

Nutrition Therapy in the Patient with COVID-19 Disease Requiring ICU Care

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Intensive care units (ICU) worldwide have become overwhelmed with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) induced respiratory failure leading to COVID-19 disease. Good supportive care remains the cornerstone in managing critically ill patients with COVID-19. The need to address the provision of critical care nutrition remains an integral component of these supportive measures. The nutritional management of the ICU patient with COVID-19 is in principle very similar to any other ICU patient admitted with pulmonary compromise. Given the lack of direct evidence on patients with COVID-19, especially those with shock, many of these recommendations are based on indirect evidence from critically ill patients in general and those with sepsis and ARDS.

The 2016 SCCM/ASPEN Guidelines for Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient are slightly outdated because the literature search supporting them ended in December 2013.^{1,2} ESPEN also has critical care nutrition guidelines³ and just produced a new paper that does address COVID-19 (not yet published). This brief review will address timing, route, and monitoring of nutritional therapy based on best available evidence, but also provide guidance on management specific to COVID-19 disease, while taking into consideration key guiding principles related to this disease process.

Guiding Principles for SARS-CoV2 Management

Like all interventions related to the care of the patient with COVID-19, the delivery of nutrition in critically ill patients should take into consideration the following principles:

1. “Cluster care,” meaning all attempts are made to bundle care to limit exposure.
2. Adhere to Centers for Disease Control (CDC) recommendations to minimize aerosol/droplet exposure with an emphasis on hand hygiene and utilization of personal protective equipment (PPE) to protect healthcare providers and limit spread of disease.

3. Preserve use of personal protective equipment (PPE), which is becoming a depleted resource in various regions of the United States, by limiting the number of staff providing care and optimizing other PPE preserving strategies.

Recommendation 1: Nutrition Assessment

We recommend all healthcare providers, including dietitians, nurses, and other healthcare professionals involved in the nutrition assessment should follow PPE standards set forth by the CDC for all patients with COVID-19 disease and adhere to their institutional recommendations. PPE includes protective eyewear, isolation gown, a face shield, and an N95 respirator (<https://www.coronavirus.gov>). Pragmatically, with limited PPE supply, many dietitians are not entering ICUs or patient rooms of patients in isolation and not performing a nutrition focused physical examination but rather relying on other providers to collect physical data on those patients. Dietitians are using other means to collect assessment data including calling the patient or family, and using telehealth visits (virtual and telephone) including various platforms (audio and visual). It is more important than ever the dietitian document assessment findings, where/how the information was received, and collaborate and coordinate with the medical teams to develop a safe nutrition care plan.

Recommendation 2: Timing of Nutrition Delivery

The most important issue is timing of nutrition delivery. Initiating early enteral nutrition (EN) within 24-36 hours of admission to the ICU or within 12 hours of intubation and placement on mechanical ventilation should be the goal. In the patient unable to maintain volitional oral intake, early EN is recommended by both 2016 SCCM/ASPEN and 2019 ESPEN guidelines.¹⁻³ Meta-analyses of randomized controlled trials conducted between 1979 and 2012 show that provision of early EN to interventional patients improved mortality and reduced infections compared to controls for whom such therapy was delayed or withheld.^{1,2} Assuming the patients were nutritionally replete prior to contracting SARS-CoV-2 and the acute phase of illness is limited, the general guidelines for ICU nutrition care from these societies are sufficient. The majority of patients with sepsis or circulatory shock have been shown to tolerate early EN at a trophic rate.⁴ Unless escalating vasopressors combined with enteral feeding intolerance with symptoms of ileus (abdominal distention, vomiting) are present, COVID-19 disease with shock should not be seen as a contraindication to trophic EN.⁴

Early PN should be initiated as soon as possible in the high-risk patient for whom early gastric EN is not feasible.^{1,2} High-risk patients include those with sepsis or shock requiring escalating or multiple vasopressors, or when high pressure respiratory support is required (NIV, CPAP, or PEEP). Bowel ischemia is rare in shock, with clinical trials reporting an overall incidence of 0.3%.⁴ However, in this unusual circumstance of COVID-19 disease where concern for ischemic bowel may be greater and a prolonged ICU stay is expected, the threshold for switching to PN may need to be lower. Early PN will subvert concerns for ischemic bowel and reduce droplet aerosol transmission to healthcare providers by avoiding procedures involved in the initial placement and maintenance of an enteral access device.

