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Nutrition Therapy in Critically Ill Patients With Coronavirus Disease 2019

Robert Martindale, PhD, MD[1]; Jayshil J. Patel, MD[2]; Beth Taylor, DCN, RD-AP[3]; Yaseen M. Arabi, MD[4]; Malissa Warren, RD[5]; and Stephen A. McClave, MD[6]

Abstract

In the midst of a coronavirus disease 2019 (COVID-19) pandemic, a paucity of data precludes derivation of COVID-19–specific recommendations for nutrition therapy. Until more data are available, focus must be centered on principles of critical care nutrition modified for the constraints of this disease process, ie, COVID-19–relevant recommendations. Delivery of nutrition therapy must include strategies to reduce exposure and spread of disease by providing clustered care, adequate protection of healthcare providers, and preservation of personal protective equipment. Enteral nutrition (EN) should be initiated early after admission to the intensive care unit (ICU) using a standard isosmolar polymeric formula, starting at trophic doses and advancing as tolerated, while monitoring for gastrointestinal intolerance, hemodynamic instability, and metabolic derangements. Intragastric EN may be provided safely, even with use of prone-positioning and extracorporeal membrane oxygenation. Clinicians should have a lower threshold for switching to parenteral nutrition in cases of intolerance, high risk of aspiration, or escalating vasopressor support. Although data extrapolated from experience in acute respiratory distress syndrome warrants use of fiber additives and probiotic organisms, the lack of benefit precludes a recommendation for micronutrient supplementation. Practices that increase exposure or contamination of equipment, such as monitoring gastric residual volumes, indirect calorimetry to calculate requirements, endoscopy or fluoroscopy to achieve enteral access, or transport out of the ICU for additional imaging, should be avoided. At all times, strategies for nutrition therapy need to be assessed on a risk/benefit basis, paying attention to risk for both the patient and the healthcare provider. (*JPEN J Parenter Enteral Nutr.* 2020;44:1174–1184)

Keywords

ARDS; COVID-19; enteral nutrition; nutrition ECMO; nutrition support teams; parenteral nutrition; sepsis

Introduction

Over 2 million patients worldwide have been affected by coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Approximately 5% develop critical illness requiring an intensive care unit (ICU) admission. Unfortunately, no cure exists, and therapeutic interventions remain largely experimental; thus, supportive care remains the cornerstone for managing critically ill patients with COVID-19.

As with any other critically ill patient, managing nutrition is an integral component of good supportive care. Worldwide reports have revealed patterns that may be important to consider when planning nutrition support

From the [1]Department of SurgeryOregon Health and Science University, Portland, Oregon, USA; [2]Division of Pulmonary & Critical Care Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin, USA; [3]Barnes-Jewish Hospital, St Louis, Missouri, USA; [4]King Abdullah International Medical Research Center, King Saud Din Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia; [5]Department of Surgery, Oregon Health and Science University and Portland VA Health Care Center, Portland, Oregon, USA; and the [6]Division of Gastroenterology Hepatology and Nutrition, School of Medicine, University of Louisville, Louisville, Kentucky, USA.

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Corresponding Author:
Robert Martindale, PhD, MD, Professor of Surgery, Department of Surgery, Oregon Health and Science University, Portland, OR, USA.
Email: martindr@ohsu.edu

in critically ill patients with COVID-19. Clinical predictors of infection severity and mortality include advanced age, obesity, diabetes mellitus, and clinical evidence of systemic inflammation (eg, elevated C-reactive protein, ferritin, and interleukin-6 levels). Whereas most patients complain of fever, cough, and shortness of air, some COVID-19 patients present with gastrointestinal (GI) symptoms (diarrhea, nausea, vomiting, abdominal discomfort, and in some cases, bleeding) and evidence of acute kidney injury (AKI). These variables have implications for nutrition interventions: (1) older patients' risk for preexisting disease and sarcopenia, which increases their risk for preexisting malnutrition and increased risk of refeeding syndrome; (2) severe acute respiratory distress syndrome (ARDS) with refractory hypoxemia, which may require prone positioning and/or extracorporeal membrane oxygenation (ECMO); (3) circulatory failure and concomitant feeding, which may increase the risk of gut ischemia and feeding intolerance; (4) multiple organ failure (MOF) and the need for early enteral nutrition (EN) to attenuate or mitigate gut derived inflammation; and (5) cytokine release syndrome, which alters nutrient utilization (especially lipid).

