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Gastrointestinal Manifestations of COVID-19: Impact on Nutrition Practices

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Abstract

Although Coronavirus disease 2019 (COVID-19) is primarily a respiratory disease, growing evidence shows that it can affect the digestive system and present with gastrointestinal (GI) symptoms. Various nutrition societies have recently published their guidelines in context of the pandemic, and several points emphasize the impact of these GI manifestations on nutrition therapy. In patients with COVID-19, the normal intestinal mucosa can be disrupted by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, and this could result in GI symptoms and a compromise in nutrient absorption. Optimization of oral diet is still recommended. However, given the GI effects of COVID-19, a fraction of infected patients have poor appetite and would not be able to meet their nutrition goals with oral diet alone. For this at-risk group, which includes those who are critically ill, enteral nutrition is the preferred route to promote gut integrity and immune function. In carrying this out, nutrition support practices have been revised in such ways to mitigate viral transmission and adapt to the pandemic. All measures in the GI and nutrition care of patients are clustered to limit exposure of healthcare workers. Among patients admitted to intensive care units, a significant barrier is GI intolerance, and it appears to be exacerbated by significant GI involvement specific to the SARS-CoV-2 infection. Nevertheless, several countermeasures can be used to ease side effects. At the end of the spectrum in which intolerance persists, the threshold for switching to parenteral nutrition may need to be lowered. (*Nutr Clin Pract.* 2020;35:800–805)

Keywords

COVID-19; digestive system; enteral nutrition; gastrointestinal symptoms; gastrointestinal tract; nutrition support; parenteral nutrition; SARS-CoV-2

Introduction

Coronavirus disease 2019 (COVID-19) is a respiratory illness caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It has become a public health emergency, classified as a pandemic by the World Health Organization in March 2020. Although primarily a respiratory disease, growing evidence shows that it affects the digestive system and presents with various symptoms, such as anorexia, diarrhea, nausea, and vomiting.[1] Nutrition societies have recently published their guidelines in the context of this pandemic, and several points emphasize the role of gastroenterology in nutrition therapy. Given the interrelatedness of gastroenterology and nutrition, this article aims to review relevant data of the 2 fields in relation to COVID-19. Specifically, the implications for the approach in the management of preexisting gastrointestinal (GI) diseases, as well as GI intolerance and challenges to nutrition therapy related to COVID-19, will be discussed. By doing so, this review could aid in the development of policies and recommendations to guide nutritionists, gastroenterologists, and other healthcare professionals in their clinical practice.

Methods

This review is based on case reports, retrospective clinical studies, review articles, and society recommendations relating to nutrition and the digestive system from articles published in PubMed, EMBASE, and different international nutrition and gastroenterology society websites. Relevant literatures were reviewed from the websites of the American

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Society for Parenteral and Enteral Nutrition (ASPEN), European Society for Clinical Nutrition and Metabolism (ESPEN), Philippine Society of Parenteral and Enteral Nutrition (PHILSPEN), American Gastroenterological Association, American College of Gastroenterology, Asian Pacific Association of Gastroenterology (APAGE), and the Society of Critical Care Medicine. An extensive hand searching of references, papers, reports, and articles with cross-referencing were done. The search terms used include "2019-nCoV," "SARS-CoV-2," or "COVID-19," combined with "nutrition," "gastrointestinal," and "digestive system."

Results

Understanding the GI Tract, COVID-19, and Related Nutrition Issues

SARS-CoV-2 is the pathogen responsible for COVID-19. It is a novel, enveloped RNA betacoronavirus that attaches to the angiotensin-converting enzyme 2 (ACE2) receptor to allow its entry into the target cell and facilitate replication. Although the ACE2 receptors are primarily seen in the respiratory lining, these receptors are also abundantly expressed in the digestive system, specifically the enterocytes in the lining of the ileum and colon.[2,3] The attachment of the SARS-CoV-2 virus on the ACE2 receptors of the digestive system is believed to disrupt the normal intestinal flora, leading to different GI symptoms-especially diarrhea.[4] Evidence has also shown the presence of SARS-CoV-2 RNA in feces, supporting its pathologic mechanism in the gut.[5]

