Nutrición Hospitalaria

Trabajo Original

Paciente crítico

Feeding intolerance during prolonged prone position in overweight and obese patients with severe COVID-19

Intolerancia a la alimentación durante el prono prolongado en pacientes con COVID-19 y sobrepeso y obesidad

Iván Armando Osuna-Padilla[1,2], Nadia Rodríguez-Moguel[2,3], Laurie Abril López-Orduña[2], Ana Lucía Gómez-Rodríguez[1], Alan García-Grimaldo[1], Sebastián Rodríguez-Llamazares[1], Ismael Maldonado-Beltrán[1], Martín Armando Ríos-Ayala[1], Carmen Margarita Hernández-Cárdenas[1]

[1]*Respiratory Intensive Care Unit. Department of Critical Areas. Instituto Nacional de Enfermedades Respiratorias (INER). Mexico City, Mexico.* [2]*Tecnológico de Monterrey. School of Medicine and Health Sciences. Monterrey, Nuevo León. Mexico.* [3]*Department of Infectious Diseases Research. Instituto Nacional de Enfermedades Respiratoria (INER). Mexico City, Mexico*

Abstract

Objective: the aim of this study was to compare the incidence rate of feeding intolerance (FI) during supine (SP) or prone positioning (PP) in critically ill COVID-19 patients.

Methods: this was a retrospective cohort study of critically ill patients with overweight or obesity who received enteral nutrition (EN) in prone or supine positioning continuously during the first five days of mechanical ventilation. Nutritional risk, anthropometric measurements and body composition were assessed at the first 24 hours upon Intensive Care Unit (ICU) admission. Biochemical and clinical variables (Sequential Organ Failure Assessment [SOFA], Acute Physiology and Chronic Health Evaluation II [APACHE II], Acute Kidney Injury [AKI] or comorbidities diagnosis) were collected. Pharmacotherapy (prokinetics, sedatives or neuromuscular blocking agents) and FI incidence (gastric residual volume [GRV] ≥ 200 ml or ≥ 500 ml, vomiting or diarrhea) were daily recorded. Constipation was defined as the absence of evacuation for five consecutive days.

Results: eighty-two patients were included. Higher rate of prophylactic prokinetic prescription was observed in PP (42.8 *vs* 12.5 %, p = 0.002). GRV ≥ 200 in supine position was not different when compared to PP (p = 0.47). Vomiting episodes in supine compared to PP showed no difference between groups (15 % *vs* 24 %, p = 0.31). No differences in diarrhea events were detected (10 % *vs* 4.7 %, p = 0.36). Constipation was common in both groups (95 % *vs* 82 %, p = 0.06).

Conclusion: FI during prone position was not different in comparison to supine position. Routinely use of prokinetics in continuous prone position may help to prevent FI incidence. Algorithm development is necessary for FI prevention and treatment so to avoid EN interruptions and adverse clinical outcomes.

Correspondence:

Carmen Margarita Hernández-Cárdenas. Respiratory Intensive Care Unit. Department of Critical Areas. National Institute of Respiratory Diseases (INER). Calzada de Tlalpan, 4502, Colonia Sección XVI. 14080, Mexico City, Mexico
e-mail: cmhcar@hotmail.com

Resumen

Objetivo: comparar la incidencia de intolerancia a la alimentación entre pacientes críticos en posición supino (PS) o prono (PP).

Métodos: cohorte retrospectiva de pacientes bajo ventilación mecánica por distrés respiratorio por COVID-19 y sobrepeso y obesidad, quienes recibieron nutrición enteral (NE) en PP o PS. Se evaluaron riesgo nutricional, mediciones antropométricas y composición corporal en las primeras 24 horas de ingreso a la Unidad de Cuidados Intensivos (UCI). Se recolectaron variables bioquímicas y clínicas (Sequential Organ Failure Assessment [SOFA], Acute Physiology and Chronic Health Evaluation II [APACHE II], lesión renal aguda y otras comorbilidades). Se registró el esquema de farmacoterapia prescrita durante los primeros cinco días (procinéticos, sedantes y bloqueadores neuromusculares). Se evaluó la incidencia de intolerancia a la alimentación, definida como la presencia de residuo gástrico (RG) ≥ 200 o ≥ 500 ml, vómito, diarrea o estreñimiento.

