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CASE STUDY

Challenges to Provision of Adequate Medical Nutrition Therapy in a Critically Ill COVID-19 Patient Fed in the Prone Position

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Adults with acute respiratory distress syndrome (ARDS) may experience enteral nutrition (EN) intolerance. They often require mechanical ventilation and other specialized management including prone positioning. There is a controversy as to whether patients fed in prone position experience more EN intolerance than when they are in supine position. This narrative review synthesizes the literature published between 2001 and 2021 in adults with ARDS who are fed EN while in the prone position to determine safety and tolerance. A case of an adult patient with Down syndrome who developed ARDS due to COVID-19 and required EN while in prone position is presented. **Key words:** *ARDS*, *COVID-19*, *critical care*, *Down syndrome*, *enteral nutrition*, *feeding intolerance*, *mechanical ventilation*, *prone position*, *respiratory failure*, *tube feeding*

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ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) is a serious inflammatory lung condition defined by pulmonary edema, which results in severe hypoxia

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and ultimately respiratory failure.[1,2] Acute respiratory distress syndrome impacts approximately 10.4% of patients admitted to the intensive care unit (ICU) and can be caused by various conditions including sepsis, pneumonia, aspiration, severe trauma, and coronavirus disease 2019 (COVID-19).[3] The Berlin criteria can be used to classify ARDS severity into 3 major categories: mild (200 mm Hg $<$ Pa_{O_2}/F_{IO_2} $\leq$ 300 mm Hg), moderate (100 mmHg $<$ Pa_{O_2}/F_{IO_2} $\leq$ 200 mm Hg), or severe (Pa_{O_2}/F_{IO_2} $\leq$ 100 mm Hg).[2] The estimated mortality rate for ARDS increases in a stepwise fashion and ranges from 27% to 45% depending upon disease severity.[2] Individuals who develop ARDS require mechanical ventilation and, under certain circumstances, may also require prone positioning to optimize oxygenation and potentially decrease the risk of mortality.[4] The estimated prevalence of prone positioning in patients with ARDS is 16.3%.[3] Prone positioning occurs when a patient is rotated from his or her back (supine position [SP]) to lying face down on his or her abdomen for more than 12 hours.[5] This maneuver can lead to increased abdominal pressure.[6] In addition, Bordejé and colleagues[6] postulated that patients with ARDS who require mechanical ventilation and enteral nutrition (EN) may experience feeding intolerance due to this increased intra-abdominal pressure. This may contribute to difficulty feeding these individuals who will likely require alternate nutrition support in the form of EN.

Enteral nutrition may be beneficial in modulating the immune response, maintaining gut integrity, and reducing disease severity.[7] The 2016 Society of Critical Care Medicine (SCCM) and the American Society for Parenteral and Enteral Nutrition (ASPEN) nutrition support recommendations for the critically ill advise the use of early EN within the first 1 to 2 days of ICU admission with a standard polymeric formula; however, this can be challenging to accomplish due to actual or perceived gastrointestinal intolerance of EN.[7] Enteral nutrition intolerance can be defined as high gastric residual volume (GRV), diarrhea, emesis, aspiration, and abdominal pain or distention.[7] It is a common occurrence that can impact about 50% of patients who are critically ill and can contribute to inadequate nutrition support due to frequent EN interruptions.[7] This is a major problem as these patients are already hypermetabolic and often catabolic, which can cause cumulative calorie deficit, depletion of lean mass, and malnutrition.[7]

Because of the potential risk for EN intolerance as a consequence of prone positioning and critical illness, it is important to determine the appropriateness of EN for use in this patient population. The primary objective of this narrative review and case report is to synthesize the literature on enteral feeding of patients who are mechanically ventilated and fed in the prone position (PP) to determine whether it is safe and well tolerated. Since 2001, 4 prospective, observational studies have investigated the use of EN in patients who are mechanically ventilated because of respiratory failure and requiring prone positioning to improve oxygenation.[8-11] This narrative review and case report investigate clinical outcomes, such as EN intolerance (ie, high GRV, emesis, regurgitation, and diarrhea) and nutritional adequacy to determine whether EN is well tolerated.