These aforementioned factors may lead to prolonged illness, which often requires artificial nutrition therapy through the enteral and/or parenteral route. The nutrition management of the ICU patient with COVID-19 is, in principle, very similar to any other ICU patient admitted with pulmonary compromise. However, because of the limited evidence specifically regarding nutrition therapy in patients with COVID-19, the recommendations put forth in this document are based on indirect evidence from critically ill patients in general and those with sepsis and ARDS. Furthermore, the 2016 Society of Critical Care Medicine (SCCM)/American Society for Parenteral and Enteral Nutrition (ASPEN) Guideline for Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient is based on literature published up through December 2013; thus, updated modifications to this information are necessary for this report.[1,2] In this manuscript, we will address timing, route, and monitoring of nutrition therapy based on best available evidence but also provide guidance on management relevant to COVID-19 by taking into consideration key guiding principles related to this disease process.

Guiding Principles for COVID-19 Management

Nutrition therapy is an integral component of critical illness supportive care measures. Critical illness exists in phases and includes an early acute phase, the immediate postacute phase, and the recovery period. The acute phase is dominated by a hypercatabolic state in which amino acids are mobilized as substrate for acute-phase protein and immune-system products. Furthermore, the rapid breach in gut barrier function, the immune dysregulation, and the ensuing dysbiosis propagate and accentuate the inflammatory response.

Like all interventions related to the care of the patient with COVID-19, the delivery of nutrition therapy 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. Adherence to the Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO) 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 the virus
3. Preservation of use of PPE, which in many healthcare settings is becoming a depleted commodity, by limiting the number of staff providing direct patient care, decreasing the number of entries into the COVID-19 patient rooms, and optimizing other strategies to reduce consumption of these resources

Recommendation 1: Nutrition Assessment

Recommendation 1

We recommend all healthcare providers, including dietitians, nurses, and physicians, follow PPE standards set forth by the CDC and/or WHO and adhere to their institutional guidelines when conducting bedside nutrition assessments for all patients with confirmed or suspected COVID-19 disease. PPE includes protective eyewear, isolation gown, a face shield, and an N95 respirator (https://www.coronavirus.gov).

Rationale

Pragmatically, with limited PPE supply, many dietitians are not entering ICUs or the rooms of patients in isolation and are not performing a nutrition-focused physical examination but rather relying on other providers to collect physical examination data on the COVID-19 patients. Dietitians are using other means to collect assessment data, such as ICU remote-monitoring capabilities, calling the patient or family, and using telehealth visits involving various platforms (audio and visual). It is more important than ever that the dietitian document assessment findings, document where/how the information was received, and collaborate and coordinate with the medical teams to develop a safe and effective nutrition care plan.

Recommendation 2: Route and Timing of Initiation of Nutrition Therapy

Recommendation 2A

We recommend initiating early EN within 24–36 hours of ICU admission or within 12 hours of intubation and placement on mechanical ventilation.

Rationale

The timing of nutrition delivery should be of primary focus. In patients unable to maintain adequate volitional oral intake, early EN is recommended by both 2016 SCCM/ASPEN and 2019 European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines.[1-3] Meta-analyses of randomized controlled trials (RCTs) conducted between 1979 and 2015[4] show that provision of early EN to interventional patients improved mortality and reduced infections compared with controls, for whom such therapy was delayed or withheld.[1,2] Assuming patients were nutritionally replete prior to contracting COVID-19 and the acute phase of illness is limited, the major societal guidelines for initiating and maintaining ICU nutrition will suffice. Most patients with sepsis or circulatory shock have been shown to tolerate early EN at a trophic rate.[5] Unless vasopressor dose is escalating and/or enteral feeding intolerance ensues (eg, ileus, abdominal distention, vomiting), circulatory shock associated with SARS-CoV-2 should not be seen as a contraindication to trophic EN.[5]

