



Effect on mortality of early enteral nutrition in critically ill patients with COVID-19

Efecto de la nutrición enteral precoz en la mortalidad de pacientes críticos con COVID-19

Efeito da nutrição enteral precoce na mortalidade em doentes críticos com COVID-19

Araceli Alejandra Soto-Novia¹, Luisa Mariana Calvillo-Centeno¹, Andrea Virginia Aguilar-Espinosa¹, Pamela Sapien-Olea¹, Paola Renata Lamoyi-Domínguez¹, Jesús Ortiz-Ramírez², Sathia González-Guzmán¹.

Received: 14 de febrero de 2023. Accepted: 9 de abril de 2023

Posted online: 9 de abril de 2023

<https://doi.org/10.35454/rncm.v6n2.511>

Summary

Background: Early enteral nutrition (EEN) has shown favorable clinical outcomes, such as lower risk of death, fewer frequency of infection and lower health-care costs. Different societies recommend the provision of enteral nutrition within the first 24 to 48 hours of admission to the Intensive Care Unit in patients with COVID-19.

Methods: Retrospective cohort study including adult patients with severe COVID-19 and orotracheal intubation. Demographic and clinical characteristics, as well as use of drugs with nutritional relevance, such as vasopressors and steroids, as well as biochemical results (serum electrolytes) were registered. EEN was defined as the provision of enteral feeding within the first 24-48 hours of invasive mechanical ventilation (IMV). The primary outcome was in-hospital all-cause mortality.

Results: Overall, 404 patients were included in the study. EEN was achieved in 74% of all patients. EEN significantly reduced mortality in the bivariate model (RR 0.88, 95% CI 0.80 - 0.95) and in the multivariate model (adjusted OR 0.42, 95% CI 0.19 - 0.90). No differences in hospital length of stay and days on IMV in survivors were found.

Conclusions: EEN was associated with a lower risk of death in critically ill patients with COVID-19. Additional studies are

Resumen

Antecedentes: la nutrición enteral temprana ha demostrado resultados clínicos favorables, tales como menor riesgo de mortalidad, menor frecuencia de infecciones y menores costos en salud. Diferentes sociedades recomiendan la provisión de nutrición enteral dentro de las primeras 24 a 48 horas del ingreso a la unidad de cuidados intensivos (UCI) en pacientes con enfermedad por coronavirus de 2019 (COVID-19).

Métodos: estudio de cohorte retrospectiva en pacientes adultos con COVID-19 grave e intubación orotraqueal. Se registraron las características demográficas y clínicas, así como el uso de fármacos con relevancia nutricional, como vasopresores y corticoides, y los resultados bioquímicos (electrolitos séricos). La nutrición enteral temprana se definió como la provisión de alimentación enteral en las primeras 24-48 horas de ventilación mecánica invasiva. El resultado primario fue la mortalidad hospitalaria por todas las causas.

Resultados: se incluyeron en el análisis a 404 pacientes. El 74 % de los casos recibió nutrición enteral temprana. La nutrición enteral temprana se asoció con una reducción estadísticamente significativa en la mortalidad por todas las causas en el modelo bivariado (riesgo relativo [RR]: 0,88; intervalo de confianza [IC] del 95 %:

Resumo

Introdução: a nutrição enteral precoce (NEP) tem mostrado resultados clínicos favoráveis, como menor risco de morte, menor frequência de infecção e menores custos de saúde. Diferentes sociedades recomendam o fornecimento de nutrição enteral nas primeiras 24 a 48 horas após a admissão na Unidade de Terapia Intensiva em pacientes com COVID-19.

Métodos: estudo de coorte retrospectivo incluindo pacientes adultos com COVID-19 grave e intubação orotraqueal. Foram registradas as características demográficas e clínicas, bem como o uso de medicamentos com relevância nutricional, como vasopressores e esteróides, e os resultados bioquímicos (eletrólitos séricos). A NEP foi definida como o fornecimento de alimentação enteral nas primeiras 24-48 horas de ventilação mecânica invasiva (VMI). O desfecho primário foi mortalidade intra-hospitalar por todas as causas.

Resultados: quatrocentos e quatro pacientes foram incluídos no estudo. A NEP foi alcançada em 74% de todos os pacientes. A NEP reduziu significativamente a mortalidade no modelo bivariado (RR 0,88, 95% IC 0,80 a 0,95) e no modelo multivariado (OR ajustado 0,42, 95% IC 0,19 - 0,90). Não foram encontradas diferenças no tempo de internação e nos dias de VMI nos sobreviventes.



necessary to further clarify the effects of early enteral feeding on patient outcomes.

Key words: Early enteral nutrition, mortality, COVID-19, critically ill patients, invasive mechanical ventilation.