Resultados: fueron incluidos 82 pacientes. Se observó una mayor prescripción de procinéticos como terapia profiláctica en PP (42,8 *vs.* 12,5 %, p = 0,002). No se observaron diferencias en RG ≥ 200 ml (p = 0,47) ni vómito (p = 0,31) entre ambos grupos. No se observaron diferencias en episodios de diarrea (10 % en PS *vs.* 4,7 % en PP, p = 0,36). El estreñimiento fue común en ambos grupos de estudio (95 *vs.* 82 %, p = 0,06).

Conclusiones: la PP no se relaciona con una mayor incidencia de intolerancias a la alimentación. El uso rutinario de procinéticos durante la PP continua puede ayudar a prevenir la incidencia de dichas intolerancias. Es necesario el desarrollo de algoritmos para la prevención y tratamiento de las intolerancias a la alimentación para evitar interrupciones en la NE y desenlaces no deseados.

Palabras clave:

Nutrición enteral. Valoración nutricional. Paciente crítico. Posición prono. Disfunción gastrointestinal.

INTRODUCTION

Enteral nutrition (EN) is the preferred feeding route for critically ill patients on mechanical ventilation (MV) (1), and it is associated with better immunological and clinical outcomes when started within 48 hours after admission (2). EN interruption is common during ICU stay due to procedural-related fasting, vasopressors doses, and other potentially avoidable causes (3). Feeding intolerance (FI), defined as gastrointestinal (GI) dysfunction resulting in a reduction in the delivery of enteral feeding, regardless of the underlying cause, is another common cause of EN interruption (4). Different definitions of GI symptoms are currently used in studies (5), and include vomiting, regurgitation, abdominal distension, gastric residual volume, absent/abnormal bowel sounds, abdominal pain, absence/presence of stool, diarrhea, high intra-abdominal pressure and GI bleeding (6).

Prone positioning (PP) is commonly used in acute respiratory distress syndrome (ARDS) patients (7,8), and may be a cause of EN interruptions due to higher episodes of vomiting and gastric residual volume (GRV) (9), intra-abdominal hypertension (IAH), and gut dysmotility, which can also be exacerbated by pharmacotherapy (7,10,11). Furthermore, the incidence of ARDS is higher in obese patients, and could be beneficiated by PP (12,13). Since obesity has been associated with a higher risk of impaired gastric motility and EN intolerance, due to IAH (14,15) and comorbidities such as diabetes (16), there is a lack of knowledge about the safety of EN provision in overweight and obese patients in PP. The aim of this study is to compare the incidence of FI during the supine or prone position in overweight and obese patients on MV.

METHODS

This was a retrospective cohort of consecutive patients that were admitted to the Intensive Care Unit (ICU) from November 2020 to December 2021. COVID-19 patients (confirmed by SARS-CoV-2 real-time polymerase chain reaction) on MV due to ARDS were included (17). Patients were categorized as PP if they required this management during the first five days of EN, or supine positioning (SP) if not required during that same period.

PP was considered when PaO_2/FiO_2 was below 150 according to current treatment guidelines (18). Patients were excluded if they did not have overweight/obesity (body mass index [BMI] < 25 kg/m²), or if their management required either MV or PP for less than five days, or position changed during the same period. This study was reviewed and approved by the Institutional Review Board (Register #C51-29).

DATA COLLECTION

Demographic information including sex and age was collected from patient records. Prescribed drugs with nutritional implications (steroids, benzodiazepines, opioids, neuromuscular blocking agents [NBA], sedatives, dexmedetomidine, prokinetics and vasopressors) along with medical history of non-communicable diseases were also registered. According to our unit standard, PP was achieved with foam wedges and pillows, alternating head, and neck rotation every four hours. Duration of PP cycle is continuous (24 hours) without cycles SP changed.

NUTRITIONAL ASSESSMENT

Nutritional assessment was performed on all patients during the first 24-48 hours after ICU admission. Body weight and height were estimated by means of validated equations using anthropometric measurements (19). BMI was calculated and classified using the World Health Organization (WHO) criteria (20). Waist circumference was measured at the midpoint of the line between the rib or costal margin and the iliac crest; measurements were made using a tape graduated in centimeters with 0.1 cm precision (SECA® 201, Germany). Body composition was assessed by bioelectrical impedance (BIA) using a multi-frequency device (InBody S10®, InBody Co., Ltd., Seoul, Korea). Fat mass in kg and phase angle were recorded from the machine output. The nutritional risk of each patient was calculated using a modified NUTRIC-Score due to the unavailability of the IL-6 determinations. High nutritional risk was established with a score ≥ 5 (21).

