Relevant Nutrition Therapy in COVID-19 and the Constraints on Its Delivery by a Unique Disease Process

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Abstract

Worldwide, as of July 2020, >13.2 million people have been infected by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. The spectrum of coronavirus disease 2019 (COVID-19) ranges from mild illness to critical illness in 5% of cases. The population infected with SARS-CoV-2 requiring an intensive care unit admission often requires nutrition therapy as part of supportive care. Although the various societal guidelines for critical care nutrition meet most needs for the patient with COVID-19, numerous factors, which impact the application of those guideline recommendations, need to be considered. Since the SARS-CoV-2 virus is highly contagious, several key principles should be considered when caring for all patients with COVID-19 to ensure the safety of all healthcare personnel involved. Management strategies should cluster care, making all attempts to bundle patient care to limit exposure. Healthcare providers should be protected, and the spread of SARS-CoV-2 should be limited by minimizing procedures and other interventions that lead to aerosolization, avoiding droplet exposure through hand hygiene and use of personal protective equipment (PPE). PPE should be preserved by decreasing the number of individuals providing direct patient care and by limiting the number of patient interactions. Enteral nutrition (EN) is tolerated by the majority of patients with COVID-19, but a relatively low threshold for conversion to parenteral nutrition should be maintained if increased exposure to the virus is required to continue EN. This article offers relevant and practical recommendations on how to optimize nutrition therapy in critically ill patients with COVID-19. (*Nutr Clin Pract.* 2020;35:792–799)

Keywords

COVID-19; enteral nutrition; nutrition support; nutrition therapy; pandemic; parenteral nutrition; SARS-CoV-2

Introduction

Great difficulties are incurred by the clinicians charged with managing the patient with coronavirus disease 2019 (COVID-19), as the result of several factors. First, the range of presentation spans an entire spectrum, from asymptomatic individuals who are not even aware that they have contracted the disease to the most critically ill patient treated in the setting of an intensive care unit (ICU).[1] Second, participation in the care of these patients impacts not only the professional life but also the personal life of those clinicians to an extent that none have ever experienced. And third, a plethora of new information regarding disease management is made available to these healthcare providers at an incredibly rapid rate and in a wide variety of formats, such as social media, news outlets, professional colleagues, personal experience, and international observational studies, but rarely in the form of trusted, peer-reviewed randomized controlled trials (RCTs).

This report will discuss the scope of the COVID-19 pandemic and delineate which principles of critical care nutrition apply to this disease process. Recommendations for the patient with COVID-19 are surprisingly routine, similar to the nutrition therapy that would be provided to any critically ill patient. But more importantly, this article will delineate the constraints of this disease, which impact the choices clinicians are forced to make and limit clinicians' ability to deliver that nutrition regimen.

Scope of Disease

Regarding proper terminology, the disease is called COVID-19. The virus itself is the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).[1] The virus is in the family

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of coronavirus but appears to be unique to other members of that family seen previously. Predictive models estimate that ultimately 50%–60% of the world's population will be infected, with some questioning whether that number could approach 80%.[2] Similar pandemics have occurred around the globe in recent past. The SARS pandemic in 2002 had a mortality rate of 11%, whereas the Middle Eastern respiratory syndrome in 2012 had a mortality rate of 35%–50%.[3] In contrast, the mortality rate for COVID-19 worldwide is estimated at around 4%, being slightly lower in the US at 2.3%.[1,3]

Never has the role of public health officials been more appreciated than what has been demonstrated in this pandemic, as these experts in communicable disease strive to protect the populace. Most impressive has been their directives on social distancing, which has been clearly shown to reduce exposure, slow the onslaught of new cases, and control the demands on our healthcare system. A key problem is the fact that there are asymptomatic carriers and a disease process with a long incubation time of 12–14 days and symptoms not becoming evident for 3–5 days postexposure.[1,3] Adequate testing is critical. It is important to know who has had the disease, who has not had it, and whether a person who has had the disease is now subsequently protected. It is still very early in this process, and time is needed to develop RCTs for therapy to know whether a vaccine will ever be developed against this organism and to understand the significance of antibody levels postinfection. Questions regarding whether antibodies in the convalescent serum of survivors afford protection in the future, whether that benefit falls off or erodes with time, and whether that effect can be used as therapy to treat others with more severe disease all need to be answered.

