

Statement

Nutrition Management of Acute Respiratory Distress Syndrome (ARDS) - COVID-19 in Mechanically Ventilated Patients

Patients with Acute Respiratory Distress Syndrome (ARDS) – Disease Background & Nutrition Risk

Patients with COVID-19 are likely to present to the intensive care with acute severe respiratory failure/ acute respiratory distress syndrome (ARDS). They may also suffer from multiorgan dysfunction syndrome. They are highly likely to require ventilation support; a significant number may also require renal replacement therapy, due to a high prevalence of acute kidney injury (AKI).⁽¹⁾

A recent study in 21 critically ill patients with COVID-19 in Washington State, US, shows that ARDS was observed in 100% of patients requiring mechanical ventilation (71% of total patient group) and 53% of them developed severe ARDS by 72 hours.⁽²⁾

A significant proportion of infected patients are older adults, with a higher prevalence of frailty and associated comorbidities (e.g. diabetes, cardiovascular disease, chronic obstructive pulmonary disease [COPD]).^(3,4)

“Older adults are at much higher risk for developing serious complications from this contamination. The current analysis shows that mortality rates are about 15% in contaminated subjects over 80 years, whereas it is less than 0.5% in people < 50 years old”.⁽²⁾

Malnutrition risk is high due to the nature of the disease process, impact on oral intake, older age, presence of comorbidities and expected duration of intensive care unit (ICU) stay.^(1,3,5)

Which Guidelines Could I Follow When Providing Nutrition Support to Patients with Acute Respiratory Failure or ARDS?

The nutritional therapy of critically ill patients with COVID-19 and ARDS should be in line with the new ESPEN COVID-19 guideline⁽⁶⁾, with reference also to the ESPEN ICU guidelines⁽⁵⁾. However, several local clinical nutrition societies, e.g. BAPEN, SEEN, have published recommendations dedicated to the nutrition therapy of COVID-19 patients.

Links to Useful Documents

- SFNCM (Société Francophone Nutrition Clinique et Métabolique) - France <https://www.sfncm.org/1204-covid19-avis-experts>

- SEEN (Sociedad Española de Endocrinología y Nutrición) - SPAIN
<https://www.seen.es/portal/contenidos/apartados/listado.aspx?idTipoApartado=FCUKB6%2fX264tx8sZzRkhiQ%3d%3d>
- BRASPEN (Brasileira de Nutrição Parenteral e Enteral) - Brazil
<https://slaninternacional.org/POPUP/BRASPEN-AMIB.pdf>
- BDA (British Dietetic Association) - United Kingdom
<https://www.bda.uk.com/resource/critical-care-dietetics-guidance-covid-19.html>
- BAPEN (British Association of Parenteral and Enteral Nutrition) - United Kingdom
<https://www.bapen.org.uk/pdfs/bifa/covid-19-national-pyrexia-plan-for-hpn-patients-testing-available.pdf>
- ESPEN 2020 COVID-19 Guideline
[https://www.clinicalnutritionjournal.com/article/S0261-5614\(20\)30140-0/pdf](https://www.clinicalnutritionjournal.com/article/S0261-5614(20)30140-0/pdf)

When Should I Provide Clinical Nutrition Therapy?

Patients unable to meet nutritional requirements orally and staying > 48 h in the ICU, should be considered for clinical nutritional therapy.⁽⁵⁾

When there are no contraindications to enteral nutrition, then early enteral nutrition (EEN) within 48 h can safely be started in these patients.^(4,5)

If there is a contraindication for oral or enteral nutrition, then parenteral nutrition (PN) should be started within 3-7 days.⁽⁵⁾

Conditions requiring low dose Enteral Nutrition Patients:

- Receiving therapeutic hypothermia and increasing the dose after rewarming
- With intra-abdominal hypertension without abdominal compartment syndrome, whereas temporary reduction or discontinuation of EN should be considered when intra-abdominal pressure values further increase under EN
- In patients with acute liver failure when acute, immediately life-threatening metabolic derangements are controlled with or without liver support strategies, independent on grade of encephalopathy.