LITERATURE SEARCH

The CINAHL, MEDLINE, and PubMed databases were explored to answer the following population, intervention, control, and outcome (PICO) question: Among adult patients receiving mechanical ventilation **(P),** what is the impact of receiving EN in the PP **(I)** compared with the SP **(C)** on clinical outcomes **(O)?** The search terms included key terms and medical subject headings of mechanical ventilation or mechanically ventilated or artificial ventilation AND enteral feeding or tube feeding or enteral nutrition or gastric feeding tube AND prone position or prone positioning or prone AND supine position or supine positioning or supine. The

search strategy was completed on September 22, 2021. Articles were restricted to primary research articles published in the English language, included adults older than 18 years, and published between 2001 and 2021. References were searched for additional studies that met the criteria for inclusion. The exclusion criteria consisted of non-English language, publications before 2000, patients who were 18 years of age or younger, no supine control group, review articles, and nonhuman studies. Although 31 records were found during the database search, following title and abstract screening only 10 remained and were evaluated for eligibility. Four original research studies met the criteria for further review and analysis as shown in the Figure.[12] The studies received a quality rating based on the Academy of Nutrition and Dietetics Evidence Analysis Library (EAL) Quality Criteria Checklist: Human Subjects.[13]

Data collection

Study type and design, number of patients, EN regimen, and clinical outcomes were extracted and recorded for each study.[8-11] A summary of the 4 studies that explored the safety and efficacy of EN in mechanically ventilated patients who were being fed in PP can be found in Supplemental Digital Content Table 1, available at: http://links.lww.com/TIN/A34.

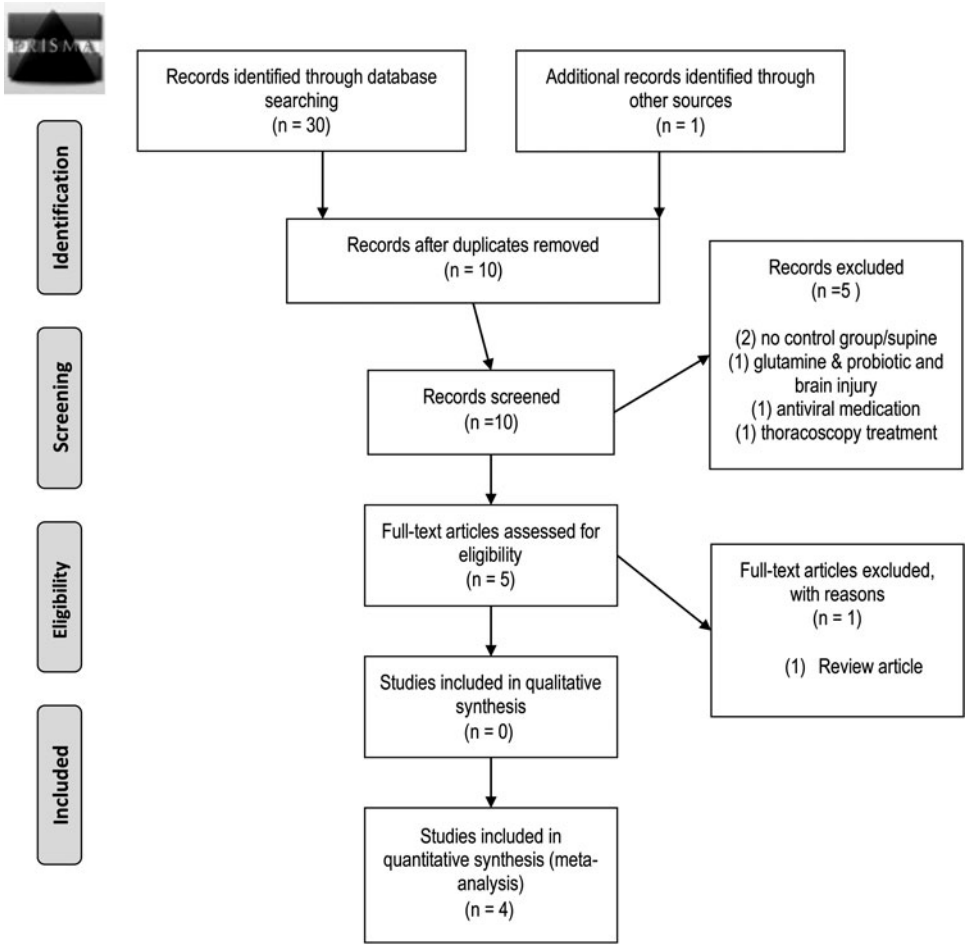

Figure. PRISMA 2009 flow diagram. From Moher et al.[12] For more information, visit: www.prismastatement.org.