The wide range of susceptibility is a problem in itself.[1,4] At one end of this spectrum are young people who are much more likely to be asymptomatic from the infection, who seem to be (with few exceptions) protected from mortality, and who are less motivated to conform to the need for social isolation. At the other end of the spectrum is the elderly nursing home population, who appear most vulnerable, who experience a devastating effect from this disease process, and whose mortality rate exceeds 80%–85%.[5] The mortality rate does not go up appreciably until the fourth or fifth decade, continuing to climb with increasing age such that by the eighth decade, survival drops to <10%–15%.[5] Overall, 80% of those infected will present as mild cases, with 50% of the total being completely asymptomatic. Approximately 20% have symptoms severe enough to require hospitalization, with 5% being critically ill and needing placement in the ICU, the majority of which (75%) will require mechanical ventilation.[1,4]

Age is the most important risk factor for contracting COVID-19, but diabetes mellitus, hypertension, and obesity are also key factors in susceptibility.[1] The link between this respiratory disease and obesity may relate to the fact that the angiotensin-converting enzyme 2 protein receptor site to which the SARS-CoV-2 binds is present on both the type 2 pneumocyte in the lungs and the adipocyte in adipose tissue. Other risk factors include multiple comorbidities and ethnicity, as shown by greater disease severity and higher mortality in African American and Hispanic populations. Early data also suggest that lower socioeconomic class increases risk, presumably because of reduced access to good medical care, poor dietary habits, and lower education with poorer understanding of the social distancing and interpersonal restrictions required to limit spread of the disease.[1]

Another aspect of this pandemic is the surge effect, the position of a community or healthcare institution on the curve of new cases and disease-related deaths, and the steepness of that curve. With a steeper curve, a greater impact occurs regarding hospital bed capacity, options for treatment, available equipment, a sufficient number of healthcare providers, and the ability to deliver nutrition therapy.

There are many aspects of the patient with COVID-19 that are different from the typical critically ill patient in an ICU with acute respiratory distress syndrome (ARDS). An overwhelming high infectivity exists for this disease. Humans are naïve and have never been exposed to this virus, and thus we are exquisitely sensitive. The major mode of transmission is aerosolized droplets, which means that coughing or sneezing can expel viral-laden secretions for ≥4–5 feet (hence the 6-foot rule for social distancing).[6] Up to 30% of infected patients will shed the SARS-CoV-2 virus in their feces, which adds the component of a fecal-oral route of transmission for this disease.[7,8]

A good understanding of this unique pandemic is critical, as consideration for potential strategies of nutrition therapy must take into account recommendations from the Center for Disease Control and the World Health Organization for the management of every patient with this disease process. Those recommendations emphasize the need to provide clustered care, minimize exposure, and preserve use of personal protective equipment (PPE).[3] These concepts have tremendous implications for the nutrition support clinician. Hospital or ICU rooms dedicated to patients with COVID-19 are sealed, and registered dietitians may be restricted from even entering the unit (in addition to physical and occupational therapists, pharmacists, etc). The frequency of interactions between the healthcare provider and the patient, meaning the number of times that provider enters the room, has to be minimized. Clustering of care means that the nurse batches together as many aspects of care as possible, enters the room once to deliver those therapies, and then exits until a subsequent time when another group of treatments is needed. For the non-ICU patient in the ward, the nurse may enter only at the beginning, middle, and end of a long 8–12 hour shift.