ENTERAL NUTRITION PRESCRIPTION

Orogastric tube placement was used over other short-term accesses as a common institutional practice to avoid epistaxis and sinus infection. Following radiographic confirmation of the correct tip position, EN was initiated. Calories and protein were prescribed according to recommendations by the American Society of Parenteral and Enteral Nutrition (ASPEN) and European Society for Clinical Nutrition and Metabolism (ESPEN), with a general target of 25 kcal/kg and 1.3 g/kg, respectively (22,23). Adjusted body weight was used in patients with a BMI > 30 kg/m² and was calculated using Hamwi equations. An algorithm for EN progression was used: 10 kcal/kg, 15 kcal/kg, and 20 kcal/kg on days 1, 2 and 3, respectively. Next, 25 kcal/kg on day 4 was prescribed in patients with high nutritional risk, and 20 kcal/kg during the first 4-7 days on low nutritional risk. Calories derived from non-nutritional sources were factored into the nutrition prescriptions to avoid overfeeding. In case of FI and interruption during EN advancement, prokinetics were administered and same nutritional support prescription from the previous day was maintained.

MAIN OUTCOME DEFINITION

FI incidence was defined as the presence of any of the following clinical conditions: diarrhea (frequency of bowel movement > 3 times/day Bristol 6 or liquid stools), vomiting, constipation (no evacuation during five consecutive days) and gastroparesis (gastric residual volume ≥ 200 and ≥ 500 ml, because there are common cut-off values used in hospital setting) (24,25). GRV was measured one time at day before EN initiation by aspirating the orogastric tube with a 50-ml syringe.

STATISTICAL ANALYSIS

Data were analyzed using Stata Intercooled (version 14, Stata Corporation, College Station, TX, USA). The normality of the distribution of quantitative variables was verified by the Shapiro-Wilk test. Descriptive statistics were used for the analysis of categorical variables (absolute and relative frequency) and quantitative variables (mean and standard deviation [SD] or median and interquartile range [IQR]). Clinical data between PP and SP were compared using the Student's t-test, Mann-Whitney U test or the χ^2 test. Statistical significance was defined as $p < 0.05$. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement.

RESULTS

A total of 180 patients were admitted to the ICU. Only 82 patients were included in this analysis (mean age ± SD: 45.3 ± 12.1; 70 % males) (Fig. 1). Overweight was identified in 59 % and obesity in 41 % according to BMI, with higher fat mass (%) in PP males (35 ± 10.8 vs 29.1 ± 8.9, p = 0.02) but not in females.

Statistical toward of low phase angle was observed in PP males (6.2 ± 1.4 vs 5.6 ± 0.9, p = 0.06), but not in females (Table I). Differences in FI were reported in table II; constipation was common in both groups (92 % vs 97 %, p = 0.11). GRV ≥ 200 (18 % vs 12 %, p = 0.38) and ≥ 500 ml (5 % vs 5 %, p = 0.92), vomiting (8 % vs 16 %, p = 0.23) and diarrhea events (8 % vs 2.3 %, p = 0.26) were similar in SP and PP groups (Fig. 2).
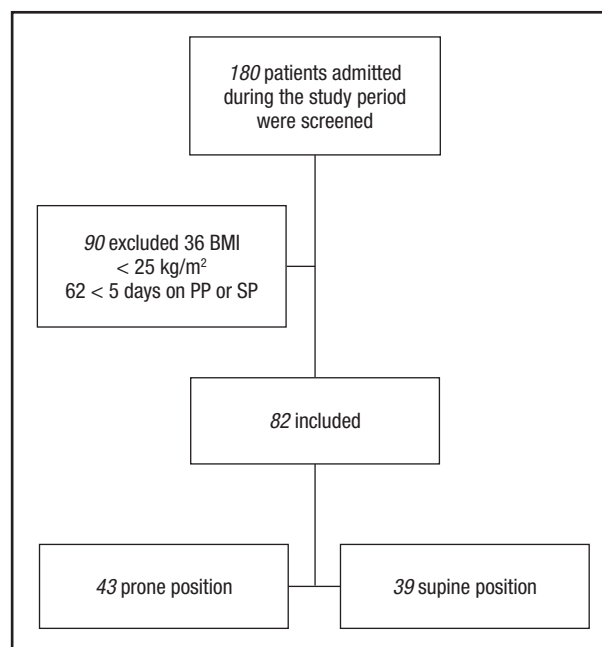
Figure 1.