Recommendation 3: Route, Tube Placement and Method of Nutrition Delivery

EN is preferred to parenteral nutrition (PN). Infusion of formula into the stomach via 10-12 Fr feeding nasogastric tube requires minimal expertise and facilitates earlier initiation of feeding. If gastric feeding is unsuccessful due to enteral feeding intolerance, use of a prokinetic agent to enhance motility is recommended as the second step. Post pyloric EN delivery is recommended only after these strategies fail. To minimize breach of airborne isolation and limiting exposure to healthcare providers, patients requiring a post pyloric feeding tube should undergo bedside placement with techniques that do not require use of endoscopy or fluoroscopic guidance. Placement strategies using real time FDA approved electromagnetic or integrated imaging guidance may eliminate the need for placement confirmation abdominal x-ray if this adheres to the institution's policy and procedures. In many cases a large bore nasogastric (NGT) or orogastric (OGT) tube may be placed at time of intubation. Initiating tube feeding via the tube that is already available is appropriate. Confirmatory abdominal x-rays should be clustered with chest x-ray timing. Placement of any enteral access device may provoke coughing and should be considered an aerosol generating procedure. If possible, keep the patient's mouth covered during placement in the nares and follow CDC guidelines regarding the use of N-95 masks and PAPR during tube placement. Post-pyloric feeding tubes tend to be smaller caliber and therefore are more likely to become clogged with decreased flushing than a larger bore NGT/OGT, which may occur with clustering of care and goal to limit patient contact. In addition, in these high-risk patients, frequent abdominal exams should occur which may not be ideal in these patients given potential shortages of PPE. Lastly, placement of post-pyloric feeding tubes may take longer to place than gastric tubes, increasing exposure time of the healthcare practitioner.

Continuous rather than bolus EN is strongly recommended, this is supported by both the ESPEN and SCCM/ASPEN guidelines.¹⁻³ Multiple meta-analyses have shown a significant reduction in diarrhea with no differences in other outcome parameters with continuous EN.³ In addition, since bolus EN delivery would require more frequent patient interaction, continuous EN delivery decreases exposure of the healthcare team to SARS-CoV-2. If the patient room allows for pumps to be placed "outside" the room, this should also include the feeding pump and bag set if possible. Use as much extension tubing as possible that allows for proper flow and is compatible with EN connectors and delivery system. Consult the pharmacist for concerns regarding medication administration via the enteral feeding tube.

Early EN may not be preferential in a subset of patients with COVID-19 with gastrointestinal (GI) involvement.⁵ Before the onset of respiratory symptoms, some patients initially present with diarrhea, nausea, vomiting, abdominal discomfort and in some cases gastrointestinal bleeding.⁵ Some evidence suggests that the development of GI symptoms indicates greater disease severity.⁵ The presence of viral RNA components has been documented in the feces and respiratory specimens of such patients (one trial showing 53% testing positive by stool studies alone).⁶ Further GI involvement has been confirmed by the presence of an ACE2 protein (a cell receptor for SARS-CoV-2) found in glandular cells on biopsy of esophageal, gastric, duodenal and rectal mucosa.^{6,7} These findings suggest a fecal-oral route of transmission for the SARS-CoV-2 virus, and a possible mode of entry into the host cells.^{6,7} Although the exact mechanism of COVID-19-induced GI symptoms largely remains elusive, when present early use of PN should be considered, transitioning to EN when GI symptoms subside.

Critically ill patients with COVID-19 disease have been reported to be older with multiple co-morbidities. Such patients are often at-risk of refeeding syndrome. Thus, identifying pre-existing malnutrition or other risk factors for refeeding syndrome in critically ill patients is vital. If refeeding syndrome risk is present, we recommend starting at approximately 25% of caloric goal, in either EN or PN fed patients, combined with frequent monitoring of serum phosphate, magnesium and potassium levels as calories are slowly increased. The first 72 hours of feeding is the period of highest risk.

Recommendation 4: Nutrition Dose, Advancing to Goal, and Adjustments

Feeding should be initiated with low dose EN, defined as hypocaloric or trophic, advancing to full dose EN slowly over the first week of critical illness to meet energy goal of 15-20 kcal/kg actual body weight (ABW)/day (which should be 70-80% of caloric requirements) and protein goal of 1.2-2.0 gm/kg ABW/day. If PN is necessary, conservative dextrose content and volume should be used in the early phase of critical illness, slowly advancing to meet the same energy goals as outlined above. While energy requirements can ideally be determined by indirect calorimetry, the principle of “clustering” of care is particularly important and we recommend instead using weight-based equations to estimate energy requirements as a practical matter for the COVID-19 patients. Nutrition requirements should take into consideration the use of propofol in terms of lipid calories and total calories needed.