The total number of healthcare providers that enter the sealed room of the patient with COVID-19 needs to be limited as well. An effort is made to restrict all members of the primary team from entering the room, allowing instead for just a single representative, along with the nurse and only essential ancillary personnel. Every time the healthcare provider enters and exits the room, a new set of PPE (gown, gloves, eye ware, protective face shield, and N95 respirator) is used, with only a portion of that able to be reused for subsequent visits. In many units, the head of the bed is positioned closer to the door, which allows for the intravenous fluid pumps and computer for the electronic medical record to be placed in the hallway outside the patient's room. If pumps are left in the room, their alarms may not be heard through the closed sealed door, necessitating the use of baby monitors.

No aspect of nutrition therapy should increase exposure for the healthcare provider beyond that which is absolutely necessary. If supplements are ordered for protein, soluble fiber, or probiotics, they may need to be given together only once, or at most twice, per day. The practice of gastric residual volumes as a monitor for enteral nutrition (EN) should be eliminated. Ordering bolus feeding to be infused every 2 hours is not reasonable but instead should be given as "incidental syringe feeding" of a variable volume of formula every time the nurse enters the room to deliver clustered care. Energy requirements should be calculated by simple weight-based equations, as use of indirect calorimetry would involve entry of more healthcare providers into the room and added equipment that has to be decontaminated. Similarly, techniques for achieving enteral access should avoid endoscopy or transport out of the ICU to a radiology suite for tube placement under fluoroscopic guidance. Placement of any feeding tube should be recognized as an "aerosol-generating procedure," and if not performed by the most experienced intensivist trained with rapid intubation and use of PPE, switching earlier to parenteral nutrition (PN) should be considered.[6] Nutrition support clinicians should perform face-to-face assessment, not by entering the sealed room but by peering through the glass door or window to communicate with nursing service and visually confirm, as much as possible, the daily deferred physical exam performed originally by the primary team. Each hospital must make site-specific changes to overcome the obstacles created by the constraints of this disease process.

Shortages have tremendous influence on what nutrition therapy is ultimately delivered. The sheer number of intravenous fluid pumps required to infuse antibiotics, vasopressor agents, sedatives, and other medications in a surge situation may result in an insufficient number of pumps to provide these therapeutic agents. These are the same pumps needed to infuse PN. Shortages may extend to involve the separate pumps required to deliver continuous infusion of enteral formula. Nutrition support clinicians instead have to improvise by switching to gravity drain or bolus infusion. With a shortage of mechanical ventilators, intensivists have had to resort to "co-venting," in which 1 machine is used to simultaneously ventilate 2 separate patients. Although the Society of Critical Care Medicine (SCCM) does not recommend this strategy, the organization acknowledges that its use may be necessary in extreme surge situations.

The clinical consequences of COVID-19 affect delivery of the prescribed nutrition regimen and impact the patient's ability to assimilate infused exogenous nutrients.[1] The most common unifying clinical presentation is a rapid, persistent refractory hypoxemic respiratory failure. The most critically ill patients with this disease process have an incredible hyperinflammatory response described as the cytokine storm syndrome. Laboratory tests confirm not only diffuse systemic inflammation, as suggested by high levels of C-reactive protein and erythrocyte sedimentation rate, but also severe inflammation throughout multiple organ systems, as evidenced by elevated myoglobin (skeletal muscle), troponins (heart), aspartate aminotransferase/alanine aminotransferase (liver), and blood urea nitrogen/creatinine (kidney). With this cytokine storm comes a number of metabolic derangements that reflect futile substrate cycling, intolerance, and errors in fuel use. There is a severe insulin resistance due to not only predisposing diabetes mellitus and obesity but also the severe inflammatory process and cytokine storm. Patients with COVID-19 are very sensitive to volume overload, so conservative fluid volume resuscitation is required. Patients tend to be hypernatremic because of insensible fluid loss from fever and inflammation, development of acute kidney injury (AKI), and an osmotic diuresis from glucosuria. A pseudohyponatremia effect from elevated glucose levels means that sodium levels may be even higher than what appears in the laboratory values. Hyperphosphatemia occurs because of muscle breakdown, mitochondrial failure, and progression to AKI. Hypocalcemia is common, as the high phosphate levels chelate available calcium. Hyperkalemia results from the catabolic response unless AKI develops with a renal tubular pathology, resulting in loss of potassium in the urine and a refractory hypokalemia. The severe insulin resistance leads to ketonemia and hypertriglyceridemia, made worse with infusion of soy-based intravenous lipid emulsion (ILE) for PN or propofol for sedation. Over 85% of ICU patients with COVID-19 are hypercoagulable, which accounts in large part for the ventilation/perfusion mismatch in the lungs leading to hypoxemia, the presentation of some patients with stroke and myocardial infarction, and the need for anticoagulation with heparin.[9] ICU patients with COVID-19 tend to show severe deconditioning and immobilization, which lead to an accelerated proteolysis just short of rhabdomyolysis. It is anticipated that a postviral syndrome