Early EN may not be preferred in a subset of COVID-19 patients with GI symptoms.[6] Before the onset of respiratory symptoms, some COVID-19 patients first present with diarrhea, nausea, vomiting, abdominal discomfort, and in some cases, GI bleeding.[6] In a meta-analysis of 60 studies, including 4243 patients (although not all these patients were critically ill), the prevalence of anorexia was 26.8%, nausea/vomiting 10.2%, diarrhea 12.5%, abdominal pain/discomfort 9.2%, and "any" GI symptom 17.6%.[7] 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 of such patients (1 trial showing 53% testing positive by stool studies alone).[8] Further, GI involvement has been confirmed by the presence of an angiotensin converting enzyme 2 (ACE2) protein (a cell receptor for SARS-CoV-2) found in glandular cells on biopsy of esophageal, gastric, duodenal, and rectal mucosa.[8,9] These findings suggest a fecal-oral route of transmission in addition to the aerosolized droplet respiratory mode of transmission for the SARS- CoV-2 virus, and another possible route of entry into the host cells.[8,9] Patients with severe GI symptoms and/or enteral feeding intolerance should be considered for early parenteral nutrition (PN). The transition back to EN should be attempted when symptoms subside.

Recommendation 2B

We recommend starting early PN as soon as possible in patients for whom early gastric EN is contraindicated or not feasible and who are at high nutrition risk, are malnourished, or have an expected prolonged ICU stay.[1,2] Contraindications for EN may include patients with GI symptoms, shock requiring escalating vasopressor support, or use of noninvasive positive-pressure ventilation (NIPPV) such as bilevel or continuous positive airway pressure (CPAP). PN may be delayed in patients at low nutrition risk for 5–7 days, unless this level of risk changes.[2]

Rationale

NIPPV has been utilized for management of respiratory failure related to COVID-19, although there are controversies about its effectiveness in preventing the need for intubation. Practically, enterally feeding a patient on NIPPV may increase the risk for complications, such as aspiration due to the gastric insufflation[10] associated with this mode of ventilator support. In addition, placement of a feeding tube into a patient on NIPPV increases the risk for aerosolization and exposes healthcare personnel to virus transmission. Thus, instituting early PN in this population is advised, particularly when NIPPV is utilized without interruptions for oral intake, when there is increased concern for aspiration, and for those who are at high nutrition risk or malnourished. Continuous positive-pressure ventilation through helmet has been used extensively in Italy for COVID-19 patients, and nutrition may be provided more effectively and safely than with mask NIPPV, but data are needed. Nonocclusive bowel ischemia is rare with use of EN in shock, with observational and contemporary RCTs reporting an overall incidence of 0.3%.[4] However, in the unusual circumstance of COVID-19 disease for which concern for ischemic bowel may be greater and a prolonged ICU stay is expected, the threshold to initiate PN in lieu of EN should be lower. Early PN, as compared with no artificial nutrition therapy, has been shown to improve mortality in patients with preexisting malnutrition.[5] PN may subvert concerns for ischemic bowel and may reduce droplet aerosol transmission to healthcare providers by avoiding procedures involved in the initial placement and maintenance of an enteral access device.

Recommendation 3: Tube Placement and Method of Delivery for Early EN

Recommendation 3A

We recommend EN be infused into the stomach via a 10–12-French (F) orogastric (OG) or nasogastric (NG) feeding tube. If a larger-bore OG/NG tube was placed at time of intubation, it may be used for feeding.

Rationale

Infusion of formula into the stomach via an OG/NG tube requires minimal expertise and facilitates earlier initiation of feeding. If gastric feeding is unsuccessful because of enteral feeding intolerance, use of a prokinetic agent to enhance motility is recommended as the second step. These agents have been associated with QT prolongation, predisposing to cardiac arrhythmias, which should be monitored. Postpyloric EN delivery is recommended only after these strategies fail.[11] To minimize breach of airborne isolation and limiting exposure to healthcare providers, patients requiring a postpyloric feeding tube should undergo bedside placement with techniques that do not require use of endoscopy or fluoroscopic guidance. Placement strategies using real-time US Food and Drug Administration–approved electromagnetic or integrated imaging guidance may eliminate the need for placement confirmation by abdominal x-ray if this adheres to the institution's policy and procedures. Confirmatory abdominal x-rays should be clustered with chest x-rays as feasible. 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 and WHO guidelines regarding the use of N95 masks or a powered, air-purifying respirator. Postpyloric feeding tubes tend to be smaller caliber and therefore are more likely to become clogged with decreased flushing than a larger-bore NG/OG tube, which may occur with clustering of care and the goal to limit patient contact. In addition, use of EN in these high-risk patients often necessitates monitoring by more frequent abdominal exams, which may not be ideal given potential shortages of PPE. Lastly, postpyloric feeding tubes may take longer to place than gastric tubes, increasing the absolute exposure time of the healthcare practitioner.