Several studies have shown varied GI symptoms as part of the manifestations of the COVID-19 infection.[4,6] Fever, cough, and fatigue remain to be the most common symptoms, but data have shown that GI symptoms (such as anorexia, nausea, vomiting, diarrhea, and abdominal pain) can also occur, although to a lesser extent than respiratory symptoms. A meta-analysis comprised of 60 studies with 4243 patients showed a pooled prevalence of GI symptoms at 17.6% (95% CI, 12.3-24.5).[7] In this study, anorexia was the most commonly reported symptom (26.8%, [95% CI, 16.2-40.8]), followed by diarrhea (12.5%, [95% CI, 9.6-16.0]), nausea and vomiting (10.2%, [95% CI, 6.6-15.3]), and abdominal discomfort (9.2%, [95% CI, 5.7-14.5]). These GI manifestations of COVID-19 pose huge challenges in feeding the patients to achieve their nutrition targets. Patients who are fed orally are expected to be mostly affected, given their poor appetite.

Despite the viral effects of SARS-CoV-2 in the digestive system, enteral nutrition (EN) is still the preferred method of nutrition therapy if oral intake fails, as it stimulates the gut. It has been established that the lack of nutrient contact with intestinal mucosa could lead to atrophy of lymphoid tissue and functional decline of the immune system, as well as intensification in bacterial translocation.[8] Studies in the pre–COVID-19 era have also shown that EN decreases length of hospital stay, costs, mortality rate, and septic complications compared with parenteral nutrition (PN).[9] Given these multiple benefits of gut nutrition, EN should be preferred in patients with COVID-19 who require nutrition support.

There are very few studies relating to the effects of SARS-CoV-2 infection on preexisting GI disorders and the role of nutrition therapy. The APAGE stated that exclusive EN is a safe and effective option to induce remission in Crohn's disease without risking the development of or worsening COVID-19, but comanagement with a dietitian is advised.[10] An article by the Chinese Society of Inflammatory Bowel Disease states that active-stage inflammatory bowel disease (IBD) with malnutrition is a potential risk factor for SARS-CoV-2 infection, and if biologics are not available, EN may serve a therapeutic role in addition to medications given for IBD.[11] No study has discussed COVID-19 and its effects on patients with other preexisting GI disorders, such as pancreatitis, short-bowel syndrome, celiac disease, or irritable bowel syndrome. Given that GI manifestations, specifically diarrhea, can occur in patients with COVID-19, studies in these population groups are recommended, as the coronavirus infection may complicate these preexisting conditions, resulting in potential malabsorption of nutrients and severe malnutrition.

With the growing field of the gut microbiome and the use of probiotics in different disease states, probiotics have been proposed for patients with COVID-19, most especially for patients presenting with diarrhea. It is important to emphasize that different medications used for COVID-19, such as antibiotics and antivirals, could lead to alteration of the gut microbiota, and this opens a new therapeutic target in which probiotics could play a role.[12] China's National Health Commission has advocated the use of probiotics for the treatment of patients with severe COVID-19 to mitigate intestinal dysbiosis and possibly reduce bacterial translocation and secondary infection.[13] However, this practice is based on indirect evidence, and further understanding of the pathogenesis of the SARS-COV-2 infection and its effect on gut microbiota is recommended.[14]

Innovating Nutrition Practices in the COVID-19 Pandemic

Basic nutrition principles still apply in the COVID-19 pandemic, but some key GI and nutrition practices are altered to observe safety of the healthcare workers and patients. Most of these measures are apparently due to the implications of the viral effects to the digestive system. The protocols for nutrition delivery, as well as access and timing of feeding, are innovated in such a way that care is clustered and structured to limit the exposure of healthcare workers. Most of the practices discussed in this paper are based on

the recommendations of the ASPEN, the ESPEN, and the PHILSPEN.[15-17]