When initiating EN:

- Start EN early within 24¬36 hours ICU admission, or within 12 hours of intubation and placement on mechanical ventilation.
- Infuse EN into the stomach via a 10¬12 Fr tube. A large-bore orogastric or nasogastric tube placed at time of intubation is appropriate to use if that is the only enteral access device available.
- If EN delivery is limited due to intolerance, add a prokinetic agent before attempting post-pyloric tube placement into the small bowel.
- Use of a feeding tube placed by bedside electromagnetic guidance or integrated imaging is recommended over one placed by endoscopic or fluoroscopic guidance (which often requires transport out of the ICU).
- Any abdominal films required to confirm tube placement should be clustered with attainment of chest x-rays requested by the primary team.
- Use of continuous EN infusion is recommended over bolus infusion to decrease exposure to the healthcare provider. In case of pump shortages, infusion by gravity drain is preferred over bolus infusion.
- Initiate trophic low-dose EN and advance slowly over 1 week to:
  - Energy goal of 70¬80% of caloric requirements (15¬20 kcal/kg ABW/day)
  - Protein goal of 1.2¬2.0 g/kg ABW/day
- In obesity, calculate goals by:
  - Energy at 11¬14 kcal/kg ABW per day for BMI 30¬50, 22¬25 kcal/kg IBW/day for BMI >50
  - Protein at 2.0 (Class I, II) or 2.5 (Class III) g/kg IBW/day
- Use a standard isosmotic polymeric formula.
- Consider supplementation with soluble prebiotic fiber and probiotics and switching to a mixed fiber formula once tolerance of the EN regimen is established.
- Withhold EN if there is a rising lactate level, or hemodynamic instability with the need for escalating vasopressor support.
- Switch from EN to PN if there is significant EN intolerance, as evidenced by unexplained abdominal pain, vomiting, diarrhea, abdominal distention, pneumatosis intestinalis, or dilated loops of bowel with air/fluid levels.

Figure 1. Nutrition recommendations for early EN in patients with COVID-19.[10] ABW, actual body weight; BMI, body mass index; EN, enteral nutrition; IBW, ideal body weight; ICU, intensive care unit; PN, parenteral nutrition.

with debilitation will become apparent in those severely ill patients who manage to survive COVID-19.

Overall Recommendations for Nutrition Therapy

In mid-March 2020, as the pandemic was just beginning to expand in this country, the SCCM released its Surviving Sepsis Campaign guidelines for the management of the patient with COVID-19. When it was noted that no recommendations for nutrition therapy were included in these guidelines, a group of nutrition experts were recruited from SCCM and the American Society for Parenteral and Enteral Nutrition (ASPEN) to develop COVID-19–specific recommendations for such support. Immediately evident was a paucity of data in the literature to make any recommendations specific to COVID-19. So, instead, the group of experts compiled recommendations based on principles of critical care nutrition, modified by the constraints of this disease process, resulting in other words with COVID-19–relevant recommendations for nutrition therapy.[10]