LITERATURE REVIEW

In a prospective, observational study, Savio et al[8] evaluated the impact of early EN within 24 to 48 hours of ICU admission on gastrointestinal tolerance in 47 adult patients who were diagnosed with ARDS, had an Acute Physiology and Chronic Health Evaluation (APACHE) II score of 26.8 ± 9.2, and required mechanical ventilation. During the study, the clinical outcomes were measured on the same patients when in PP and again when they were in the SP.[8] A registered dietitian (RD) completed a subjective global assessment, estimated nutritional needs using the SCCM/ASPEN 2016 guidelines[6] (25-30 kcal/kg for calories and 1-1.5 g/kg for protein), and prescribed a 1.2 to 2.1 kcal/mL enteral formula via a nasogastric (NG) or orogastric feeding tube for study participants.[8] Gastric residual volume was measured every 6 hours and a GRV greater than 250 mL was defined as high.[8] The total duration of EN interruptions was 3.3 times greater for prone positioning than for supine positioning.[8] In addition, prone positioning had no EN interruptions due to diarrhea, gastroparesis, or nausea/emesis while supine positioning had EN turned off for gastroparesis (6.6%) and nausea/emesis (1.4%).[8] Although the aforementioned results were not clinically significant, a statistically significant increase in GRV was found when patients were in PP compared with SP (PP: 15 ±18.5 mL, SP: 5.3 ± 3.9 mL, $P = .03$).[8] Patients in SP met 80.8% while those in PP met 75% of their protein goal ($P = .025$).[8] There was no statistically significant difference in caloric intake between patient groups (SP: 83.2% and PP: 79.6%, $P = .12$).[8]

In a prospective, observational, crossover study, Saez de la Fuente et al[9] investigated the safety and efficacy of EN in 34 patients with ARDS on a mechanical ventilator who were in a medical-surgical ICU. The majority of the study participants had an APACHE II score of less than 20.[9] Enteral nutrition was provided via NG tube and was gradually increased until 100% of estimated nutrition needs (ESPEN guidelines[14]: 25 kcal/kg) were met on day 4 using Jevity (Abbott Nutrition, Columbus, Ohio), Impact (Nestle Health Science, Bridgewater, New Jersey), or Oxepa (Abbott Nutrition, Columbus, Ohio).[9] Supplemental parenteral nutrition was initiated when unable to meet nutrition needs via EN alone.[9] Gastric residual volume was checked every 6 hours on day 1, 12 hours on day 2, and once a day thereafter.[9] Enteral nutrition intolerance was defined as GRV of 500 mL and greater, emesis, or regurgitation.[9] They found no significant difference in daily GRV when patients were in PP compared with SP (PP: 189.2 ± 203.2 mL, SP: 126.6 ± 132.1 mL, $P = .054$).[9] Those fed in SP experienced fewer complications such as high GRV, emesis, and regurgitation than those fed in PP; however, the results were not statistically significant ($P = .39$, $P = .53$, and $P = .51$, respectively).[9]

Van der Voort and Zandstra[10] provided early EN within 24 hours of ICU admission to 19 adult patients who were critically ill and had a mean APACHE II score of 25.5 ± 8.98 in a prospective study to determine whether EN would be well tolerated. Study patients were prescribed an EN formula via NG tube at an infusion goal rate of 80 mL/h as long as GRV less than 150 mL while placed in PP and SP for 6 hours per position in a crossover design.[10] Gastric residual volume was checked every 3 and 6 hours.[10] Ten patients experienced higher GRV when they were in PP compared with SP while 8 patients had higher GRV in SP.[10] In addition, 1 patient vomited while in PP.[10] Overall, there was not a statistically significant difference in median 6-hour GRV between SP and PP (PP: 110 mL and SP: 95 mL, $P = .85$).[10]