Recommendation 3B

We recommend continuous rather than bolus EN in critically ill patients with COVID-19.

Rationale

The recommendation for continuous EN delivery 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, because 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, pumps should to be placed "outside" the room to minimize patient exposure and avoid contamination and particularly during shortages where pumps needs to be shared; this should also include the feeding pump and bag set if possible. As much extension tubing as needed may be utilized, as long as it allows for proper flow and is compatible with EN connectors and delivery system.

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

Recommendation 4A

We recommend initiating low-dose EN, defined as hypocaloric or trophic, and advancing slowly over the first week of critical illness to meet the energy goal of 15–20 kcal/kg actual body weight (ABW)/day (which should be 70%–80% of energy requirements) and protein goal of 1.2–2 g/kg ABW/day. This adjusts to 11–14 kcal/kg ABW/day in patients with body mass index (BMI) in the range of 30–50 and 22–25 kcal/kg ideal body weight/day in patients with BMI $>$ 50 and a protein goal of 2–2.5 g/kg ideal body weight. 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.

Rationale

Contemporary RCTs comparing low- (hypocaloric and trophic) with full-dose EN during the first week of critical illness have demonstrated no difference in clinical outcomes.[12-14] Although energy requirements can ideally be determined by indirect calorimetry, this technology would involve contamination of equipment and additional exposure to healthcare providers. Thus, we recommend utilizing weight-based equations instead of indirect calorimetry 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 energy and total energy needed.

Recommendation 4B

EN should be withheld in the patient with rising lactate levels and hemodynamic instability requiring escalating vasopressor support.

Rationale

Resuscitation of the critically ill patient takes priority. Introducing EN into a severely hypoperfused gut increases the risk for enteral feeding intolerance and nonocclusive bowel ischemia. 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 $\geq$65 mm Hg.[5,15]

Recommendation 4C

We recommend switching from EN to PN in patients with persistent or significant enteral feeding intolerance as manifested by unexplained abdominal pain, unremitting vomiting, unexplained diarrhea (eg, antibiotic-induced or clostridial colitis), abdominal distention, dilated loops of bowel with air/fluid levels, or pneumatosis intestinalis.[15,16]

Rationale

COVID-19 patients have been reported to have prolonged mechanical ventilation, lasting weeks. Insufficient nutrition therapy due to enteral feeding intolerance predisposes the patient to a greater energy deficit, negative nitrogen balance, and deterioration of nutrition status. Furthermore, enteral feeding intolerance may predispose bedside personnel to more frequent patient exposures, increasing the risk of virus transmission and PPE utilization. Early PN in this population may reduce energy deficits and provide amino acids to improve nitrogen balance. Recent pragmatic studies comparing early EN with PN in critically ill patients have shown no increased infectious risk with early PN and no difference in mortality, suggesting early PN is safe and feasible when early EN cannot or will not be provided. [17,18]

Recommendation 4D

We recommend obtaining a history and performing a bedside assessment, when possible, to identify preexisting malnutrition and risk factors for refeeding syndrome.

Rationale

We recognize some healthcare institutions have limited bedside patient access to avoid exposure to SARS-CoV-2. When bedside examination is restricted, obtaining history and performing a nutrition assessment can be conducted in conjunction with a non–nutrition expert under the principle of clustering care. Critically ill patients with COVID-19 tend to be older with multiple comorbidities. Such patients are often at risk of refeeding syndrome.[19,20] Thus, identifying preexisting malnutrition or other risk factors for refeeding syndrome in critically ill patients is vital. If risk for refeeding syndrome is present, we recommend starting at approximately 25% of energy requirements while advancing slowly to goal (70%–80% of requirements) over 4–7 days, in either EN- or PN-fed patients, combined with frequent monitoring of serum phosphate, magnesium, and potassium levels. The first 72 hours of feeding is the period of highest risk.