When Providing Nutrition Therapy Which Route Should I Use?

Gastric access should be first choice, provided by a fine bore nasogastric tube.⁽⁵⁾ However, there is a risk of gastrointestinal (GI) intolerance (e.g. high gastric residuals, vomiting) related to the use of medications (sedatives and neuromuscular blockage) and prone positioning, that may be implemented in this patient group. Therefore, close monitoring of GI tolerance is essential when commencing early enteral nutrition.^(1,5,7,8)

ASPEN/SCCM and the Surviving Sepsis Campaign recommend the **use of prokinetics** metoclopramide (10 mg three times a day) and erythromycin (3-7 mg/kg/day) in the case of feeding intolerance in critically ill patients.⁽⁹⁾

However, several prokinetics (Erythromycin, Metoclopramide and Domperidone) are contraindicated in patients treated with Chloroquine or Hydroxychloroquine. These drugs may increase QTc on ECG and the combination may be associated with a high risk of severe ventricular arrhythmias.

In case of **contraindications to oral and EN, PN** should be implemented **within 3-7 days**.⁽⁵⁾

Early and progressive PN can be provided instead of no nutrition in case of contraindications for EN in severely malnourished patients.⁽⁵⁾

In patients who do not tolerate full dose EN during the first week in the ICU, the safety and benefits of **initiating PN** should be weighed on a case-by-case basis.⁽⁵⁾

To avoid overfeeding, early full EN and PN shall not be used in critically ill patients (not in the first 48 h) but shall be prescribed within three to seven days. **Progressive introduction of EN and PN** may limit the risk of overfeeding and refeeding syndrome.⁽⁵⁾

Can Patients in the Prone Position Still Receive Enteral and Parenteral Nutrition?

Patients in the prone position can still safely receive enteral nutrition. To improve GI tolerance, **when feasible, raise the head of the bed slightly by 20-25° and consider early or prophylactic prokinetics**.^(1,5,8,9)

In those at high risk of GI intolerance or with ongoing GI intolerance (e.g. high gastric residuals, vomiting), despite prokinetics, the placement of a **post pyloric (e.g. nasojejunal) feeding tube can be performed**.^(1,5,9)

When placement of a post pyloric feeding tube is not possible, alternative options including nasogastric feeding, with a peptide-based formula, or PN can be considered.⁽¹⁾

SEEN (Sociedad Espanola de Endocrinologia y Nutricion) recommends the **use of PN** when enteral nutrition is not possible or does not reach nutritional targets, for example in the need of prone position or an inadequate GI tolerance.

How Should I Determine the Patients Nutritional Requirements?

Energy requirements:

It is unlikely that Indirect calorimetry is feasible for use in COVID-19 patients, due to an increased risk of infection. Furthermore in practice, due to the workload, indirect calorimetry is not used in majority of ICUs. ESPEN ICU Guidelines recommend in the absence of IC, and during emergency times, **the predictive equation 20 kcal/kg/d could be used, and energy increased to 50-70% of the predicted energy at day 2 and 80-100% at day 4**.⁽⁶⁾

Protein requirements: During critical illness, **1.3 g/kg protein equivalents per day** can be delivered progressively, **to reach target by day 3-5**.^(5,6) In case of using PN containing amino

acids this corresponds to 1.56 g amino acids (AA)/kg/d based on the fact that 100 g parenteral AA mixture is equivalent to 83 g high-quality dietary protein.⁽¹⁰⁾

For persons with obesity, where body composition measurements are not possible, use of adjusted body weight is recommended. *Adjusted body weight = ideal bodyweight + (actual bodyweight – ideal body weight) * 0.33.*⁽⁶⁾