Patients included in this analysis. BMI: body mass index; PP: prone position; SP: supine position.

Table I. Demographical characteristics of critically ill COVID-19 patients

	Supine (n = 39)	Prone (n = 43)	p value
Age	45.3 ± 13	45.3 ± 11.6	0.97
Sex Female (%)	7 (18 %)	17 (40 %)	0.03
Diabetes (%)	11 (28 %)	11 (26 %)	0.78
Hypertension (%)	11 (28 %)	14 (33 %)	0.66

(Continues on next page)

Table I (Cont.). Demographical characteristics of critically ill COVID-19 patients

	Supine (n = 39)	Prone (n = 43)	p value
AKI (%)	18 (47 %)	11 (27 %)	0.06
SOFA scale	9 ± 2	10 ± 2	0.24
APACHE II	19 ± 4	19 ± 5	0.77
Nutric-score	4 ± 2	4 ± 1	0.78
Benzodiazepines	36 (92 %)	34 (79 %)	0.09
Days	3.9 ± 1.4	4.3 ± 1.0	0.25
Opioids	39 (100 %)	42 (98 %)	0.33
Days	4.6 ± 0.8	4.6 ± 0.7	0.65
Propofol	9 (23 %)	16 (37 %)	0.16
Days	4.1 ± 1.0	3.8 ± 1.5	0.53
Neuromuscular blocking agents	30 (77 %)	36 (84 %)	0.43
Days	3 ± 1.4	4 ± 1.2	0.009*
PEEP cmH$_2$O	11 ± 3	12 ± 2	0.18
> 10 cmH$_2$O	31 (79 %)	41 (98 %)	0.009*
PCR baseline (mg/dl)	13.1 (8.8-18)	13.8 (6.7-25.5)	0.95
Waist circumference (cm)	109.7 ± 12	111.3 ± 11.5	0.54
Weight (kg)	86.1 ± 17.9	88 ± 18.6	0.64
BMI (kg/m^2)	30.5 ± 6.6	31.1 ± 5.3	0.63
Overweight	25 (68 %)	21 (51 %)	0.14
Obesity	12 (32 %)	20 (49 %)	
Fat mass (%)			
Male	29.1 ± 8.9	35 ± 10.8	0.02*
Female	40.7 ± 6.9	41.2 ± 9.0	0.92
Phase angle (°)			
Males	6.2 ± 1.4	5.6 ± 0.9	0.06
Females	4.7 ± 0.4	4.9 ± 0.9	0.66
Prokinetic use	5 (12.5 %)	18 (42.8 %)	0.002*
Day 1	3 (8 %)	4 (9 %)	0.79
Day 2	3 (8 %)	11 (26 %)	0.03*
Day 3	2 (5 %)	13 (30 %)	0.003`*
Day 4	2 (5 %)	12 (28 %)	0.006*
Day 5	1 (3 %)	14 (33 %)	< 0.001*
Vasopressors use			
Day 1	21 (54 %)	19 (45 %)	0.43
Day 2	22 (56 %)	17 (40 %)	0.15
Day 3	18 (46 %)	11 (27 %)	0.07
Day 4	20 (51 %)	12 (29 %)	0.04*
Day 5	16 (41 %)	14 (34 %)	0.52
Norephinefrine dose (mcg/min)			
Day 1	2.6 (1.3-7.9)	2.3 (0.6-5.3)	0.57
Day 2	2.3 (0.6-5.3)	3.9 (1.3-6.6)	0.34
Day 3	1.9 (1.3-2.9)	3.3 (1.0-7.9)	0.71
Day 4	2.3 (1.3-6.3)	2.8 (1.0-6.3)	0.65
Day 5	1.4 (0.6-3.3)	3.9 (1.8-6.6)	0.02*
Antibiotic use			
Day 1	7 (17 %)	8 (19 %)	0.60
Day 2	13 (33 %)	8 (19 %)	0.33
Day 3	14 (36 %)	10 (23%)	0.59
Day 4	16 (41 %)	14 (32 %)	0.22
Day 5	18 (46 %)	11 (26 %)	0.25
Clinical outcomes			
Mortality	5 (13 %)	13 (30 %)	0.06
Days on mechanical ventilation	16 (10-28)	15 (10-26)	0.87

AKI: Acute Kidney Injury; SOFA: Sequential Organ Failure Assessment; APACHE: Acute Physiology and Chronic Health Evaluation II; PEEP: positive end-expiratory pressure; BMI: body mass index.