0,80 a 0,95) y en el modelo multivariado ajustado (*odds ratio* [OR] ajustado: 0,42; IC 95 %: 0,19 a 0,90). No se encontraron diferencias significativas en la duración de la estancia hospitalaria ni en los días de VMI en los supervivientes.

Conclusiones: la nutrición enteral temprana se asocia con menor mortalidad por todas las causas en pacientes críticos con COVID-19. Son necesarios estudios adicionales para aclarar los efectos de la nutrición enteral temprana en los resultados de los pacientes.

Palabras clave: nutrición enteral temprana, mortalidad, COVID-19, pacientes críticos, ventilación mecánica invasiva.

Conclusões: a NEP foi associada a menor risco de morte em pacientes gravemente doentes com COVID-19. Estudos adicionais são necessários para esclarecer melhor os efeitos da alimentação enteral precoce nos resultados dos pacientes.

Palavras-chave: nutrição enteral precoce, mortalidade, COVID-19, pacientes críticos, ventilação mecânica invasiva.

¹ Department of Clinical Nutrition, Hospital General Ajusco Medio. Mexico City, Mexico.

² General Management, Hospital General Ajusco Medio. Mexico City, Mexico.

*Corresponding author: Sathia González-Guzmán.
nutricionclinica.ajuscomedio@gmail.com

INTRODUCTION

Different societies recommend the provision of enteral nutrition within the first 24 to 48 hours of admission to the Intensive Care Unit (ICU) in patients with COVID-19⁽¹⁾. Early enteral nutrition (EEN) has shown favorable clinical outcomes, such as lower risk of death, fewer frequency of infection and less healthcare costs^(2,3). Benefits of early enteral nutrition are summarized in Table 1. On the other hand, delayed enteral nutrition (DEN), started after day 4 of invasive mechanical ventilation (IMV), is associated with longer hospital stay, longer stay in the ICU and more days on IMV. It is reported that the most common reasons for the delay in enteral feeding in critically ill patients with COVID-19 are hemodynamic instability (requiring high vasopressor doses) and provider fear of aspiration, particularly with the patient in prone position⁽⁴⁾. Current guidelines suggest that critically ill patients in prone position or with gastric residual volume within the suggested thresholds can and should be fed^(1,5). There is evidence to suggest that dietitian involvement in the multidisciplinary team providing care to critically ill patients improves the achievement of protein and energy targets, development and implementation of nutrition algorithms and, most importantly, early initiation of enteral nutrition⁽⁶⁾.

Patients infected with SARS-CoV-2 often develop acute respiratory distress syndrome (ARDS) and around 5% of all confirmed COVID-19 cases will require critical care and IMV⁽⁷⁾.

We conducted a retrospective cohort study to evaluate the effect of EEN on mortality in patients with COVID-19 who required IMV.

METHODS

For this single-center cohort study, data were retrospectively collected using medical records of adult patients (>18 years) admitted with confirmed SARS-CoV-2 infection between June 2021 and January 2022 to a referral center in Mexico City. All consecutive patients admitted with laboratory confirmed COVID-19 who were under IMV for more than 72 hours were included. Patients transferred from other units, who had previously been on IMV, or who had been started on IMV before transfer were excluded.

Out of a total of 455 patients, a sample size of 293 patients was considered statistically significant. Sample size was calculated using the formula for finite population, a confidence level of 95%, an acceptable margin of error of 0.05, an occurrence probability of 0.95 and a non-occurrence probability of 0.05.

Table 1. Early Enteral Nutrition Benefits

Early Enteral Nutrition Benefits		
Cardiovascular system	Respiratory system	Musculoskeletal system
Attenuate oxidative stress by decreasing the systemic inflammatory response syndrome.	Reduce lung axis of inflammation by maintaining the mucosal associated lymphoid tissue and increasing the production of secretory A immunoglobulin at epithelial surfaces.	Help maintaining muscle reserve, function, mobility and return to baseline function.
Gut	Immune system	Gastrointestinal system
Maintain gut integrity by decreasing gut permeability, supporting commensal bacteria and stimulating oral tolerance. Increase butyrate production and promote insulin sensitivity by decreasing hyperglycemia.	Increase dominance of anti-inflammatory Th2 over pro-inflammatory Th1 responses; modulate adhesion molecules to decrease transendothelial migration of macrophages and neutrophils.	Provide antioxidants, micro and macronutrients. Maintain lean body mass, decrease muscle and tissue glycosylation, increase mitochondrial function and protein synthesis to meet metabolic demands, increase absorptive capacity, decrease virulence of pathogenic organism and favors motility and contractility.

Adapted from: McClave SA et al. Crit Care Med. 2014;42(12):2600-10.