The basis for these recommendations was centered on the presumption that the most important aspect of nutrition therapy for severely ill patients with COVID-19 was to bathe the intestinal mucosa with luminal nutrients, to maintain gut barrier defenses, to attenuate the systemic inflammatory response syndrome, and to support the microbiome.[11,12] Because the gastrointestinal tract is the largest immune organ in the body with the greatest microbial burden, the gut can act as an accelerator to the hyperinflammatory response seen in this disease process. On the flip side of this precept is an opportunity to use the gut through early EN to modulate immune responses, oppose dysbiosis, and promote an anti-inflammatory pattern of recovery.[10]

Regarding actual recommendations for nutrition therapy in the patient with COVID-19, the principles follow, in cookbook fashion, those for critical care nutrition in general for any ICU patient (see Figures 1–3).[13-15] EN is preferred over PN. Intragastric EN should be initiated early after admission to the ICU, especially if the patient requires intubation and placement on mechanical ventilation. In most cases with acute deterioration of clinical status,

When initiating PN:

- Initiation of PN should be considered as soon as possible in the following patients for whom gastric feeding is contraindicated or not feasible:
  - High nutrition risk
  - Malnourished, poor nutrition status
  - Expected prolonged intensive care unit length of stay
  - Gastrointestinal involvement of COVID-19 with significant intolerance
- Delay initiation of PN in the low-risk patient for 5¬7 days.
  - Limit use of ω-6 soy-based ILE for the first week, either by restricting use of an ILE altogether or switching to a mixture of lipids such as SMOF
- Monitor serum triglyceride levels closely if propofol or soy-based ILEs are used.

Figure 2. Nutrition recommendations for parenteral nutrition (PN) in patients with COVID-19.[10] COVID-19, coronavirus disease 2019; ILE, intravenous lipid emulsion; SMOF, soy, medium-chain triglycerides, olive oil, and fish oil.

Additional guidance for nutrition therapy:

- Do not use gastric residual volumes as a monitor for delivery of EN.
- Obtain patient history, perform face-to-face assessment without entering sealed patient room, identify pre-existing malnutrition, and identify risk for refeeding syndrome.
- Monitor by daily deferred physical examination (done originally by primary team), confirm passage of stool and gas, record % goal energy/protein delivered.
- With prone-positioning, deliver intragastric EN starting at trophic doses, advancing as tolerated over the first week. Elevate head of bed 10¬25 degrees to reduce risk of aspiration, facial edema, and intra-abdominal hypertension.
- With use of extracorporeal membrane oxygenation, initiate intragastric EN at trophic doses, advancing slowly over the first week to goal.
- With AKI requiring CRRT, dose protein at 2.0¬2.5 g/kg/day. Monitor and replete micronutrients in AKI on CRRT (especially zinc, iron, selenium, vitamin D, and vitamin C).

Figure 3. Additional recommendations to guide nutrition therapy for patients with COVID-19.[10] AKI, acute kidney injury; COVID-19, coronavirus disease 2019; CRRT, continuous renal replacement therapy; EN, enteral nutrition.

the most experienced intensivist will expediently perform intubation, establish a central line, and often place a large bore orogastric or nasogastric tube at 1 setting. Patients should then be monitored for tolerance, as EN started at trophic doses is advanced slowly over the first week to goal for energy and protein provision. The biggest difference for the patient with COVID-19 is that clinicians should lower their threshold for switching from EN to PN. Evidence of intolerance may harbor a greater danger of complications, such as ischemic bowel and the need for postpyloric tube placement, and would necessitate an additional aerosol-generating procedure, and the need for noninvasive positive pressure ventilation might preclude use of a feeding tube altogether (because of difficulty establishing a seal or tight mask fit with a feeding tube in place). Once the decision is made, the actual delivery of PN for the patient with COVID-19, again, is routine, following usual principles for critical care nutrition. The only exception would be the need to use strategies that avoid infusion of proinflammatory, pure soy-based ILE for the first week after admission to the ICU, either by restricting use of ILE altogether or by switching to

a less inflammatory mixture of lipids, such as SMOF (soy, medium-chain triglycerides, olive oil, and fish oil) or olive oil–based ILE.[13]