Nutrition Delivery and Access

According to the existing nutrition guidelines for COVID-19, EN is advised to maintain gut barrier and immune function. However, oral diet is preferred for patients who are able to eat.[18] Specifically, the optimization of oral diets and addition of oral nutrition supplements (ONSs) are recommended to be part of the armamentarium to meet the patient's nutrition targets.[16] Patients are advised to ingest a high-calorie and high-protein diet to maintain metabolic functions, muscle mass, and body weight. The caloric intake should be ≥1500–2000 calories, with protein of 75–100 g/d.[19] If a patient has a poor appetite, and nutrition counseling is not sufficient for the patient to reach nutrition goals, ONSs should be given within 24 to 48 hours of hospitalization to help meet nutrition needs. Supplements should be given for ≥1 month and provide ≥400 kcal/d and ≥30 g/d of protein.[16]

EN via nasogastric tube (NGT) route is recommended if the patient's nutrition requirements cannot be met orally, especially in the polymorbid medical inpatients and in older persons with a reasonable prognosis.[16] In these cases, the use of EN may be superior to PN because of the lower risk of infectious complications and earlier gut function. In addition, PN has been postulated to induce deleterious changes in physiology.[9] Nevertheless, complications can also arise in patients in whom EN is initiated. These GI complications can be present with diarrhea, nausea, or vomiting; mechanical issues, which include aspiration and tube-related complications; and metabolic complications, which include electrolyte imbalance and hyperglycemia.[20] Close monitoring should be given to patients fed enterally to safeguard against these complications and side effects.

PN should be considered if targets can't be reached with EN and if all strategies to maximize EN intolerance have been attempted. PN includes nourishment by central and peripheral veins.[9] It can be administered as full PN when EN is not safe or tolerated or as supplemental PN when it is used as additional nutrition support. Onset of PN-related complications, such as PN-associated liver disease and catheter-related blood stream infections, should be monitored. In the context of the pandemic, there is no evidence regarding increased risk of these complications. However, these should be considered for patients who require PN for an extended duration.[21]

Aside from PN, nasointestinal feeding is also an option when gastric feeding is not tolerated. ESPEN has actually recommended the nasointestinal route in cases with large gastric residual volume (GRV) > 500 mL.[16] However, it has been more practical to feed parenterally instead because of the risk of exposure to healthcare workers in the placement of the postpyloric feeding tube either in bedside or in the endoscopic unit. Moreover, the tube can be easily dislodged from its position, especially when putting the patient into prone position. Studies have also shown that postpyloric feeding tubes do not significantly decrease the risk of aspiration.[22] Table 1 shows the different routes of nutrition and their indications.

For the safety of the healthcare workers, it is important to note that the placement of enteral access, such as an NGT, is an aerosol-generating procedure, as it may provoke coughing.[15] It is recommended that proper personal protective equipment (PPE) be used, based on the Centers for Disease Control and Prevention guidelines, which includes an N95 or higher-level respirator, eye protection or face shield, gloves, and a gown. During the placement of these tubes, it is recommended to limit the number of people and equipment in the room. Confirmatory abdominal x-ray should be clustered with chest x-ray timing. A large-bore NGT may be used, as it has reduced risk of tube occlusion during feeding and would not require frequent change of NGT.[15]

Timing of Nutrition Delivery

For the critically ill patient, early EN is advised to start at trophic rates (10–20 mL/hr), with a goal to reach at least 15–20 kcal/kg actual body weight (ABW) per day.[15] The early acute phase of critical illness is usually represented as the period of greatest risk of EN intolerance, in which vomiting, ileus, and mesenteric ischemia can occur. A meta-analysis has shown that low-dose EN is favored over the full dose in the first week of critical illness.[23] During critical illness, the protein goal is set at 1.2–2.0 g/kg ABW/d, as this target has been shown to improve survival of frail patients.[15,16] Continuous feeding is recommended over bolus feeding to reduce the incidence of diarrhea. It also optimizes blood glucose control and entails less healthcare worker interaction, thereby limiting exposure.[18]