Data collection

Demographic and clinical characteristics (comorbidities, in-hospital length of stay [LOS], days on IMV and survival) as well as biochemical parameters (serum electrolytes) were registered. Data on the use of drugs with nutritional relevance, such as vasopressors and steroids were also collected. Gastrointestinal intolerance was defined as the presence of gastric residual volume >500 mL every six hours in supine position, and >300 mL every four hours in prone position, the presence of emesis or diarrhea (defined as more than 3 stool or a total stool volume of more than 750 mL in 24 hours)^(8,9).

Nutritional parameters

Data on nutritional intake (energy and protein) during the first 72 hours after orotracheal intubation were collected. Causes of interruptions in enteral feeding were collected from medical charts. Prone position and the presence of gastric residual volumes lower than those previously stated were considered unjustified reasons for delaying enteral feeding. EEN was defined as the provision of enteral feeding in the first 24-48 hours of IMV. Weight and height were estimated using Rabito formulas in patients who could not be weighed before orotracheal intubation^(10,11). Refeeding syndrome risk was defined as patients with a BMI <18.5 kg/m², unintentional weight

loss >10% in the past 3 to 6 months, little or no nutritional intake for >5 days at the moment of admission, history of alcohol or drug abuse (including insulin, chemotherapy, antacids, or diuretics), low baseline levels of potassium, phosphate or magnesium before feeding⁽¹²⁾, as well as refeeding hypophosphatemia (phosphate <2 mg/dl o or a drop of >0.5 mg/dl after the first 72 hours of enteral nutrition initiation or increase)⁽⁸⁾.

Study endpoints

The primary outcome was in-hospital all-cause mortality. Secondary outcomes included hospital LOS and days on IMV in survivors.

Statistical analysis

Categorical variables were reported in absolute and relative frequencies. Quantitative variables were reported using mean and standard deviation or median and interquartile range, according to each variable distribution as assessed by the Shapiro-Wilk test. Comparisons between groups were made using Chi-squared, Fisher exact test and Student's t test for variables with normal distribution, or the two-sample rank sum test for variables with no normal distribution. A bivariate analysis was performed in order to find associations between in-hospital all-cause mortality and baseline characteristics. Relative risk and 95% confidence intervals were

calculated. A logistic regression model was constructed to find independent associations between in-hospital all-cause mortality and the variables of interest. Interactions were assessed using the Cochran-Mantel-Haenszel Chi. A two tailed p value of less than 0.05 was considered significant. The STATA version 14 software package (Texas, USA) was used.

Ethical approval

This study complies with the Declaration of Helsinki and with the General Health Law of Mexico.

RESULTS

During the study period, 455 patients were considered eligible for inclusion. We excluded 78 patients for the reasons described in Figure 1. Overall, 404 patients were included in the study. The demographic characteristics and clinical features are shown in Table 2.

EEN was achieved in 74% of all patients. The mean age was 59 (48-71) years, 65.8% were male and 42% were obese. Significant differences were observed between the EEN and DEN groups for chronic kidney disease on renal replacement therapy (CKD-RRT) and vasopressor or steroid use. A total of 332 patients (82%) died. Surviving patients were ventilated for 15 (10-24) days. Surviving patients who received EEN (62) were ventilated for 17 (10-24) days and had a LOS of 39 (28-50) days. Surviving patients in the DEN group (10) were ventilated for 13 (7-19) days and had a LOS of 30 (13-35) days.

Early Enteral Nutrition versus Delayed Enteral Nutrition

EEN was significantly associated with a lower risk of death in the bivariate model (RR 0.88, 95% CI 0.80 a 0.95) and in the multivariate model (adjusted OR 0.42, 95% CI 0.19 – 0.90) adjusted by sex, age, obesity, hypertension (HTN), type 2 diabetes (T2DM), CKD-RRT, stroke, human immunodeficiency virus (HIV), liver disease, refeeding syndrome risk and vasopressors and steroid use (Figure 2). The model included those variables considered by the investigators as having biological importance. Colinear variables (e.g., chronic obstructive pulmonary disease, malignancy, heart disease, connective tissue disease) were excluded from the model.

Delayed Enteral Nutrition

Most common causes for DEN were hemodynamic instability and metabolic acidosis. Other causes included lack of access, gastrointestinal intolerance, and unjustified reasons (Table 3).

DISCUSSION

This study shows a significant association between EEN and reduced mortality in critically ill patients with COVID-19. Our results support current recommendations for the provision of EEN and similar evidence. A recent systematic review and meta-analysis⁽¹³⁾ of four studies and 1682 patients found a significant reduction in risk of death with a RR of 0.89 (95% IC, 0.79-1.0).