Patients may require higher amounts of protein, but this should be assessed on an individual basis.⁽⁵⁾ ASPEN/SSCM recommends that sufficient (high-dose) protein should be provided. Protein requirements are expected to be in the range of 1.2–2.0 g/kg actual body weight per day and may likely be even higher in burn or multi-trauma patients.⁽⁹⁾

Fluid requirements: Patients with acute respiratory failure may require a restricted fluid strategy.^(1,11) Therefore, this needs to be considered when providing enteral and/or parenteral nutrition.^(1,5,11)

Micronutrients: Ensure adequate daily provision. If unable to meet full requirements from nutritional formula, consider additional supplementation. Avoid providing high doses of antioxidants without proven deficiency.⁽⁵⁾

How Should I Prescribe Enteral Nutrition?

To determine the dose of enteral nutrition, first assess if there is any condition that would affect providing full EN dose.⁽⁵⁾**

** Contraindications to early enteral nutrition

*Conditions contraindication to EN: uncontrolled shock, life-threatening hypoxemia, hypercapnia or acidosis, active upper GI bleeding, overt bowel ischemia, high-output intestinal fistula if reliable feeding access distal to the fistula is not achievable, abdominal compartment syndrome; gastric aspirate volume is above 500 ml/6 References

When and How to Prescribe Parenteral Nutrition?

Reintam-Blaser et al 2019, provide an algorithm for decision making in nutrition, which aims to assist clinicians to implement the ESPEN ICU Guidelines. It includes a clear guidance when and how to use PN.⁽¹²⁾

PN should be implemented in case of contraindications to EN which includes, e.g.: uncontrolled hypoxemia and acidosis, uncontrolled upper GI bleeding, gastric aspirate > 500 ml/6 h, bowel ischemia, bowel obstruction, abdominal compartment syndrome, and high-output fistula without distal feeding access.⁽¹²⁾

PN should also be used in case of relative contraindications to EN and when nutritional targets are not achieved (e.g. vomiting, diarrhea, abnormal bowel sounds, gastric residual volume, bowel dilatation).