Nutrition Therapy During Prone Positioning

COVID-19 leads to severe ARDS in a relatively small number of those infected, estimated at 12% requiring mechanical ventilation (14% require ICU admission, of which 75% end up on mechanical ventilation [or 12% of the total COVID-19 patient population]).[1] In the patients who develop refractory hypoxemia, prone positioning is an inexpensive technique to improve oxygenation and increase bronchial secretion clearance. Although some controversy still exists regarding the use of EN while patients are in the prone position, most literature now supports the concept that EN during prone positioning is safe and effective.[16,17] Voluntary prone positioning can be used when the patient is awake, can breathe spontaneously, and can self-assist with the prone positioning. When the patient is heavily sedated or paralyzed and ventilated, a number of healthcare

providers may be required to turn the patient into the prone position. Several retrospective and small prospective trials have shown that EN during prone positioning is not associated with increased risk of gastrointestinal or pulmonary complications.[17-19] Most patients in the prone position tolerate EN delivered into the stomach, but on occasion, postpyloric placement of the feeding tube may be indicated. Placement of postpyloric tubes increases exposure to SARS-CoV-2, and thus their use should be considered only on a case-by-case basis in patients with COVID-19. 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.[20]

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.[21] No COVID-19–specific data are currently available regarding delivery of nutrition therapy for the ECMO patient. One of the major obstacles to early EN for patients requiring ECMO is the perception that ECMO patients are at significant risk of delayed gastric emptying and bowel ischemia. Data from several observational trials and a review article support the safety and tolerability of EN delivery during ECMO.[22] Large database studies on prospectively collected data of several thousand patients report that early EN resulted in decreased mortality, with no significant increase in episodes of ischemic bowel.[23,24] Thus, early EN may be initiated during use of ECMO, starting at trophic doses, with slow advancement over the first week of critical illness in patients with COVID-19.

Additional Nutrition Therapies

As COVID-19 has spread across the globe, numerous untested nutrition strategies have been proposed and widely circulated on the internet and social media for the patient suffering from infection by the SARS-CoV-2 virus. Many of these nutrition strategies are not based on sound scientific principles. Caution and transparency must be used when providing suggestions from untested or unstudied nutrition agents to avoid being a detriment to patients and their families. In a fast-moving pandemic, no therapeutic intervention for these patients should be driven by fear and misinformation, which often supersede the scientific evidence. The following nutrition interventions may be considered but are thought to be hypothesis-generating, at best, for the COVID-19 population.

Coronavirus, along with several other viruses, cause ≥30% of upper respiratory infections (URIs) in humans.[25]

Although not specifically evaluated in COVID-19, the use of probiotics for URIs has shown benefit. In a meta-analysis of 12 studies comparing placebo vs probiotics, the probiotic-supplemented groups showed fewer URIs and a decrease in the mean duration of URI symptoms when compared with the placebo groups.[26]

Inconsistency in the nutrition literature regarding supplementation of any of the B vitamins or vitamin E in viral illnesses in ICU care precludes any specific recommendations for their use in COVID-19. Several protocols for the use of vitamin D in COVID-19 have circulated on social media. Vitamin D has been shown to be beneficial in viral infection in certain animal models, as well as some very limited human studies.[27] Caution must be exercised, however, as 2 recent large ICU trials evaluating vitamin D supplementation in patients admitted to the ICU with documented deficiency of vitamin D reported no benefit.[28,29] Using an animal model (chickens), 1 study showed that a vitamin A–deficient diet led to increased susceptibility to coronavirus (not SARS-CoV-2),[30] whereas a second trial showed that supplementation with vitamin C increased resistance to coronavirus.[31] Both a meta-analysis published in 2019 and a large prospective trial in septic ICU patients with ARDS reported no benefit from vitamin A supplementation in ICU patients.[32]

In the nutrition management of patients with COVID-19, the trace minerals selenium and zinc have received the most attention. 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. Again, as the overall data are inconsistent, consequently, no recommendation can be made for additional selenium other than the standard ICU recommendations found in the societal guidelines.[13,15] Adequate zinc is essential for the development and function of both the innate and humoral immune response. 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 from the measles virus, although data are inconsistent.[33,34] As with selenium, no recommendations for supplemental zinc, above the levels recommended for any ICU patient, can be supported until more data are available.