Recommendation 5: Formula Selection

Recommendation 5A

We recommend using a standard high-protein (≥20% protein) polymeric iso-osmotic enteral formula in the early acute phase of critical illness. As the patient's status improves and vasopressor requirements and GI dysfunction abate, addition of fiber should be considered. A fiber-containing formula or supplement provides non-nutrition benefits to the gut microbiota.

Rationale

In animal models and small human trials, fish oil–containing formulations have been shown to benefit immune modulation and clearance of viral infections. The end-products of fish-oil metabolism (resolvins and protectins, or specialized proresolving mediators) seem to be the active components.[21] A paucity of data from human trials prevents making a formal recommendation at this time. Although theoretical benefits are described for other types of formulas to modulate immune responses (arginine/fish-oil formulas) or to enhance tolerance (small-peptide/medium-chain triglyceride [MCT] formulas), failure to improve outcome in a similar population of patients in a medical ICU as well as added cost does not warrant a recommendation for their routine use in COVID-19 patients. Any supplemental nutritional modules such as protein packets, probiotics, or soluble fibers should be given once or, at most, twice per day in order to cluster care.

Recommendation 5B

We recommend limiting use of pure soy-based lipid emulsions if PN is required in the first week of ICU stay during the acute inflammatory phase of COVID-19.[3] This can be accomplished by withholding soy-based lipid or using alternative mixed lipid emulsions.

Rationale

Mixed intravenous lipid emulsions are now available in the United States and include a variety of alternative, less inflammatory oils such as olive oil, MCTs, and fish oil.[22]

Recommendation 5C

We recommend monitoring serum triglycerides in patients receiving propofol and/or intravenous lipid emulsions early in their course, taking into consideration and context that elevated serum triglyceride levels may be due to secondary hemophagolymphocytic histiocytosis (HLH), which is a hyperinflammatory response secondary to cytokine storm that occurs in a subset of COVID-19 patients.[23]

Rationale

There have been numerous anecdotal reports from several centers from around the world that COVID-19 patients who receive propofol or pure soy-based lipid rapidly develop severe hypertriglyceridemia. Elevated serum triglyceride in patients receiving propofol may, in fact, be due to secondary HLH, which occurs in a subset of COVID-19. Serum triglyceride is a component of criteria for identifying secondary HLH, and it is vital to distinguish secondary HLH from propofol-related hypertriglyceridemia. The pathogenesis for elevated serum triglyceride in secondary HLH is unclear.

Recommendation 6: Monitoring Nutrition Tolerance

Recommendation 6A

We recommend not checking gastric residual volumes (GRVs) in patients receiving EN.

Rationale

Enteral feeding intolerance is common during the early and late acute phases of critical illness. Early experience with critically ill COVID-19 patients suggests that GI symptoms (which might manifest as enteral feeding intolerance) are associated with greater severity of illness. 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.[24] Furthermore, per the guiding principles in caring for the critically ill patient with COVID-19 disease, this recommendation is relevant to decrease the risk of COVID-19 transmission to the healthcare provider.

Recommendation 6B

We recommend patients be monitored by daily physical examination and confirmation of passage of stool and gas and that these observations should be "clustered" with other provider activities to minimize healthcare team virus exposure. As with any ICU patient, the percent of energy and protein delivered should be recorded for both EN and PN.

Rationale

Enteral feeding intolerance is common during the acute phase of critical illness. Abrupt worsening of clinical status has been observed in COVID-19 patients, hallmarked by heightened inflammation, worsening oxygen requirements, and MOF. These conditions increase the risk for enteral feeding intolerance. Thus, where available, bedside assessment through physical examination remains imperative to guide further delivery of EN or the need for transitioning to PN.

Recommendation 7: Nutrition for the Patient Undergoing Prone Positioning

Recommendation 7

We recommend delivering early EN into the stomach and elevating the head of bed 10–25° in critically ill COVID-19 patients undergoing prone positioning.