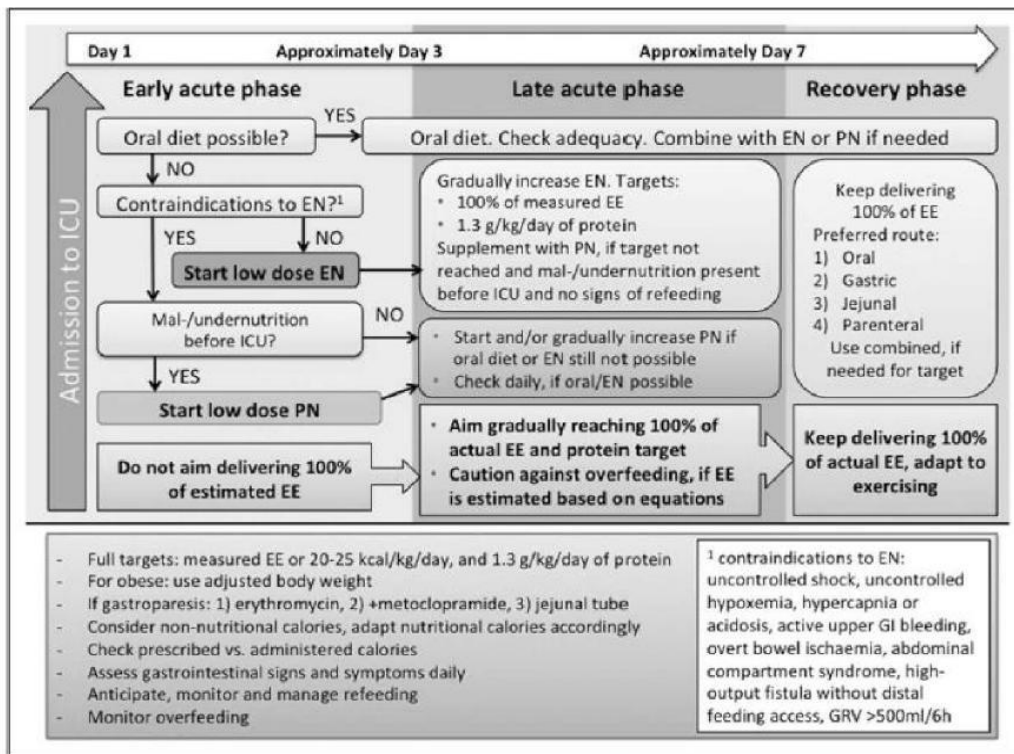


FIGURE 1. Flow chart for decision-making on nutrition. EE, energy expenditure; EN, enteral nutrition; GRV, gastric residual volume; PN, parenteral nutrition.

Source: Reintam Blaser A, Deane AM, Starkopf J et al. Translating the European Society for Clinical Nutrition and Metabolism 2019 guidelines into practice. *Curr Opin Crit Care* 2019, 25:314–321.

Same as for EN, also for PN progressive start and ramp up is recommended.⁽⁵⁾

How Should I Adjust the Nutrition Regimen if the Patient is on Propofol?

Propofol is a lipid containing infusion (containing 1.1 kcal /ml). It can be provided at a 1% or 2% concentration. **When provided at an infusion rate exceeding 20 mL/h, the caloric value**

of the propofol in combination with feeds can lead to significant excess of energy delivery.

Excessive energy delivery is associated with hyperglycemia, fatty liver, hypertriglyceridemia, and excess CO² production.

When all criteria below are met, reduce the feeding rate:⁽⁷⁾

- Propofol provided as an hourly infusion (not as a bolus).

- Propofol already provided for > 24 h.
- Propofol expected to continue for an additional > 24 h.
- Propofol average hourly infusion rate > 20 mL/h.

Example of How to Reduce the Enteral Feed Rate for Patients on Propofol Infusion.⁽⁷⁾

Energy Density of Enteral Feed: 1.0-1.2 kcal/ml feed (e.g. Fresubin Original)	Energy Density of Enteral Feed: 1.5-2.0 kcal/ml feed (e.g Fresubin HP Energy)
Action: Reduce the enteral feed rate equivalent to the propofol infusion rate.	Action: Reduce enteral feed rate by 50% (1/2) the rate of the propofol infusion rate.
Example Propofol infusion rate @ 30ml/hr Decrease enteral feed rate by 30ml/hr	Example Propofol Infusion rate @ 30ml/hr Decrease enteral feed rate by 15ml/hr

For patients on higher infusion rates of 1% propofol concentration, discuss with the physician in charge if a 2% propofol concentration solution can be considered, to reduce the propofol infusion volume, and allow patients to achieve the feeding volume.

If PN is indicated, non-nutritional sources such as glucose solution for drug dilution or lipids from propofol/clevidipine or citrate from continuous renal replacement therapy (CRRT) should be taken into account as a non-nutritional calorie intake.

What Type of Enteral Nutrition Formula Should I Choose?

Patients with acute respiratory failure or ARDS often require a restricted fluid strategy. They are at risk of GI intolerance to higher volume enteral nutrition, especially those in a prone position.^(1,5,13) **Therefore, a high calorie and protein, low volume enteral nutrition formula should be first choice unless there are other conditions**^(1,13,14) **(see below).** EN enriched with omega 3 fatty acids within nutritional doses can be administered.⁽⁵⁾

High calorie feeds (> 1.5kcal/ml) may reduce gastric emptying time in some patients, especially in the acute phase of illness, or in a prone position, and the benefits of meeting nutritional requirements must be balanced against risk of GI intolerance.⁽¹⁾

What About Carbohydrate to Fat Ratio of Formulas?