EN should be withheld in the patient with hemodynamic instability requiring vasopressor support at high or escalating doses, patients on multiple vasopressor agents, or rising lactate levels. EN may be initiated/restarted after the patient is adequately resuscitated and/or has been on a stable vasopressor dose with sustained mean arterial pressure of ≥ 65 mmHg.^{4,8}

EN should be held and PN strongly considered in patients with gastrointestinal intolerance as manifested by unexplained abdominal pain, nausea, diarrhea, significant abdominal distention, dilated loops of small and large bowel with air/fluid levels, pneumatosis intestinalis or increasing nasogastric outputs in previous 6 to 12 hours with start of trophic feeds or prior to initiation of EN.^{8,9}

Recommendation 5: Formula Selection

A standard high protein ($\geq 20\%$ protein) polymeric isosmotic enteral formula should be used in the early acute phase of critical illness. As the patient’s status improves and vasopressor requirements abate, addition of fiber should be considered. If there is significant GI dysfunction a fiber free formula may be better tolerated. As soon as GI dysfunction improves, a fiber containing formula or supplement should be attempted for the non-nutritional benefits to the gut microbiota. Animal models and a few small human trials suggest that fish oil containing formulations may be of benefit in immune modulation and helping to clear viral infections. The fish oil metabolites (Specialized Pro-resolving Mediators) seem to be the active participant. Currently with only animal data and a few human trials, inadequate specific human trials are available to make this a formal recommendation. While theoretical benefits are described with other types of formulas to enhance tolerance (small peptide/MCT oil formulas), failure to improve outcome in a similar population of patients in a medical ICU does not warrant their

added cost. Any supplemental nutritional modules such as protein packets, probiotics, or soluble fibers should be given once per day in order to cluster care.

If PN is required in the first week of ICU stay during the acute inflammatory phase of COVID-19, limiting steps should be taken for use of pure soybean lipid emulsions as outlined in published guidelines.³ This can be accomplished by withholding soybean lipids or using alternative mixed lipid emulsions. There have been anecdotal reports that these patients who receive propofol are rapidly developing severe hypertriglyceridemia. Monitor serum triglyceride levels in these patients receiving propofol and/or intravenous lipid emulsions early in their course (perhaps within 24 hours) after initiation of lipid containing products. While we recommend checking serum triglyceride in patients receiving propofol, a subset of SARS-CoV2 patients develop a cytokine storm which resembles secondary hemophagocytichistiocytosis (secondary HLH), and a serum triglyceride is part of the criteria for identifying secondary HLH. We recommend taking into consideration and context other secondary HLH criteria when interpreting an elevated triglyceride, to distinguish secondary HLH from propofol-related hypertriglyceridemia.¹⁰

Recommendation 6: Monitoring Nutrition Tolerance

Enteral feeding intolerance (EFI) is common during the early and late acute phases of critical illness. Early experience with COVID-19 patients suggests that gastrointestinal symptoms (which might manifest as EFI) are associated with greater severity of illness. Gastric residual volume (GRV) monitoring is not reliable for detection of delayed gastric emptying and risk of aspiration, has been shown to be a deterrent to the delivery of EN, and should not be utilized as a monitor of feeding tolerance.¹¹ Per the guiding principles in caring for the critically ill patient with COVID-19 disease, this recommendation is relevant to decrease the risk of SARS-CoV-2 transmission to the healthcare provider.

Patients should be monitored by daily physical examination and confirmation of passage of stool and gas. These observations should be “clustered” with other provider activities to minimize healthcare team virus exposure. As with any ICU patient, recording of the percent of calories and protein delivered should be recorded for both EN and PN.

Recommendation 7: Nutrition for the Patient Undergoing Prone Positioning

SARS-CoV-2 may lead to acute respiratory distress syndrome (ARDS), necessitating invasive mechanical ventilation with lung protective and open lung ventilation. Despite these measures, some ARDS patients develop refractory hypoxemia and prone positioning is an inexpensive technique to improve oxygenation and increase bronchial secretion clearance. This strategy has been associated with decreased ventilator-induced lung injury and increased survival in patients with severe acute respiratory distress syndrome (ARDS) with refractory hypoxemia.^{12,13}

Several retrospective and small prospective trials have shown EN during prone positioning is not associated with increased risk of gastrointestinal or pulmonary complications, thus we recommend the patient requiring prone positioning receive early EN.¹⁴