Rationale

COVID-19 may lead to 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 ARDS with refractory hypoxemia.[25,26] Several retrospective and small prospective trials have shown EN during prone positioning is not associated with increased risk of GI or pulmonary complications.[27-30]

Many patients tolerate EN delivered into the stomach while in the prone position, but on occasion, postpyloric placement of the feeding tube may be indicated. However, placement of postpyloric tubes increases exposure to SARS-CoV-2, and thus their use should be evaluated on a case-by-case basis in COVID-19 patients. When EN is introduced during prone positioning, elevating the head of the bed (reverse Trendelenburg) 10–25° may decrease the risk of aspiration, facial edema, and intra-abdominal hypertension.[23,31]

Recommendation 8: Nutrition Therapy During ECMO

Recommendation 8

We recommend early initiation of EN at trophic doses, with slow advancement over the first week of critical illness in COVID-19 patients undergoing ECMO.

Rationale

ECMO is a supportive care strategy to oxygenate and ventilate patients with severe ARDS with refractory hypoxemia and/or hypercapnia.[32] No data are available for nutrition support during ECMO specifically in COVID-19 disease. One of the major barriers to EN during ECMO is the perception that ECMO patients are at increased 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.[33] Other observational data show safety and tolerability of gastric EN delivery during ECMO.[34] 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 ECMO, Ohbe found early EN, compared with delayed EN, was associated with a reduction in 28-day mortality, with no cases of bowel ischemia reported.[35] Park et al noted similar experience, finding that increased EN energy and protein delivery were associated with a decreased 90-day mortality.[36]

Recommendation 9: Patients Requiring Continuous Renal Replacement Therapy

Recommendation 9A

We recommend providing protein at a dose of 2–2.5 g/kg ABW/day (or 2.5 g/kg ideal body weight/day in those patients with BMI $\geq$ 30) in critically ill patients with AKI undergoing renal replacement therapy (RRT).[1,37]

Rationale

Critically ill patients with AKI undergoing RRT lose up to 10 g of amino acids per day in the dialysate. Observational data have demonstrated that up to 2.5 g/kg/d is well tolerated and is associated with a positive nitrogen balance.[1,37]

Recommendation 9B

We recommend monitoring and repletion of micronutrients in critically ill patients undergoing RRT as recommended in the 2016 ASPEN/SCCM and 2018 ESPEN guidelines.[1-3]

Rationale

Micronutrients in the critically ill with severe AKI has been recently evaluated by Ostermann et al. They reported plasma levels below the reference range for zinc, iron, selenium, vitamin D3, vitamin C, and several amino acids in patients undergoing continuous RRT. They concluded micronutrient levels were low in patients with AKI regardless of the RRT modality.[38]

Potential Nutrition Interventions Based on Theory, Extrapolations, and Anecdotes in COVID-19 Patients

Disclaimer

Supplementation with several specific vitamins, minerals, probiotics, and pharmaconutrients have been proposed in several ICU populations over the past 40 years, with some studies demonstrating benefit. As we navigate untested therapeutic strategies in the COVID-19 population, we acknowledge no COVID-19–specific data for their use are available. Providing false hope with untested or unstudied nutrition agents will only be a detriment to our patients and their families. We acknowledge any intervention (not just nutrition ones) for our patients cannot be driven by fear and misinformation, which often supersedes the scientific evidence. Thus, the information for the following nutrition interventions are, at best, hypothesis-generating in the COVID-19 population.

Probiotics

Coronavirus, along with several other viruses, can cause upper respiratory infections (URIs) in humans.[39] These include viruses such as respiratory syncytial virus, adenovirus, human coronavirus, and human parainfluenza virus. These viruses are responsible for up to 30% of URIs in adults globally. The use of probiotics for URIs (not specifically COVID-19) has shown benefit in patients with viral URIs. In 12 studies comparing placebo vs probiotics, the probiotic-supplemented groups showed fewer URIs and were noted to be better than placebo in reducing the mean duration of URI symptoms.[40]

Vitamins

No consistency is noted in supplementation of the B vitamins in viral illnesses or ICU care. The literature is so widely variable that at this point, no recommendation is made other than that supported by the societal guidelines.