Reignier et al[11] evaluated the safety and efficacy of early EN in 71 adult patients (n = 37 SP and 34 PP) who were mechanically ventilated with comparable Simplified Acute Physiology Scores II (SP: 52 ± 14 and PP: 52 ± 30) and a diagnosis of ARDS in a prospective, comparative study. Patients were fed in PP or SP. The EN goal was to provide 2000 mL of Isosource (Nestle Health Science, Bridgewater, New Jersey) by initiating tube feeds at 30 mL/h on day 1 and increase by

30 mL until the goal rate was achieved on day 4.[11] Gastric residual volume was checked every 6 hours and would be held for GRV greater than 250 mL or emesis.[11] Reignier et al[11] found that PP led to significantly higher GRV compared with SP on day 1 ($P = .001$), day 2 ($P = .001$), and day 4 ($P < .01$) of the 5-day study. Enteral nutrition interruptions occurred in 82% of the PP group and 49% of the SP group ($P < .01$).[11] The most common reasons for EN interruptions were emesis (PP: 39 episodes, SP: 27 episodes) and high GRV defined as greater than 250 mL (PP: 24 episodes, SP: 15 episodes).[11] The SP group received more volume of EN during days 1 through 5 of the study compared with the PP group (SP: 572-1837 mL and PP: 169-1200 mL, $P < .05$).[11]

The results of 3 studies indicate that tolerance is comparable when EN is administered to patients on a mechanical ventilator who were fed in either PP or SP[8-10]; however, Reignier and colleagues[11] found that tolerance was better in SP. Enteral nutrition intolerance can also hinder the ability to meet the patient's nutritional needs. All of the studies were performed at single centers, not randomized, unblinded, and lacked a power analysis.[8-11] Various EN formulations were used including standard polymeric ± fiber,[8,9] immune enhancing,[9] and pulmonary[9]; some were not identified.[8,11] Savio et al[8] used supplemental parenteral nutrition. Each study defined high GRV differently. For instance, Savio et al[8] and Reignier et al[11] used more than 250 mL, Saez de la Fuente et al[9] used 500 mL and more, and van der Voort and Zandstra[10] used more than 150 mL to define high GRV. Savio et al[8] and Saez de la Fuente et al[9] used established nutrition support guidelines to determine nutritional needs, and van der Voort and Zandstra[10] and Reignier et al[11] did not specify what guidelines were used. Finally, the heterogeneous nature of ICU patients coupled with varying ICU protocols makes it difficult to definitively conclude whether EN tolerance is comparable in patients in PP compared with SP. Large-scale randomized clinical trials or pooled data from multicenter trials are needed to definitely answer this question. Because of the lack of published studies with a positive quality rating, health care practitioners must use clinical judgment to determine whether EN should be used with caution in critically ill, mechanically ventilated patients being fed in PP.

The following case report, which is utilized with permission, delineates the course of care for an adult patient with COVID-19 and ARDS who required mechanical ventilation and EN while in PP. This case demonstrates some of the challenges health care professionals face when providing EN support to mechanically ventilated patients with COVID-19–related ARDS who are fed in PP.

CASE REPORT

R.M. was a 38-year-old White man with Down syndrome who resided in a group home until he was admitted to the hospital in August 2020 with a 1-day history of a 39.3°C fever (102.7° F), cough, and shortness of breath. He subsequently tested positive for COVID-19 and was diagnosed with severe acute respiratory syndrome coronavirus-2 (SARS-CO-V2) viral pneumonia. His past medical history was significant for hypertension, seizure disorder, hypothyroidism, type 2 diabetes (DM), hyperlipidemia, and pneumonia 2 years prior to admission (PTA) requiring mechanical ventilation. He had a supportive sister who was his medical power of attorney and she provided the RD with information regarding his nutrition and weight history via phone due to a no visitor policy at the hospital during the COVID-19 surge. He was 177.8 cm, weighed 132.4 kg at admission, ideal body weight (IBW) of 75.5 kg, and had a body mass index of 41.9 kg/m^2. The patient weighed 113.6 kg at 4 months and 128.6 kg at 2 weeks PTA. According to his sister, he denied any nausea, vomiting, or diarrhea PTA, but he did have a history of becoming constipated very easily. His last bowel movement was at an unspecified time PTA. While at the

