger patients.²³ However, another study could not demonstrate a significant difference in quadriceps muscle layer thickness between older or younger ICU patients (1.2 ± 0.5 cm vs 1.4 ± 0.7 cm, respectively; $P=0.57$).²²

Route or timing of nutrition therapy

Two RCTs and 1 retrospective observational study were included, with sample sizes ranging from 141–325 patients (online Supplementary Table S3). The first RCT investigated the effect of enteral nutrition (EN), parenteral nutrition (PN), and combined EN with supplemental PN.²⁴ Patients on PN had a higher rate of infectious and non-infectious complications than the other 2 groups. In contrast, mechanical ventilation (MV) duration, ICU and hospital LOS, and 20-day mortality were all significantly lower in the combined EN and supplemental PN groups compared to EN or PN group. The energy and protein received by each group was not reported.²⁴ The second RCT assigned patients to postpyloric vs gastric EN, and found that the incidences of ventilator-associated pneumonia, vomiting and abdominal distension were significantly lower in the postpyloric group. However, this was not translated into lower use of renal replacement therapy, shorter MV duration, ICU and hospital LOS, or a lower rate of ICU and hospital mortality.²⁵ Lastly, an observational study among older ICU patients with thermal injuries reported that early (<24 h), compared with late (>24 h) EN initiation was associated with a shorter ICU and hospital LOS, and a lower risk of sepsis, superficial skin infection, pneumonia and mortality.²⁶

Determination of energy and protein requirements

Three prospective and 2 retrospective observational studies were included (online Supplementary Table S4), with sample sizes ranging from 25–103 patients. All studies included MV patients and found that predictive equations were not ideal in predicting resting energy expenditure (REE) measured by indirect calorimetry (IC) in older patients.^{27–31}

Among 8 unique predictive equations with their variants, 1 study found that the Penn State (PSU) equation that included the Mifflin-St Jeor equation was the best equation for non-obese older (≥ 60 years) ICU patients.²⁸ Among obese older ICU patients, the PSU (modified) equation may be the best choice.²⁹ In another study comparing 6 predictive equations (without the PSU equation), the Harris-Benedict equation with a correction factor of 1.2 agreed most closely with IC measurements.³⁰

In studies comparing older vs younger patients, measured resting metabolic rate (after controlling for basal metabolic rate)³² or REE³¹ was not different between groups. However, the absolute deviation (either over- or underestimation) of predicted (25 kcal*ideal body weight in kg) from measured REE was significantly higher in older vs younger patients (9.3 ± 6.9 vs 6.3 ± 6.6 kcal/kg, respectively; $P < 0.01$).³¹ In critically ill trauma patients, the incidence of azotaemia (blood urea nitrogen > 25 mg/dL) was higher among older than younger patients with similar protein intake.³²

Energy and protein intake

Four retrospective observational studies were included, with sample sizes of 55–1,279 (online Supplementary Table S5).

Three retrospective studies were conducted on critically ill trauma patients. The first study investigated a hypocaloric (21–25 kcal/kg/day), high protein (≥ 2 g/kg/day) regime for > 10 days. No differences in nitrogen balance or clinical outcomes were found between older vs younger group.³³ Another study found that nitrogen balance can only be improved with a protein intake of > 1.5 g/kg/day in older patients, compared with > 0.99 g/kg/day in younger patients.³⁴ The third study showed that the calories received did not predict the time-to-discharge alive from the hospital for both older and younger groups.³⁵ Among MV COVID-19 patients, a retrospective analysis found no correlation between calories and protein intake with ICU LOS, hospital LOS, length of vasopressor use, and duration of MV in the older or the younger group.³⁶

Pharmaconutrition

Four studies (3 RCTs and 1 non-randomised interventional trial) investigated the effect of pharmaconutrition (intravenous [IV] glutamine, EN glutamine or IV fish oils) in older ICU patients (online Supplementary Table S6).