Vitamin D has been shown to be beneficial in some animal viral infection models as well as some human studies. Several articles widely speculating on the effects of vitamin D on either prevention or treatment of COVID-19 are being published as we navigate this new pandemic.[41] Caution must be exercised before wide acceptance of unsubstantiated or unstudied recommendation are made in patients with COVID-19 infections. Two recent ICU trials evaluated vitamin D supplementation in patients admitted to the ICU with documented deficiency of vitamin D. Both well-done studies showed no benefit of diets supplemented with vitamin D.[42,43] Vitamin A has been studied in an animal model (chickens) given a diet low in vitamin A. The deficient animals did show an increased susceptibility to coronavirus. This was not COVID-19. No human trials have been done.[44] Like vitamin A, vitamin E has been shown to benefit viral infections in animal studies (murine and bovine), but no data are available in human ICU trials. Vitamin C has also been studied in chickens, and it was reported that the animals showed increased resistance to coronavirus.[45] A meta-analysis published in 2019 reported inadequate supportive data to make a specific recommendation for supplemental vitamin C in ICU patients. In a more recent large human RCT in septic patients with ARDS, vitamin C was given over a 96-hour infusion at a relatively high dose.

When compared with placebo, the supplemental vitamin C reported no benefit.[46]

Trace Minerals

The trace minerals selenium and zinc have received a lot of attention in viral infections. Selenium has been shown in vitro and in some animal studies to alter viral replication and reduce the viral-induced oxidative stress. Selenium has well-described benefits as a cofactor for several antioxidant enzymes such as superoxide dismutase, thioredoxin reductase, and glutathione peroxidase. The data are inconsistent across these studies regarding dosing, timing of delivery, and documentation of any preexisting deficiency state.[47] No recommendation can be made other than the standard ICU recommendations found in the societal guidelines.[1,3]

Zinc is important in the development and function of the immune system, both innate and humoral. It has also been reported that zinc is required for the antioxidant complex metallothionein production in response to lung stretch. This has led to the suggestion by some to be protective in mechanical ventilation.[48] In vitro experiments have shown that zinc impairs viral replication and has beneficial effects on RNA viruses like coronavirus. Zinc supplementation in children documented to be deficient has been shown to decrease mortality, although data are inconsistent.[49,50] No consistent data show zinc supplementation in intensive care patients to be of benefit.[51] As with selenium, the dosing, timing, and target population of those patients most likely to benefit from zinc supplementation are yet unknown. As a result, no recommendations for supplemental zinc, above the levels recommended for any ICU patient, can be supported until more data are available.

Lessons Learned From the Field

Anecdotal real-time lessons learned from the field are coming to light rapidly. Although not necessarily evidence-based, these observations may be helpful to frontline clinicians in addressing barriers imposed by the current pandemic and important implications to consider.

Assessment and Monitoring the COVID-19 Patient

In efforts to preserve PPE and reduce exposure, many nutrition professionals are finding ways to evaluate their patients away from the bedside, including chart review and caregiver interviews. Bedside nurses provide invaluable information regarding GI function and physical assessment. However, some nursing staff and providers, especially those coming from a variety of (non-ICU) work areas, may not place as high a level of importance on documentation or face time constraints resulting in inconsistent documentation of EN, PN, and oral intake, as well as urine, stool, and drain outputs. Nutrition providers must be diligent in their communication with bedside staff and providers on the importance of these parameters and how best to obtain the information. Coordinating phone calls with providers or less ill patients may be beneficial. Fortunately, CMS has lifted many restrictions and expanded coverage for telehealth visits (virtual and telephone), including using various platforms such as FaceTime, Blue Jeans, Zoom, Skype, and Google Duo (audio and visual). This applies to all providers (physicians, NPs, PAs, and dietitians). Clinicians should check with their facility for specific support and application of state licensure rules.