group home, he was reportedly on a regular diet and had been eating well. His sister was concerned about his weight gain and attributed this to eating junk food while at the group home. She requested that he receive a "diabetic" diet when feasible. He had no known food allergies or intolerances.

R.M.'s clinical course was complicated by hypoxia, shock, and ARDS requiring him to be sedated and mechanically ventilated using a low tidal volume ventilation strategy on hospital day (HD) 1. His hospital medications included propofol, fentanyl, Synthroid, Lantus, methylprednisone, heparin, remdesivir, pantoprazole, Zofran, hydralazine, metoprolol, norepinephrine, Lovenox, Rocephin, Lipitor, and Zithromax. He also received convalescent plasma therapy for COVID-19. Supplemental Digital Content Table 2, available at: http://links.lww.com/TIN/A35, shows pertinent laboratory values and nutrition support regimens for R.M. during his hospitalization. On HD 2, his laboratory values were glucose: 270 mg/dL (normal range: 74-106 mg/dL), hemoglobin A_{1C}: 6.0% (normal range: 4.2%-5.6%), ferritin: 422.4 ng/L (normal range: 26-388 ng/mL), C-reactive protein (CRP): 8.8 mg/L (normal range: <0.29 mg/dL), lactate dehydrogenase (LDH): 494 (normal range: 87-241 units/L), fibrinogen: 426 mg/dL (normal range: 200-393 mg/dL), and aspartate transaminase (AST): 47 units/L (normal range: 15-37 units/L). R.M. was initiated on Glucerna 1.5 (Abbott Nutrition, Columbus, Ohio) at 40 mL/h via a 16 French NG tube within 4 hours of ICU admission.

NUTRITIONAL ASSESSMENT AND DIAGNOSIS

The RD completed a comprehensive nutrition assessment on HD 2 due to a physician consult for tube feeding recommendations. The RD was unable to perform a nutrition-focused physical examination due to COVID-19 precautions, which restricted entry into the patient's room for nonessential tasks to prevent unnecessary exposure. R.M. experienced a 16.5% weight gain in the preceding 4 months. His body mass index of 41.9 kg/m^2 was consistent with grade III obesity. Based on R.M.'s history of a good appetite and no indication of weight loss PTA, the RD determined that he did not meet the Academy of Nutrition and Dietetics/ASPEN criteria for malnutrition.[15] Although he did not meet the criteria for malnutrition, his combined diagnoses reflected a high risk for malnutrition. Although R.M.'s hemoglobin A_{1C} level was at the goal of less than 7.0% for an individual who has DM, he had hyperglycemia in the hospital due to DM, insulin resistance associated with inflammatory syndrome due to COVID-19–related critical illness, and steroid exacerbation. In addition, his inflammatory markers (ie, CRP, LDH, etc) were elevated because of a systemic inflammatory response syndrome. R.M. had elevated D-dimer and fibrinogen levels, which indicate a clotting abnormality that could lead to thrombus formation.[16] The RD estimated R.M.'s caloric needs at 1886 to 2263 kcal (25-30 kcal/kg IBW) or 2304 kcal using the Penn State 2003b[17] equation. His protein requirements were 151 to 189 g of protein (2-2.5 g/kg IBW) using the SCCM/ASPEN 2016 guidelines.[7] Fluid needs were estimated at 1886 to 2263 mL or 1 mL/kcal. The current EN regimen provided 1440 total kcal, 79 g of protein, and 729 mL of water. Propofol at 20.7 mL/h provided an additional 546 kcal from lipid. The EN regimen plus kilocalories from propofol met 88% to105% of caloric, 42% to 52% of protein, and 32% to 38% of fluid needs. Although not mandated by hospital policy, GRVs were checked because of simultaneous PP and EN infusion. R.M.'s residuals were less than 10 mL since EN was initiated. The appropriate Problem Etiology Signs and Symptoms statement for R.M. was inadequate EN infusion (NI-2.3)[18] due to inadequate EN rate prescribed compared with estimated nutritional needs as evidenced by meeting only 42% to 52% of protein needs.