Nutrition in the Prone Position

COVID-19 patients may develop acute respiratory distress syndrome and refractory hypoxemia despite mechanical ventilation. Prone positioning has been shown to be beneficial in the oxygenation of these patients.[24,25] There is apprehension to feed patients in prone position in view of the relatively flat body position, increase in abdominal pressure, and the use of sedative and paralytic agents in high doses on critically ill patients.[24] These factors have led to variable reports of GI intolerance.[25]

It remains largely unknown whether the prone position affects gastric emptying, but studies have shown that there is no increased risk of GI or pulmonary complications in prone patients fed enterally.[26] Hence, both ASPEN and ESPEN have recommended early EN in COVID-19 patients in prone position.[15,16] It is recommended to keep the head

Table 1. Indication and Routes of Nutrition Support.

Route	Indication	Remarks
Oral diet and oral nutrition supplements (ONSs)	If able to tolerate oral diet, take high-calorie and high-protein diet	High-calorie and high-protein diet should be advised to maintain metabolic functions and body weight[19]
	If nutrition targets are not met by oral diet, ONSs can be added	ONSs should be given within 24 to 48 hours of hospitalization with the ONSs providing ≥400 kcal/d and ≥30 g/d protein[16]
Enteral nutrition via nasogastric or nasointestinal route	If nutrition targets cannot be met orally alone (eg, polymorbid medical inpatients, older persons)	Insertion of tubes should be done with proper personal protective equipment (PPE)[15]
Parenteral nutrition	If nutrition targets cannot be met by enteral nutrition or with gastrointestinal intolerance despite different measures to address intolerance	Can be given as supplement or as parenteral nutrition[17]

Table 2. Recommendations to Address Gastrointestinal (GI) Intolerance.

GI Manifestation	Recommendation	Rationale
Nausea, vomiting, or ileus	Add prokinetics (IV erythromycin, IV metoclopramide or combination)	To enhance motility
Delayed gastric emptying	Do not concentrate enteral formula	To avoid delayed gastric emptying
	Consider postpyloric feeding	To bypass the stomach and administer feed to the small intestine because of delayed gastric emptying
Abdominal distension	Reduce feeding rate or volume	To alleviate abdominal distension and give longer time for better absorption
	Shift to energy-dense formula	To provide high-calorie feeding but with less volume for better absorption and to alleviate abdominal distension
Diarrhea	Shift to semi-elemental or predigested formula	To reduce diarrhea and for better absorption

of the bed elevated or in a reverse Trendelenburg position to ≥10–25 degrees to decrease risk of aspiration.[15] To reduce the risk of aspiration, it is recommended to hold feeding temporarily for 1 hour when shifting positions.[17] Feeding is also started at a hypocaloric prescription (10–20 mL/hr), which can be slowly progressed if with no signs of GI intolerance to reduce the risk of aspiration while optimizing adequate provision of nutrition.

The Challenge of GI Intolerance

GI intolerance is common during the early and late acute phases of critical illness, particularly for COVID-19 patients who are intubated, deeply sedated, or are in prone positions.[15] In a study by Kaafarani et al, half of the 141 COVID-19 patients admitted to the intensive care unit (ICU) developed hypomotility-related complications showing clinical or radiographic evidence of ileus.[27] GI intolerance can manifest as unexplained abdominal pain, nausea, vomiting, diarrhea, or significant abdominal distention. Dilated bowel loops with air and fluid levels and pneumatosis intestinalis may be observed on serial abdominal exams. In patients with GI intolerance, the measurement of GRV is not advised by ASPEN, as it is considered to be unreliable for detection of delayed gastric emptying, and checking the GRV will significantly increase risk of virus exposure and transmission.[15] ESPEN has recommended a cutoff > 500 mL, and PHILSPEN recommends its use only with signs of GI intolerance.[16,17]