Frequent reassessment of the patient's metabolic status and employed medical interventions is necessary to determine if an alteration in the nutrition prescription is required. COVID-19 patients receiving large doses of propofol may require a decrease in energy to avoid overfeeding and an order for triglyceride monitoring. Patients with AKI may or may not be able to start dialysis in a timely fashion, as some institutions are reporting a lack of machines. In these patients, EN/PN regimens should become fluid- and electrolyte-restricted, with the potential for short-term underfeeding or reduced protein until dialysis treatment can be initiated. Patients receiving noninvasive ventilation may require scheduled oral supplements and fortifying snacks that can be readily available at bedside to optimize energy and protein intake while off treatment, especially in those who no longer have an enteral access device. Close monitoring of oral intake is necessary, as patients recovering from COVID-19 disease are typically deconditioned and weak and often unable to meet nutrition needs with oral intake alone. If supplemental EN is needed during noninvasive ventilation, smaller-bore nasoenteric feeding tubes (<12F) may improve mask seal.

Dietitians should remain engaged in COVID-19 ICU rounds via distancing (fewer team members during rounds, wearing appropriate PPE, separated by 6 feet) and/or virtual communication. It is imperative to be "present" (in person or virtually) when the plan and goals for the day are discussed. Throughout the day, scheduling calls with bedside caregivers when they are out of the patient room can be challenging.

Shortages

Feeding pumps, EN feeding bags, and tubes may be in short supply during a surge of admitted COVID-19 patients. Priority in the distribution of EN pumps should be given to patients with mild symptoms of GI intolerance at admission or those with a small-bowel feeding tube in place. Continuous gravity feeding should be attempted if pumps and/or pump feeding sets are not available. In general, there are 20 drops per milliliter of formula. However, actual "drop rates" can be difficult to set "by hand" by the bedside nurse.

Some latitude should be accepted for the time required to deliver the daily goal volume; for example, if the patient tolerates 600 mL (trophic feeding goal) delivered over 15 hours as opposed to 24 hours, this should be considered a success. Some formulas are too viscous to flow freely via gravity drip (generally concentrated or fiber containing); this should be verified based on the manufacturer recommendations. For these formulas or when shortages of gravity bags exist, bolus feeding via the syringe method may be attempted. Administering formula in amounts equivalent to 1 unit (can, carton, or pouch) will decrease formula waste.

PN provided in multichamber bags may become necessary if institution shortages of individual components exist or there is a need to decrease pharmacist compounding time. If feasible, extension tubing should be used to locate the PN pump outside the room to decrease practitioner viral exposure and allow for easy access.

Conclusion

The delivery of nutrition therapy to the patient with COVID-19 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 that 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 instead of indirect calorimetry, avoiding use of GRV as an indicator of EN intolerance, and reducing the need for endoscopic or fluoroscopic techniques for feeding tube placement.

Like most ICU patients, those with COVID-19 are expected to tolerate EN and benefit from the favorable physiologic response to bathing the intestinal mucosa with luminal nutrients. Intragastric delivery of a standard polymeric formula should be initiated at trophic doses and advanced as tolerated to protein and energy goals over the first week. Once-daily supplementation with fiber additive and probiotic organisms is warranted, but lack of benefit precludes a recommendation for routine infusion of micronutrient vitamins or trace elements. In contrast to other populations of critically ill patients, the threshold for switching to PN for the patient with COVID-19 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 (noninvasive ventilation (NIV), CPAP, or positive end-expiratory pressure), 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.

Disclaimer

These recommendations do not constitute medical or other professional advice and should not be taken as such. To the extent that the information published herein may be used to assist in the care of patients, this is the result of the sole professional judgment of the attending healthcare professional, whose judgment is the primary component of quality medical care. The information presented is not a substitute for the exercise of such judgment by the healthcare professional. Circumstances in clinical settings and patient indications may require actions different from those recommended in this document, and in those cases, the judgment of the treating professional should prevail.

Statement of Authorship

R. Martindale and J. J. Patel equally contributed to the conception and design of the research; B. Taylor and S. A. McClave equally contributed to the design of the research; all authors contributed to the acquisition, analysis, and interpretation of the data; and R. Martindale, B. Taylor, and S. A. McClave drafted the manuscript. R. Martindale, B. Taylor, M. Warren, J. J. Patel, S. A. McClave, and Y. M. Arabi clinically revised the manuscript. All authors agree to the fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript

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