Table II. Differences in feeding intolerance according to prone or supine positioning

Postural positioning	Day 1		Day 2		Day 3		Day 4		Day 5	
	SP	PP	SP	PP	SP	PP	SP	PP	SP	PP
GRV ≥ 200 ml	0	2 (5 %)	1 (2 %)	2 (5 %)	3 (8 %)	0	0	0	4 (10 %)	0
GRV ≥ 500 ml	0	2 (5 %)	0	0	0	0	1 (2.5 %)	0	1 (2.5 %)	0
Vomiting	2 (5 %)	1 (2.3 %)	1 (2.5 %)	2 (5 %)	1 (2.5 %)	3 (7 %)	0	3 (7.0 %)	0	3 (7 %)
Diarrhea	0	0	0	0	1 (2.6 %)	1 (2.3 %)	2 (5.1 %)	1 (2.3 %)	1 (2.5 %)	0
Absence of evacuations	38 (97 %)	43 (100 %)	38 (97 %)	43 (100 %)	37 (95 %)	42 (98 %)	36 (92 %)	42 (98 %)	35 (90 %)	43 (100 %)

n (%). SP: supine position; PP: prone position; GRV: gastric residual volume.
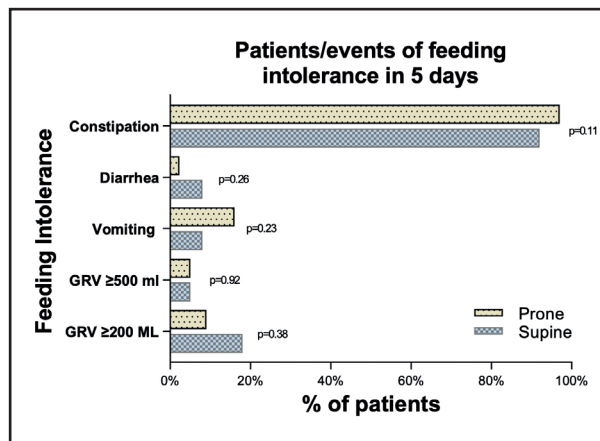

Figure 2.

Differences in patients/events of feeding intolerances during study period. GRV: gastric residual volume.

DISCUSSION

This study found no differences in FI incidence between PP and SP patients on MV due to COVID-19 ARDS. In this cohort we included only patients with BMI ≥ 25 kg/m^2 (59 % overweight and 41 % obesity) receiving EN in PP o SP continuously during the first five days of MV. No differences in BMI (p = 0.63) and phase angle by sex were observed between individuals at the SP or PP. Similar prevalence of overweight and obesity were observed by Savio R et al. in critically-ill patients with non-COVID related ARDS (49.2 % and 30.2 %, respectively) (26). Both studies showed no significant differences in FI despite SP or PP. This suggests that EN during PP is safe and does not represent a higher risk for GI dysfunction in overweight or obese individuals (27).

The use of certain drugs such as sedatives, opioids and vasopressors has also been related to FI (7). In our cohort, we found no differences in the use of benzodiazepines (p = 0.09), opioids (p = 0.33), propofol (p = 0.16) or antibiotics in SP compared to PP during the study period. The number of individuals receiving vasopressors in the SP group and the PP group was also similar, except for day 4 (51 % *vs* 29 %, p = 0.04); however, no significant differences were observed in FI events. Individuals in PP do not seem to have different or higher drug requirements compared to SP, which can be related to the fact that both groups reported a similar incidence of FI.

According to the guidelines and practice recommendations for nutritional care of critically-ill patients with COVID-19, it has been established that prokinetics use can be considered to promote gastric motility in high risk aspiration patients (28,29). In a systematic review from Lewis et al. prokinetics were associated with reduced FI; defined as GRV ≥ 150 ml, vomiting or abdominal distention (RR 0.73, 95 % CI: 0.55-0.97; p = 0.03), and high gastric residual volumes reduction (RR 0.69; 95 % CI: 0.52-0.91; p = 0.009). Nevertheless, there was no significant improvement

in the risk of vomiting, diarrhea, ICU length of stay or mortality (30). In a recent meta-analysis from Peng et al. an updated definition of FI (GRV ≥ 500 ml, presence of vomiting, diarrhea, gastrointestinal bleeding or inadequate delivery of EN < 60 % of the target or < 20 kcal/kg after 72 hours of feeding attempts) was proposed. According to this, ten of 13 studies showed that prokinetics were beneficial on FI in critically-ill patients with gastric EN, with a reduction in ICU length of stay (MD -2.03, 95 % CI: -3.96, -0.10; p = 0.04; low certainty) and hospital length of stay (MD -3.21, 95 % CI: -5.35, -1.06; p = 0.003; low certainty) (31). However, prokinetics effect on other clinical outcomes related to ICU mortality such as pneumonia, remains unclear.