Most patients tolerate EN delivered into the stomach while in the prone position, but on occasion, post-pyloric placement of the feeding tube may be indicated. As placement of post-pyloric tubes increases potential exposure to virus, use of post-pyloric tubes should be limited in COVID-19 patients. When EN is introduced during prone positioning, we recommend keeping

the head of the bed elevated (reverse Trendelenburg) to at least 10 to 25 degrees to decrease the risk of aspiration of gastric contents, facial edema and intra-abdominal hypertension.¹⁵

Recommendation 8: Nutrition Therapy During ECMO

Extracorporeal membrane oxygenation (ECMO) is a supportive care strategy to oxygenate and ventilate patients with severe ARDS with refractory hypoxemia and/or hypercapnia.¹⁶ No data is available for nutrition support during ECMO in COVID-19 disease. One of the major barriers to EN during ECMO is the perception that ECMO patients are at-risk of delayed gastric emptying and bowel ischemia. Early observational data from Ridley et al found bowel ischemia in 4.5% of 107 patients on ECMO receiving EN.¹⁷ Other observational data shows safety and tolerability of gastric EN delivery during ECMO.¹⁸ Extrapolating from observational data from the H1N1 pandemic, most patients tolerated early EN within 24 hours of initiating ECMO. In the largest observational study of EN during veno-arterial (VA) ECMO, Ohbe et al found early EN, as compared to delayed EN, was associated with improvement in 28-day mortality and zero incidence of bowel ischemia.¹⁹ Thus, we recommend starting early low dose (trophic) EN in those on ECMO with close monitoring for EFI and slow advancement to goal over the first week of critical illness. In patients where PN is utilized, there was concern because the initial ECMO filters allowed lipid infiltration into the oxygenator. However, newer ECMO circuits have negated the lipid infiltration issue.

Lessons Learned from the Field

These anecdotal real-time lessons learned from the field are coming to light rapidly. These lessons are not necessarily evidence-based but can be helpful to frontline clinicians and are important to consider.

1. CMS has lifted many restrictions and expanded coverage for telehealth visits (virtual and telephone) including using various platforms such as FaceTime and Google Duo (audio and visual). This applies to all providers (physicians, NPs, PAs and dietitians). One should check with their facility for specific support and application of state licensure rules.
2. As the number of patients who require EN increase, there may be a shortage of enteral pumps. Therefore, enteral pump distribution priority should be given to patients with small bowel feeding or those with symptoms of intolerance, and continuous gravity feeding be attempted for those not able to have a pump. Also consider alternative enteral administration sets in light of the current shortage of all EN bag products.
3. For PN, consider use of multi-chamber bag PN products as a potential way to decrease pharmacist compounding time for PN preparation, particularly if standard PN components are in shortage.
4. PN pumps can also have extension tubing placed to allow making adjustments from outside the room.
5. Consider use of the EN algorithm of care below.

Conclusion

The delivery of nutritional therapy to the patient with COVID-19 disease should follow the basic principles of critical care nutrition as recommended by European and North American societal guidelines. Specific to these patients, is the need to promote strategies which help cluster care, reduce the frequency with which healthcare providers interact with patients, minimize contamination of additional equipment, and avoid transport out of the ICU. This may be

accomplished by simple measures such as utilizing continuous rather than intermittent or bolus infusion, calculating energy requirements by weight-based equations since indirect calorimetry may not be feasible, avoiding use of gastric residual volumes as an indicator of EN intolerance, and reducing the need for endoscopic or fluoroscopic techniques for feeding tube placement.

Like most ICU patients COVID-19 patients are expected to tolerate EN and benefit from the favorable physiologic response to bathing the intestinal mucosa with luminal nutrients. In contrast to other populations of critically ill patients, though, the threshold for switching to PN for the patient with COVID-19 disease may need to be lower. Use of PN in these patients, especially those with severe septic shock or when high pressure respiratory support is required (NIV, CPAP, or PEEP), may help minimize risk of ischemic bowel and reduce droplet aerosol transmission to healthcare providers by avoiding procedures involved in the initial placement and the nursing care required to maintain an enteral access device.

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Resources

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Enteral Nutrition Care Pathway for Critically-Ill Adult Patients

https://www.nutritioncare.org/Guidelines_and_Clinical_Resources/EN_Pathway/Enteral_Nutrition_Care_Pathway_for_Critically-Ill_Adult_Patients/

Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19) https://sccm.org/getattachment/Disaster/SSC-COVID19-Critical-Care-Guidelines.pdf?lang=en-US&_zs=7wPqi1&_zl=KKtc6

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