Two RCTs from the same group of authors randomised patients into 3 groups (control vs IV glutamine vs IV glutamine + intramuscular recombinant human growth hormone)³⁷ and 2 groups (control vs IV glutamine).³⁸ IV glutamine was administered at 100 mL/day for 2 weeks. Both studies found that IV glutamine reduced Acute Physiology and Chronic Health Evaluation II (APACHE II) and multiple organ dysfunction syndrome (MODS) scores at day 14, but this was not translated into improvements in MV duration, ICU LOS, or 28-day survival rate.^{37,39}

One non-randomised trial compared standard EN vs IV fish oils at a dose of 0.2 g lipid/kg body weight over 6 hours for 3 consecutive days. No differences were found between groups for ICU LOS, duration of MV and ICU mortality.³⁸

The last study randomised patients into total parenteral nutrition (TPN) with gradual transition to full EN; EN + lower glutamine dose (0.3 g/kg/day); and EN + higher glutamine dose (0.6 g/kg/day). Compared to the TPN group, both glutamine groups had higher transferrin and prealbumin levels at day 7, and higher haemoglobin level at day 14. There was no difference in the incidence of diarrhoea and bloating between the groups at day 7 and 14. No clinical outcomes were reported.⁴⁰

DISCUSSION

This scoping review found limited evidence for nutrition therapy in older critically ill patients. There were only 5 RCTs (sample size range: 90–147 patients) for 2 topics: route or timing of nutrition therapy and pharmaconutrition. In contrast, among general critically ill patients, up to December 2008, there were already 207 RCTs with 23,091 patients across 34 topics.⁴¹ The results of each topic are discussed in the following sections.

Nutrition screening and assessments

Determination of malnutrition and its risk among ICU patients is important for prognostication and may be used to guide nutrition intervention. This is especially relevant for older patients as they may be at higher risk of malnutrition or already malnourished before ICU admission due to various physical or social factors.⁴² Of the 2 nutrition assessment tools (SGA and MNA),

only SGA could prognose poorer clinical outcomes, and it is the most validated nutrition assessment tool in the general critically ill patients.⁶ Of note, mid-arm circumference, a unidimensional assessment, may be inadequate to assess for malnutrition.

The American Society for Parenteral and Enteral Nutrition 2016 guidelines recommended using NRS-2002 and NUTRIC/mNUTRIC score to guide nutrition intervention.⁴³ Notably, only the NUTRIC/mNUTRIC was developed and validated among critically ill patients.^{44,45} Hsu et al. reported that most older ICU patients had high mNUTRIC score (91.1%), and achieving $\geq 80\%$ of prescribed calories and protein was associated with lower mortality.¹⁶ However, the result of this observational study needs to be confirmed by high-quality RCTs.

Tools such as CONUT, GNRI, PNI and OPNI use biochemical markers like serum albumin and total lymphocytes to establish malnutrition risk. However, serum albumin and lymphocytes in an acute clinical setting reflect inflammatory status and disease severity rather than nutritional status.⁴⁶ These markers may have some prognostic value but using such tools may misguide treatment as they do not respond to nutritional interventions in an acute setting.⁴⁶

Similar to general adult critically ill patients, current evidence suggests that mNUTRIC and SGA may be the best available tools to aid prognostication of clinical outcomes in older critically ill patients. High-quality RCTs are needed to determine whether these tools can identify patients who may benefit from higher nutrition delivery.

Muscle mass assessment

Skeletal muscle is the most abundant tissue and the main reservoir of amino acids for vital organs during the stressed state.^{47,48} The direct measurements of muscle mass using imaging procedures such as CT and ultrasound at ICU admission may more precisely reflect patients' nutritional status.⁴⁹ Indeed, 3 studies consistently demonstrated higher hospital mortality in older critically ill patients with low muscularity at ICU admission.¹⁷⁻¹⁹ Compared to younger patients, older patients tended to have lower skeletal muscle mass and higher prevalence of low muscularity at ICU admission.^{22,23} For this reason, older ICU patients may experience greater nutrition-related complications than younger patients. Therefore, it may be crucial for older critically ill patients to receive early nutrition assessment and intervention. Further investigation is needed to

determine whether a nutrition intervention that is tailored to age and/or muscularity status will result in improved clinical and functional outcomes.

Route or timing of nutrition therapy

First, it is well established that in haemodynamically stable patients with functional gastrointestinal tract, early rather than delayed EN is associated with significant clinical benefit.⁵⁰ Second, postpyloric EN is also known to reduce the risk of pneumonia and gastrointestinal complications without reducing the risk of mortality.⁵¹ Regarding EN vs PN, infectious complications were found to be greater in the PN group if the calories received are higher than in the EN group.⁵² However, the actual energy and protein received between groups were not reported.²⁴ The included study found significant clinical benefits of combining EN and PN;²⁴ however, this is not supported by a meta-analysis of RCTs in general ICU patients.⁵³ Overall, the evidence regarding the route and timing of nutrition therapy is limited but unlikely to be different from the findings of general critically ill patients.