NUTRITION INTERVENTION

Because of severe hypoxia, R.M. had to be in SP for 8 hours and then in PP for 16 hours to enhance oxygenation and promote alveolar recruitment.[5] The head of the bed was kept at a 30° angle while in SP and 10° to 25° angle (reverse Trendelenburg) when in PP to minimize aspiration risk from EN. The health care team was hesitant about feeding at the goal rate while in PP due to the patient's worsening hypoxia; therefore, the RD recommended increasing the Glucerna 1.5 at 40 mL/h as tolerated to a goal rate of 60 mL/h when in SP and decrease to 30 mL/h when in PP. R.M. required 1 Healthy Shot (Hormel Health Labs, Savannah, Georgia), a protein supplement, 3 times a day that provided 300 kcal and 72 g of protein. Enteral nutrition plus protein supplements would provide 1740 kcal, 151 g of protein, and 729-mL water per day at the goal rate. EN plus propofol would provide 2286 kcal, 151 g of protein, and 729 mL water. This would meet 100% of R.M.'s nutritional needs. The medical team was managing his fluid needs; therefore, the RD did not recommend a free water flush regimen. The RD suggested a bowel regimen to prevent constipation and promote laxation. The primary goal of nutrition support was to meet 80% to 100% of R.M.'s estimated nutritional needs.

MONITORING AND EVALUATION

The RD followed up on R.M. on HD 6 of admission. His current weight was 133.6 kg, which was an increase of 0.9% due to edema. Propofol was still infusing at 20.7 mL/h. He was also receiving Glucerna 1.5 at 60 mL/h when in SP, 30 mL/h when in PP, and 3 Healthy Shots (Hormel Health Labs, Savannah, Georgia). This EN regimen and propofol provided 2286 kcal and 151 g of protein, which met 100% of R.M.'s nutritional needs. Gastric residuals were 0 to 10 mL. The only change in his medication regimen was the addition of an insulin drip for steroid-induced hyperglycemia and a bowel regimen consisting of Lactulose, Senokot, Miralax, and Colace. The pertinent laboratory values included albumin: 2.5 g/dL (normal range: 3.4-5.0 g/dL), glucose: 225 mg/dL (normal range: 74-106 mg/dL), ferritin: 514.1 ng/mL (normal range: 26-388 ng/mL), D-dimer: 1.21 mg/L (normal range: <0.10-0.50 mg/L), LDH: 444 units/L (normal range: 87-241 units/L), and CRP: 1.14 mg/dL (normal range: <0.29 mg/dL). His point-of-care glucose values were 191 to 225 mg/dL. R.M.'s glucose levels improved after initiation of the insulin drip and eventually reached the target of less than 180 mg/dL. R.M.'s inflammatory markers began to trend down while his coagulopathy markers remained elevated, yet steady. Triglyceride levels increased from 90 to 175 mg/dL (normal range: <150 mg/dL) secondary to lipids from propofol.

R.M. was nil per os (NPO) on HD 9 due to pending extubation, which occurred later that day. He tested positive for *Escherichia coli* infection and was started on antibiotics. Glucerna 1.5 was restarted on HD 10 at 20 mL/h but he was being closely monitored for the need to reintubate. The current EN regimen would provide 720 kcal and 39 g of protein. Gastric residuals were 3 to 10 mL. The last documented laxation occurred on HD 8. Propofol was discontinued and he was now on Lasix for diuresis. His current weight was 120.7 kg, which was down 11.7 kg (8.8% weight loss) due to diuresis and hypermetabolic state. His pertinent laboratory values were glucose: 137 mg/dL (normal range: 74-106 mg/dL), albumin: 2.8 g/dL (normal range: 3.4-5.0 g/dL), AST: 57 units/L (normal range: 15-37 units/L), and alanine transaminase: (ALT): 104 units/L (normal range: 12-78 units/L). His laboratory values remained stable or continued to improve throughout the rest of his hospitalization except for his liver function tests. His AST and ALT began to trend upward due to shock liver due to low oxygenation and statin therapy; however, his liver function improved when the statin medication was discontinued. The RD recommended changing the EN