In our cohort, prokinetics were used routinely by some members of physician's staff in continuous PP as prevention or initiated after FI episodes; we observed that a higher frequency of individuals in our PP group received prokinetics, compared to the SP group (42.8 % vs 12.5 %, p = 0.002). In our cohort, constipation was common in both groups (97 % vs 92 %, p = 0.11). GRV ≥ 200, vomiting and diarrhea events were similar in SP and PP groups. Considering this, the initiation of prokinetics agents should be considered simultaneously at PP (7), to avoid fasting prescription previous to PP or the reduction of the rate infusion of EN as strategies for FI prevention.

Higher prevalence of obesity grade 1 (BMI ≥ 35 kg/m²) was observed in males on PP group (31 % vs 13 %, p = 0.26). This explain the higher amount of adipose tissue in males between groups. Obese patients have an increased risk of ARDS and were the group of patients that may benefit from PP. No differences were observed for phase angle between groups, which is a marker of low muscle mass and is associated with higher mortality and length of stay (32-34).

Similar to our results, other authors report no differences between positions in GRV and vomiting episodes in non-COVID-19 critically-ill patients with ARDS (26), however, BMI was not reported (35,36). Reignier et al. report that patients on PP and nasogastric tube had a higher GRV and had more vomiting episodes, however, nutritional status and BMI was not reported (37). Similarly, L'Her et al. report an incidence of high GRV in 14 % and vomiting in 12 % of patients on PP, but enteral access and BMI were not reported (38). Contrary to what can be expected, Liu et al. report that BMI ≥ 40 kg/m² is associated with decreased risk of FI, but differences between PP and SP were not analyzed. The incidence rate variation between reports may be influenced by PP, BMI and enteral access (39).

Our study offers data in COVID-19 critically-ill patients with overweight and obesity, showing that EN during PP is not different from SP and might be considered as a safe intervention, but it also has the following limitations: a) our cohort was enrolled at a single center; d) no data of interruptions or caloric debt associated with reported FI during prone were available; c) no data of the timing of the initiation of prokinetics agents as prophylactic or treatment of FI was gathered, and this may have an impact on FI rate; d) infectious complications or the incidence of ventilator-associated pneumonia (VAP) were not assessed; and e) although the follow-up period in our study was limited to the first five days

of MV, it includes the time of initiation and advancement of EN, where the deficit in its supply due to FI interruptions has been associated with adverse clinical outcomes.

CONCLUSION

FI in terms of GRV, vomiting or diarrhea during PP was not different in comparison with SP. To prevent adverse effects, a multidisciplinary intervention in critically-ill patients undergoing prone positioning is required.