Conclusion

Management of the patient with COVID-19 must respect the need to cluster care, reduce the frequency of patient interactions, limit contamination of additional equipment, and avoid transport out of the ICU. Nutrition therapy follows the basic principles of critical care nutrition. Although

most patients with COVID-19 will tolerate intragastric EN, clinicians should maintain a lower threshold for switching from EN to PN, as the perception of gastrointestinal feeding intolerance may lead to increased exposure or the need for nonessential aerosol-generating procedures. Provision of prebiotic fiber, probiotics, or added doses of protein is encouraged but should be given, if possible, by once-daily supplementation. A paucity of data preclude making a firm recommendation for micronutrient supplementation at this time. All strategies involved in the nutrition therapy of the patient with COVID-19 should be evaluated on the basis of the risk-to-benefit ratio, assessing risk both to the patient and to the healthcare provider.

Statement of Authorship

References

1. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with covid-19 in the New York city area. *JAMA*. 2020;323(20):2052-2059.
2. WebMD. How scientists predict how many people will get COVID-19. Medscape medical news. Accessed May 5, 2020. https://www.webmd.com/lung/news/20200401/how-scientists-predict-how-many-people-will-get-covid-19#1
3. Dost B, Koksal E, Terzi O, et al. Attitudes of anesthesiology specialists and residents toward patients infected with the novel Coronavirus (COVID-19): a national survey study. *Surg Infect*. 2020;21(4):1-7.
4. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72,314 cases from the chinese center for disease control and prevention. *JAMA*. 2020;323(13):1239-1242.
5. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med*. 2020;46(5):846-848.
6. Chen C, Zhao B. Some questions on dispersion of human exhaled droplets in ventilation room: answers from numerical investigation. *Indoor Air*. 2010;20(2):95-111. PMID: 20002792.
7. Pan L, Mu M, Yang P, et al. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study. *Am J Gastroenterol*. 2020;115(5):766-773.
8. Gu J, Han B, Wang J. COVID-19: Gastrointestinal manifestations and potential fecal-oral transmission. *Gastroenterology*. 2020;158(6):1518-1519.
9. Marik PE; EVMS Medical Group. EVMS critical care COVID-19 management protocol 04-06-2020. evms.edu/covidcare. April 6, 2020
10. Martindale RG, Patel JJ, Taylor B, Arabi YM, Warren M, McClave SA. Nutrition therapy in critically ill patients with coronavirus disease (COVID-19). *JPEN J Parenter Enteral Nutr*. (Submitted).
11. McClave SA, Lowen CC, Martindale RG. The 2016 ESPEN Arvid Wretlind lecture: the gut in stress. *Clin Nutr*. 2018;37(1):19-36.
12. McClave SA, Martindale RG. Why do current strategies for optimal nutritional therapy neglect the microbiome? *Nutrition*. 2019;60:100-105.
13. McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JPEN J Parenter Enteral Nutr*. 2016;40(2):159-211.
14. Barazzoni R, Bischoff SC, Krznaric Z, Pirlich M, Singer P. ESPEN expert statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection. *Clin Nutrit*. 2020;39(6):1631-1638.
15. Singer P, Blaser AR, Berger MM, et al. ESPEN guideline on clinical nutrition in the intensive care unit. *Clinical Nutrition*. 2019;38(1):48-79.
16. Reignier J, Dimet J, Martin-Lefevre L, et al. Before-after study of a standardized ICU protocol for early enteral feeding in patients turned in the prone position. *Clin Nutr*. 2010;29(2):210-216.