Determination of energy and protein requirements

In general, REE should be measured using IC when available and feasible. In situations when IC measurements are not possible, PSU (Mifflin) or PSU (modified) may be used for non-obese and obese older critically ill patients, respectively. However, the PSU equations were developed >10 years ago and based on a Caucasian population.^{28,29} It may be more appropriate to use a population-specific equation that is developed among critically ill patients, if available.^{54,55} On the other hand, the benefits of using IC in older ICU patients remain unclear since none of the included studies investigated clinical outcomes. Recently, a systematic review and meta-analysis of RCTs demonstrated that IC-targeted energy delivery significantly reduced short-term mortality.⁵⁶

Weight-based predictive equations were less accurate in older vs younger patients,³¹ and older patients were also at higher risk of azotaemia than younger patients at similar protein intake.³² Based on these limited evidence, the use of IC (if feasible) or age- and population-specific predictive equations, and careful monitoring of urea levels may be used to guide energy and protein prescription, respectively, in older ICU patients. Other protein monitoring strategies such as nitrogen balance, urea/creatinine ratio and monitoring of muscle mass trajectory may also be useful, though current evidence is lacking in this population.

Energy and protein intake

Older, compared to younger patients, required higher protein to achieve nitrogen balance (1.5 vs 0.99g/kg/day);³⁴ however, calories and protein intake were not associated with any clinical outcomes.^{35,36} This is similar to 2 meta-analyses of RCTs in general ICU patients showing that higher calories and/or protein intake were not associated with any improvement in clinical outcomes.^{57,58} Overall, the optimal energy and protein dose for older critically ill patients are yet to be determined. Physiologic data suggest that older patients require higher protein intake than younger patients;³⁴ however, caution needs to be exercised with higher protein as older patients are at a higher risk of azotaemia than younger patients at similar protein intake.³¹

Pharmaconutrition

The use of IV or EN glutamine and IV fish oils were not associated with clinical outcomes,³⁷⁻³⁹ despite 2 studies showing improvement of APACHE II and MODS scores in the IV glutamine group.^{37,39} Generally, the routine use of glutamine is not recommended except in burns and trauma ICU patients.^{43,59} A recent meta-analysis of RCTs demonstrated that fish oils as part of PN formula or administered as a standalone medication was associated with improved clinical outcomes.⁶⁰ Further studies are needed to elucidate whether the treatment effect of pharmaconutrition is different in older vs younger patients.

Limitations

The low number and poor quality of evidence of the included studies for each topic preclude any reliable conclusion or clinical recommendations. These findings will hopefully encourage more high-quality original nutrition studies in this increasing population. The selection of studies with subgroup analysis of older vs younger patients that are known to the authors may have contributed to bias in the findings. However, we disclosed this in the methodology, and the similarity of our findings with published recommendations for general critically ill patients attest to a low risk of bias.⁶¹ Future research may continue to build on our work by adding more studies that might have been missed by us into our tables.

This review did not identify studies on other aspects of critical care nutrition such as the use of micronutrients, monitoring of feeding tolerance, refeeding syndrome and glycaemic control; or the use of supplementation such as hydroxymethylbutyrate and leucine in older patients with sarcopaemia; or the effect of nutrition on functional outcomes. More studies are needed in these aspects.

CONCLUSION

The scarcity of data on nutrition therapy in older critically ill patients precludes any reliable clinical recommendations. Our review suggests that the recommendations from the general adult critically ill population are also applicable to older patients with the following exceptions. Evaluation of nutrition risk (mNUTRIC) and status (SGA) should be done early upon ICU admission to guide nutrition therapy, as older patients are at higher risk of having lower muscle mass compared to younger patients. Objective assessment of muscle mass or muscularity status using imaging methods such as ultrasound may be considered to guide and monitor the progress of nutrition therapy. IC or age- and population-specific predictive equations should be used to determine energy requirements. Older critically ill patients may require higher protein intake (~1.5kcal/kg/day) than younger patients with careful monitoring of urea level to prevent azotaemia.

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