REFERENCES

1. Preiser J-C, Arabi YM, Berger MM, Casaer M, McClave S, Montejo-González JC, et al. A guide to enteral nutrition in intensive care units: 10 expert tips for the daily practice. Crit Care 2021;25:424-37. DOI: 10.1186/s13054-021-03847-4
2. Schörghuber M, Fruhwald S. Effects of enteral nutrition on gastrointestinal function in patients who are critically ill. Lancet Gastroenterol Hepatol 2018;3:281-7. DOI: 10.1016/S2468-1253(18)30036-0
3. Uozumi M, Sanui M, Komuro T, Iizuka Y, Kamio T, Koyama H, et al. Interruption of enteral nutrition in the intensive care unit: a single-center survey. J Intensive Care 2017;5:52-7. DOI: 10.1186/s40560-017-0245-9
4. Reintam Blaser A, Deane AM, Preiser J-C, Arabi YM, Jakob SM. Enteral feeding intolerance: updates in definitions and pathophysiology. Nutr Clin Pract 2021;36:40-9. DOI: 10.1002/ncp.10599
5. Reintam Blaser A, Preiser J-C, Fruhwald S, Wilmer A, Wernerman J, Benstoem C, et al. Gastrointestinal dysfunction in the critically ill: a systematic scoping review and research agenda proposed by the Section of Metabolism, Endocrinology and Nutrition of the European Society of Intensive Care Medicine. Crit Care 2020;24:224-40. DOI: 10.1186/s13054-020-02889-4
6. Berger MM, Hurni C-A. Management of gastrointestinal failure in the adult critical care setting. Curr Opin Crit Care 2022;28:190-7. DOI: 10.1097/MCC.0000000000000924
7. Al-Dorzi HM, Arabi YM. Enteral nutrition safety with advanced treatments: extracorporeal membrane oxygenation, prone positioning, and infusion of neuromuscular blockers. Nutr Clin Pract 2021;36:88-97. DOI: 10.1002/ncp.10621
8. Behrens S, Kozeniecki M, Knapp N, Martindale RG. Nutrition support during prone positioning: an old technique reawakened by COVID-19. Nutr Clin Pract 2021;36:105-9. DOI: 10.1002/ncp.10592
9. Bruni A, Garofalo E, Grande L, Auletta G, Cubello D, Greco M, et al. Nursing issues in enteral nutrition during prone position in critically ill patients: A systematic review of the literature. Intensive Crit Care Nurs 2020;60:102899-906. DOI: 10.1016/j.iccn.2020.102899
10. Bordejé ML, Montejo JC, Mateu ML, Solera M, Acosta JA, Juan M, et al. Intra-abdominal pressure as a marker of enteral nutrition intolerance in critically ill patients. The PIANE Study. Nutrients 2019;11:2616-25. DOI: 10.3390/nu11112616
11. Yan Y, Chen Y, Zhang X. The effect of opioids on gastrointestinal function in the ICU. Crit Care 2021;25:370-83. DOI: 10.1186/s13054-021-03793-1
12. De Jong A, Verzilli D, Jaber S. ARDS in obese patients: specificities and management. Crit Care 2019;23:74-82. DOI: 10.1186/s13054-019-2374-0
13. Foy BH, Brightling CE, Siddiqui S. Proning reduces ventilation heterogeneity in patients with elevated BMI: implications for COVID-19 pneumonia management? ERJ Open Res 2020;6:00292-2020. DOI: 10.1183/23120541.00292-2020
14. Kim IB, Prowle J, Baldwin I, Bellomo R. Incidence, risk factors and outcome associations of intra-abdominal hypertension in critically ill patients. Anaesth Intensive Care 2012;40:79-89. DOI: 10.1177/0310057X1204000107
15. Lambert DM, Marceau S, Forse RA. Intra-abdominal pressure in the morbidly obese. Obes Surg 2005;15:1225-32. DOI: 10.1381/096089205774512546
16. Ye Y, Jiang B, Manne S, Moses PL, Almansa C, Bennett D, et al. Epidemiology and outcomes of gastroparesis, as documented in general practice records, in the United Kingdom. Gut 2021;70:644-53; DOI: 10.1136/gutjnl-2020-321277

17. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA 2012;307:2526-33. DOI: 10.1001/jama.2012.5669

18. Fan E, Del Sorbo L, Goligher EC, Hodgson CL, Munshi L, Walkey AJ, et al. An Official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine Clinical Practice Guideline: mechanical ventilation in adult patients with acute respiratory distress syndrome. Am J Respir Crit Care Med 2017;195:1253-63. DOI: 10.1164/rccm.19511erratum

19. Rabito EI, Mialich MS, Martínez EZ, García RWD, Jordao AA, Marchini JS. Validation of predictive equations for weight and height using a metric tape. Nutr Hosp 2008;23:614-8.

20. World Health Organization (WHO). Obesity: preventing and managing the global epidemic. Report of a WHO consultation. WHO Tech Rep Ser 2000;894(i-xii):1-253.

21. Rahman A, Hasan RM, Agarwala R, Martin C, Day AG, Heyland DK. Identifying critically-ill patients who will benefit most from nutritional therapy: further validation of the "modified NUTRIC" nutritional risk assessment tool. Clin Nutr 2016;35:158-62. DOI: 10.1016/j.clnu.2015.01.015

22. Martindale R, Patel JJ, Taylor B, Arabi YM, Warren M, McClave SA. Nutrition therapy in critically ill patients with coronavirus disease (COVID-19). J Parenter Enteral Nutr 2020;44:1174-84. DOI: 10.1002/jpen.1930

23. Barazzoni R, Bischoff SC, Breda J, Wickramasinghe K, Krznaric Z, Nitzan D, et al. ESPEN expert statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection. Clin Nutr 2020;39:1631-8. DOI: 10.1016/j.clnu.2020.03.022