ESPEN recommends an energy ratio from fat and carbohydrate between 30:70 (subjects with no respiratory deficiency) to 50:50 (ventilated patients).⁽⁶⁾

Patients with acute respiratory failure and other conditions

- **Glucose intolerance/stress hyperglycaemia:** Consider a diabetes specific formula.^(5,14)
- **Renal failure (not receiving renal replacement therapy):** Consider lower volume/ electrolyte reduced formula.⁽¹⁾
- **Malabsorption:** Consider a peptide-based formula with MCT.^(9,14)
- **Persistent diarrhoea:** Consider fibre enriched formula.⁽⁹⁾
Consider first non-feed related causes including medications (e.g. antibiotics, laxatives, prokinetics, sorbitol containing liquid preparations) & gastrointestinal infections (e.g. Clostridium difficile).
- **Burns/trauma;** Consider glutamine enriched EN and/or additional glutamine supplementation.⁽⁵⁾

For patients not on a fluid restriction or with above conditions:

- consider a standard formula.

Regardless of enteral nutrition formula, enteral nutrition should be started slowly and gradually progressed to target (see nutritional requirements section above).

What Type of Parenteral Nutrition Solutions Should I Choose?

ARDS is an overwhelming systemic inflammatory process associated with significant morbidity and mortality. It is characterized by refractory hypoxic respiratory failure with a significant global inflammatory processes and multi-organ dysfunction and pulmonary edema.⁽¹⁵⁾

Langlois et al. 2019 showed in a systematic review and meta-analysis (12 RCTs and 1280 patients were included) of omega-3 fatty acid supplementation in critically ill patients with ARDS a trend in patients receiving omega-3 fatty acids toward reduced ICU LOS and duration of mechanical ventilation.⁽¹⁶⁾

Fish oil containing PN is associated with statistically and clinically significant positive effects on clinical outcomes e.g. infection rates, sepsis rate, length of ICU and hospital stay.⁽¹⁷⁾ The ESPEN guidelines on clinical nutrition in the intensive care unit state that parenteral lipid emulsions enriched with EPA and DHA (fish oil dose 0.1-0.2g/kg/d) can be provided in patients receiving PN. ⁽⁵⁾

ESPEN ICU guidelines recommend that micronutrients (i.e. trace elements and vitamins) should be provided daily with PN to enable substrate metabolism.⁽⁵⁾

Patients with ARDS often require a restricted fluid strategy which favours to use PN bags for central application which helps to meet the nutritional targets and to avoid fluid overload.

How Can I Ensure Safety in Feed Application?

To ensure safety in feed application and to reduce risk of complications (e.g. infections, aspiration), it is essential to adhere to best practices in feed handling and administration.⁽¹⁸⁾

- **Ensure correct storage conditions of feed** in line with product recommendations.⁽¹⁸⁾
- **It is essential to practice hand hygiene and wearing of gloves** (to avoid contamination of feed, bacterial or viral transmission) when EN formula is handled, and/or administered. Check formula has not exceeded its expiration date.⁽¹⁸⁾
- **Ensure adherence to hang times:** 24-48 h; for a closed system (large volume bags or containers), 8 h; for an open system (smaller volume liquid cans, bags, or cartons), 4 h; for powdered formula requiring preparation.⁽¹⁸⁾
- **To reduce the risk of aspiration and improve gastrointestinal tolerance:** (1, 5,8,14,19)
 - Tilt the head of bed by 30-45°, 20-25° (if patient is prone), when feasible.
 - Ensure correct positioning of feeding tube prior to; commencing EN, using the tube for water, or medications administration. Check the position of feeding tube at regular intervals throughout the day as the feeding tube may become displaced.
 - Use a continuous feeding method of application.
 - Start EN at low rate e.g. 20ml/hr and gradually building up to energy and protein targets (see nutritional requirements question).
 - Monitor gastric residual volumes when initiating EEN & consider prokinetics as part of a standardised feeding protocol.
 - **Consider feed formulation (see feed formulation question).**

How Should I Monitor Patients?