17. Saez de la Fuente I, Saez de la Fuente J, Quintana Estelles MD, et al. Enteral nutrition in patients receiving mechanical ventilation in a prone position. *JPEN J Parenter Enteral Nutr*. 2016;40(2):250-255.
18. van der Voort PH, Zandstra DF. Enteral feeding in the critically ill: comparison between the supine and prone positions: a prospective crossover study in mechanically ventilated patients. *Crit Care*. 2001;5(4):216-220. PMID:11511335
19. Sams VG, Lawson CM, Humphrey CL, et al. Effect of rotational therapy on aspiration risk of enteral feeds. *Nutr Clin Pract*. 2012;27(6):808-811. PMID:2308726
20. Kallet RH. The vexing problem of ventilator-associated pneumonia: observations on pathophysiology, public policy, and clinical science. *Respiratory Care*. 2015;60(10):1495-1508.
21. Hardin CC, Hibbert K. ECMO for severe acute respiratory distress syndrome. *N Engl J Med*. 2018;379(11):1092-1093.
22. Bear DE, Smith E, Barrett NA. Nutrition support in adult patients receiving extracorporeal membrane oxygenation. *Nutr Clin Pract*. 2018;33(6):738-746.
23. Ohbe H, Jo T, Yamana H, Matsui H, Fushimi K, Yasunaga H. Early enteral nutrition for cardiogenic or obstructive shock requiring venoarterial extracorporeal membrane oxygenation: a nationwide inpatient database study. *Intensive Care Med*. 2018;44(8):1258-1265.
24. Park J, Heo E, Song IA, et al. Nutritional support and clinical outcomes in critically ill patients supported with veno-arterial extracorporeal membrane oxygenation. *Clin Nutr*. Published online November 30, 2019. https://doi.org/10.1016/j.clnu.2019.11.036.
25. Arabi YM, Fowler R, Hayden FG. critical care management of adults with community-acquired severe respiratory viral infection. *Intensive Care Med*. 2020;46(2):315-328.
26. Hao Q, Dong BR, Wu T. Probiotics for preventing acute upper respiratory tract infections. *Cochrane Database Syst Rev*. 2015;(2): CD006895.
27. Grant WB, Lahore H, McDonnell SL, et al. Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. *Nutrients*. 2020;12(4):988.
28. National Heart, Lung, and Blood Institute PETAL Clinical Trials Network, Moss M, Huang DT, et al. Early neuromuscular blockade in the acute respiratory distress syndrome. *N Engl J Med*. 2019;380(21):1997-2008.
29. Amrein K, Schnedl C, Holl A, et al. Effect of high-dose vitamin D3 on hospital length of stay in critically ill patients with vitamin D deficiency: the VITdAL-ICU randomized clinical trial. *JAMA*. 2014;312(15):1520-1530.
30. Zhang L, Liu Y. Potential interventions for novel coronavirus in China: a systematic review. *J Med Virol*. 2020;92(5):479-490.

31. Hemila H, Chalker E. Vitamin C incritically ill patients may reduce the duration of mechanical ventilation: a meta-regression analysis. *J Intens Care*. Published online February 7, 2020. https://doi.org/10.1186/s40560-020-0432-y.

32. Fowler AA 3rd, Truwit JD, Hite RD, et al. Effect of vitamin C infusion on organ failure and biomarkers of inflammation and vascular injury in patients with sepsis and severe acute respiratory failure: the CITRIS-ALI randomized clinical trial. *JAMA*. 2019;322(13):1261-1270.

33. Fani M, Khodadad N, Ebrahimi S, et al. Zinc Sulfate in Narrow Range as an In Vitro Anti-HSV-1 Assay. *Biol Trace Elem Res*. 2020;193(2):410-413.

34. Awotiwon AA, Oduwole O, Sinha A, Okwundu CI. Zinc supplementation for the treatment of measles in children. *Cochrane Database Syst Rev*. 2017;6:CD011177.