There is a gamut of countermeasures that could be implemented if there are signs of GI intolerance. The use of prokinetics is primarily advised first to enhance motility. Intravenous erythromycin or metoclopramide, or a combination of these 2 prokinetics, can be given.[18] Enteral formula should not be concentrated if there is delayed gastric emptying. Feeding volume or rate can be reduced and an energy-dense formula or a semi-elemental feeding formula can also be considered if there is abdominal distension or diarrhea. If GI intolerance persists despite various measures, postpyloric feeding can be considered.[16]

Table 2 summarizes recommendations to address GI intolerance.

For patients with COVID-19, the threshold for switching to full or supplemental PN may need to be lower than the standard pre–COVID era guidelines, especially when EN is not safe or not tolerated.[15] Patients with COVID-19 who are intubated in the ICU usually have prolonged ICU stays and inadequate feeding, resulting in increased caloric and protein deficits. Furthermore, the lower threshold is also to minimize risk of ischemic bowel and reduce viral exposure of healthcare professionals.

Discussion and Summary

The emerging literature on patients with COVID-19 shows that the effects of COVID-19 infection on the digestive system can have significant impacts on the nutrition therapy of these patients. This opens the opportunities for different interventions and nutrition modalities to address the GI side effects of the disease. Oral diet or EN are still the preferred routes because of the multiple benefits of gut nutrition. The role of EN has also been recognized in COVID-19 patients with preexisting GI disorders, such as IBD, and its practice is strongly supported by IBD societies. However, studies of its role in other preexisting GI disorders are yet to be elucidated. The role of probiotics has yet to be established.

The different GI manifestations and treatment scenarios of patients with COVID-19 have posed challenges in terms of nutrition care. The GI symptoms and signs of GI intolerance can significantly restrict achievement of nutrition goals. Alternate ways to increase dietary intake, such as the addition of energy-dense ONSs, are recommended. One practice to consider is hypocaloric nutrition during the acute phase of critical illness in the ICU. However, patients with COVID-19 usually present with decreased oral intake even before hospitalization, and the longer they are fed suboptimally may result in larger caloric and protein deficits in the long run. In addition, such patients may be at increased risk of refeeding syndrome.

As for patients with GI intolerance to EN, the threshold to switch to PN has been lowered, although there are several evidence-based measures that could be done in stepwise fashion prior to resorting to the parenteral route. One of the plausible indications of the shift to the parenteral route is when the patient presents with persistent signs of GI intolerance despite multimodal regimens to promote intestinal motility. Prone positioning, despite having proven to be feasible and safe for EN, has also proven to be challenging. In general, both GI intolerance and the frequent need for proning could increase the risk for aspiration. This could potentially be more problematic for this population group if the GI complications and nutrition care are not carefully addressed.

Finally, it is important to emphasize that all these measures of nutrition care in the context of COVID-19 should be observed with the safety of the healthcare workers and patients in mind. Nutrition access procedures, such as NGT insertion, should be done with proper PPE, and nutrition delivery via continuous route is advised to limit the exposure of healthcare workers.

In conclusion, the effects of COVID-19 infection on the digestive system could significantly impact the nutrition therapy of these patients. Nutrition support practices should be adjusted to mitigate viral transmission and adapt to the pandemic. GI intolerance can occur but can be addressed adequately. Although EN is preferred in critically ill patients, the threshold for full or supplemental PN nutrition may need to be lowered, especially when EN is neither safe nor tolerated.

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Statement of Authorship

E. J. T. Aguila contributed to the conception and design of the research. E. J. T. Aguila, V. L. M. Yabut, M. F. P. Causing, I. H. Y. Cua, and J. A. C. Fontanilla contributed to the acquisition, analysis, and interpretation of the data; and E. J. T. Aguila, V. L. M. Yabut, M. F. P. Causing, I. H. Y. Cua, and J. A. C. Fontanilla drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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