- **Assess GI tolerance (e.g. gastric residuals, vomiting) when initiating enteral nutrition, and in those with abdominal problems** during enteral nutrition.^(5,8,9,19)

Use local gastric residual cut offs or consider > 500 ml/6 h as high. In this case consider reducing feeding rate and use early/prophylactic prokinetics. For persistent high gastric residuals, over 48-72 h, if feasible place a post pyloric feeding tube, or if not possible consider starting parenteral nutrition.^(5,8,9,19)

- **Assess if nutritional goals are met:**^(5,8,9) To prevent both under and overfeeding, monitor daily volume of feed delivered vs volume of feed prescribed.
- **Nutritional status:**^(5,8,9) Monitor nutrition status at regular intervals, be mindful that bodyweight will be affected by changes in fluid status of the patient.

Therefore, use estimated dry weight when calculating nutritional requirements.

- **Monitor biochemistry e.g. for risk of refeeding syndrome:**^(5,8) At risk older frail adults contribute to a significant proportion in this group of patients. **If phosphate drops** to < 0.65 mmol/l or a drop of > 0.16 mmol/l: reduce EN for 48 h and gradually increase. Phosphate deficiency can contribute to a delay in weaning.⁽²⁰⁾
- **Monitor blood glucose levels:**^(1,5,8) Type 2 diabetes appears to be a risk factor for COVID-19, additionally stress induced hyperglycaemia may occur.

Check blood glucose at regular intervals for patients on enteral nutrition and consider starting insulin when blood glucose > 10mmol/l, reassess nutrition prescription for overfeeding (energy and carbohydrate quantity) and consider adjustment to feed formula (please see feed formulation section).

- **Reassess access route:**^(1,9) To define if current route is most appropriate to meet patients' nutritional requirements, or if an alternative route is more appropriate and/or required (e.g. combined enteral and parenteral nutrition).

How Should I Manage a Patient Following Weaning from Mechanical Ventilation?

Following weaning from mechanical ventilation, and **reintroduction of oral intake patients are at risk of swallowing problems. This should be assessed on reintroduction of oral intake**, with referral to an appropriately trained health care professional (e.g. speech and language therapist) for an expert assessment.⁽⁴⁻⁶⁾

Texture modified oral nutritional supplements should be considered to overcome swallowing problems and ensuring sufficient energy and nutrient intake (e.g. semi-solid drinks, cremes or thickeners added to liquid drinks).⁽⁶⁾

Patients are also at high risk of inadequate energy, protein and fluid intakes and therefore it is essential to monitor adequacy of oral intake and need for ongoing nutrition support.

The need for ongoing nutrition support should be individualised to the patients' needs but can include prescription of oral nutritional supplements and/or continued supplementary enteral nutrition until oral diet is adequate.⁽⁴⁾

ESPEN recommends for patients with dysphagia texture modified food be considered after extubation. If swallowing is unsafe enteral nutrition should be administered. If a high aspiration risk, despite post pyloric then parenteral nutrition should be considered with removal of nasoenteral tube whilst patient receives swallowing training.⁽⁶⁾

To ensure effective nutrition management, a timely and complete transfer of the nutrition therapy plan is needed. It is also important to closely monitor nutritional intake post discharge from the ICU to prevent deterioration of nutritional status.^(4,5)

What is the Nutritional Management of Patients Who Require Non-Invasive Ventilation?

Patients with acute respiratory failure may be treated with non-invasive ventilation. These patients are **at risk of inadequate energy and protein intakes**, and subsequent malnutrition due to restricted oral intake. Non-invasive ventilation can **also impair provision of enteral nutrition.**^(1,5,11)

Consider oral nutritional supplements first and if oral intake remains inadequate (if oral intake < 65% energy & protein needs), then progress to enteral nutrition via a nasogastric tube.^(1,5) In case of contraindications to oral and EN, PN should be implemented within 3-7 days.⁽⁵⁾

Discuss with medical team if the patient is likely to need intubation and if nasogastric feeding is technically feasible without compromising respiratory support. The use of high flow oxygen or an adapted nasogastric tube through a helmet may prevent air leaks.^(1,11)

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