regimen to Glucerna 1.5 at 50 mL/h with Healthy Shot (Hormel Health Labs, Savannah, Georgia) twice a day to provide 2100 kcal, 171 g of protein, and 911 mL. Free water flushes were given in the amount of 200 mL every 4 hours to meet fluid needs. This would meet 100% of R.M.'s nutritional needs.

R.M. was discharged to the step-down unit where the speech-language pathologist evaluated his swallowing and noted that he had a wet cough and delayed swallow. R.M. was diagnosed with severe oropharyngeal dysphagia and the speech-language pathologist recommended continued NPO status on HD 16. His prior tube feeding regimen was resumed. He tolerated EN throughout his hospitalization without any nausea, emesis, high residuals, or abdominal distention. He did not require any prokinetic agents. R.M. was successfully fed EN while in PP.

R.M. was eventually discharged to a rehabilitation facility on Glucerna 1.5 at 50 mL/h, Healthy Shot (Hormel Health Labs, Savannah, Georgia) 3 times per day, and 300-mL free water flushes every 4 hours via NG tube on HD 25. During his rehabilitation admission, R.M. was sent for a percutaneous endoscopic gastrostomy tube placement, but during the procedure, he started having seizures. R.M. was readmitted to the hospital 10 days later due to multiple seizures while at the rehabilitation facility. He coded in the emergency department and cardiopulmonary resuscitation was initiated; however, he expired from a myocardial infarction, which was thought to be related to COVID-19.

DISCUSSION

There are multiple approaches to clinically manage patients with ARDS. The nutritional care provided to R.M. was largely consistent with the Nutrition Therapy Guidelines for COVID-19 (ie, early EN initiation, defer nutrition-focused physical examination in favor of alternative methods to obtain relevant information, continuous NG tube feedings, adjustment for propofol, etc); however, there were some deviations.[19] Although the RNs were not supposed to check gastric residuals for COVID-19 patients in order to reduce exposure risk, some still did it. The RD and the infectious disease physician reeducated the nursing team on the importance of not checking GRVs for patients who have COVID-19. In addition, a diabetes-specific formula was used because of his history of DM and initiation of steroid therapy, but this required exogenous protein supplementation. A higher protein EN formula may have prevented the RNs from having to go into the room to administer protein supplements several times per day. Indirect calorimetry was not used because of COVID-19; therefore, alternate methods of assessing his nutritional needs were utilized. Unfortunately, there was no information in the literature regarding nutritional requirements for adult patients with Down syndrome who are critically ill and require nutrition support. R.M.'s nutritional needs were determined by reviewing the ASPEN 2016 Guidelines,[7] COVID-19 Nutrition Guidelines,[19] and individualizing the EN prescription based on clinical judgment. Despite providing adequate nutrition to R.M., the alterations in metabolism caused by acute catabolic illness will not stop the loss of lean mass and weight. Although R.M.'s EN goal rate was adjusted on the basis of whether he was in SP or PP, the results of the narrative review suggest that this may not be necessary. All studies used in the narrative review fed patients at the goal rate and did not adjust the rate for PP.[8-11]

CONCLUSION

The narrative review and the case report emphasize the importance of using the current guidelines and consensus statements to develop an ICU nutrition protocol to successfully provide EN to individuals with ARDS who are on a mechanical ventilator and require EN support while in PP.[7,19] Close monitoring of nutritional parameters such as nausea, vomiting, diarrhea, GRV, regurgitation, and nutritional adequacy is crucial in determining whether EN is safe

and effective. In addition, it is imperative to continuously educate members of the health care team on the facility-specific ICU nutrition protocol to ensure adherence to the protocol and maximize clinical outcomes. Further research is warranted to fully validate the reliability of administering EN in PP.

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