24. Tatsumi H. Enteral tolerance in critically ill patients. J Intensive Care 2019;7:30-9. DOI: 10.1186/s40560-019-0378-0

25. Gacouin A, Camus C, Gros A, Isslame S, Marque S, Lavoué S, et al. Constipation in long-term ventilated patients: associated factors and impact on intensive care unit outcomes. Crit Care Med 2010;38:1933-8. DOI: 10.1097/CCM.0b013e3181eb9236

26. Savio RD, Parasuraman R, Lovesly D, Shankar B, Ranganathan L, Ramakrishnan N, et al. Feasibility, tolerance and effectiveness of enteral feeding in critically ill patients in prone position. J Intensive Care Soc 2021;22:41-6. DOI: 10.1177/1751143719900100

27. Binda F, Galazzi A, Marelli F, Gambazza S, Villa L, Vinci E, et al. Complications of prone positioning in patients with COVID-19: a cross-sectional study. Intensive Crit Care Nurs 2021;67:103088-94. DOI: 10.1016/j.iccn.2021.103088

28. Chapple L-AS, Tatucu-Babet OA, Lambell KJ, Fetterplace K, Ridley EJ. Nutrition guidelines for critically ill adults admitted with COVID-19: is there consensus? Clin Nutr ESPEN 2021;44:69-77. DOI: 10.1016/j.clnesp.2021.05.003

29. Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, et al. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr 2019;38:48-79. DOI: 10.1016/j.clnu.2018.08.037

30. Lewis K, Alqahtani Z, Mcintyre L, Almenawer S, Alshamsi F, Rhodes A, et al. The efficacy and safety of prokinetic agents in critically ill patients receiving enteral nutrition: a systematic review and meta-analysis of randomized trials. Crit Care 2016;20(1):259-70. DOI: 10.1186/s13054-016-1441-z

31. Peng R, Li H, Yang L, Zeng L, Yi Q, Xu P, et al. The efficacy and safety of prokinetics in critically ill adults receiving gastric feeding tubes: a systematic review and meta-analysis. PloS One 2021;16:e0245317-36. DOI: 10.1371/journal.pone.0245317

32. Osuna-Padilla IA, Rodríguez-Moguel NC, Rodríguez-Llamazares S, Orsso CE, Prado CM, Ríos-Ayala MA, et al. Low muscle mass in COVID-19 critically-ill patients: prognostic significance and surrogate markers for assessment. Clin Nutr 2022;41:2910-7. DOI: 10.1016/j.clnu.2022.02.019

33. Osuna-Padilla IA, Rodríguez-Moguel NC, Rodríguez-Llamazares S, Aguilar-Vargas A, Casas-Aparicio GA, Ríos-Ayala MA, et al. Low phase angle is associated with 60-day mortality in critically ill patients with COVID-19. J Parenter Enteral Nutr 2022;46:828-35. DOI: 10.1002/jpen.2236

34. Lima J, Eckert I, González MC, Silva FM. Prognostic value of phase angle and bioelectrical impedance vector in critically ill patients: a systematic review and meta-analysis of observational studies. Clin Nutr 2022;4:2801-16. DOI: 10.1016/j.clnu.2022.10.010

35. 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;5:216-20. DOI: 10.1177/0115426502017005323

36. Sáez de la Fuente I, Sáez de la Fuente J, Quintana Estelles MD, García Gigorro R, Terceros Almanza LJ, Sánchez Izquierdo JA, et al. Enteral nutrition in patients receiving mechanical ventilation in a prone position. J Parenter Enteral Nutr 2016;40:250-5. DOI: 10.1177/0148607114553232

37. Reignier J, Thenoz-Jost N, Fiancette M, Legendre E, Lebert C, Bontemps F, et al. Early enteral nutrition in mechanically ventilated patients in the prone position. Crit Care Med 2004;32:94-9. DOI: 10.1097/01.CCM.0000104208.23542.A8

38. L'Her E, Renault A, Oger E, Robaux M-A, Boles J-M. A prospective survey of early 12-h prone positioning effects in patients with the acute respiratory distress syndrome. Intensive Care Med 2002;28:570-5. DOI: 10.1007/s00134-002-1258-x

39. Liu R, Paz M, Siraj L, Boyd T, Salamone S, Lite T-LV, et al. Feeding intolerance in critically ill patients with COVID-19. Clin Nutr 2022;41:3069-76. DOI: 10.1016/j.clnu.2021.03.033