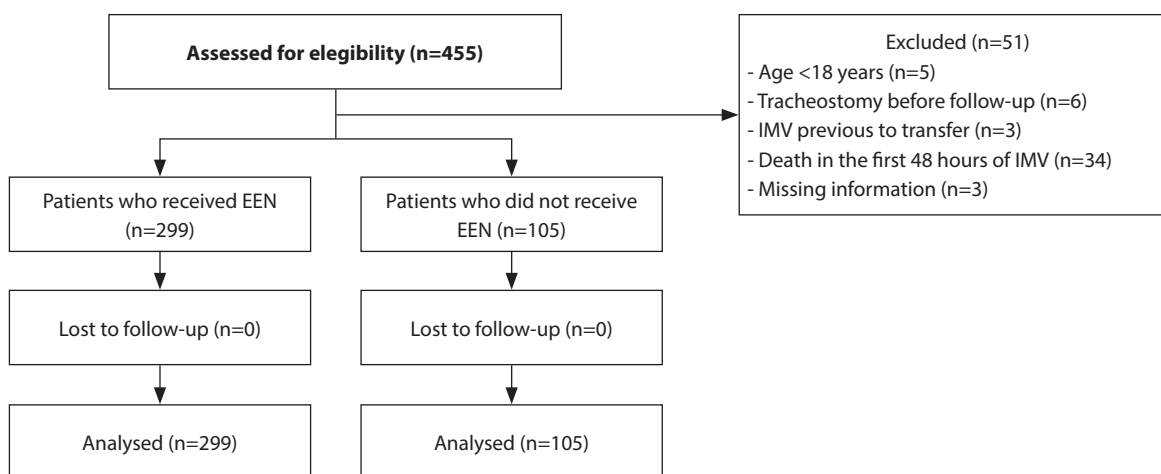


Figure 1. Study design. IMV: Invasive Mechanical Ventilation.

Table 2. Patient's characteristics.

	Total n= 404 (100%)	EEN n= 299 (74%)	DEN n= 105 (26%)	p
Male n (%)	266 (65.8)	197 (65.8)	69 (65.7)	0.97
Age ≥60 years n (%)	195 (48.2)	143 (47.8)	52 (49.5)	0.76
Body mass index, median (IQR) - (kg/m ²)	28.2 (24.9–32.9)	29.6 (28.9–30.4)	28.9 (27.5–30.3)	0.17
Obesity n (%)	170 (42%)	122 (40.8%)	41 (39%)	0.97
Hypertension n (%)	156 (38.6%)	117 (39.1%)	39 (37.1%)	0.75
Type 2 Diabetes Mellitus n (%)	168 (41.6%)	126 (42.1%)	42 (40%)	0.70
Chronic Kidney Disease – Renal Replacement Therapy n (%)	13 (3.22%)	5 (1.67%)	8 (7.6%)	0.006
Refeeding syndrome risk n (%)	50 (12.4%)	33 (11.0%)	17 (16.2%)	0.16
Chronic Obstructive Pulmonary Disease n (%)	8 (2.0%)	6 (2.0%)	2 (1.9%)	0.94
Stroke n (%)	9 (2.2%)	7 (2.3%)	2 (1.9%)	0.79
Malignancy n (%)	6 (1.5%)	4 (1.3%)	2 (1.9%)	0.67
Human Immunodeficiency Virus n (%)	3 (0.7%)	1 (0.3%)	2 (1.9%)	0.10
Heart Disease n (%)	19 (4.7%)	11 (3.7%)	8 (7.6%)	0.10
Liver Disease n (%)	9 (2.2%)	3 (1.0%)	6 (5.7%)	0.005
Connective Tissue Disease n (%)	4 (1.0%)	4 (1.3%)	0 (0.0%)	0.23
Drugs				
- Vasopressors n (%)	365 (90.3%)	264 (88.2%)	101 (96.1%)	0.018
- Steroids n (%)	338 (83.7%)	254 (84.9%)	84 (80%)	0.23
Outcomes				
- In-hospital death n (%)	332 (82.2%)	237 (71%)	95 (28%)	0.010
- Median Length of stay (IQR)	37 (26-49) (n= 72)	39 (28-50) (n=62)	30 (13-35) (n=10)	0.096
Median days of Invasive Mechanical Ventilation median (IQR)	15 (10-24) (n=72)	17 (10-24) (n=62)	13 (7-19) (n=10)	0.173

DEN: Delayed Enteral Nutrition; EEN: Early Enteral Nutrition; IQR: Interquartile range.

Our results are consistent with those of Ortiz-Martinez et al., who found positive effects on mortality. Their retrospective cohort study in 242 Mexican patients showed an OR of 0.21 (0.087-0.509) in favor of patients receiving EEN⁽¹⁴⁾. Chawla et al., in a retrospective review in 515 adults, found that EEN was associated with a lower risk of hospital mortality (adjusted HR 0.79, 95% CI, 0.63-1.0)⁽¹⁵⁾. Furthermore, late enteral

nutrition has been associated with higher hospital mortality (RR 9.00, 95% CI, 2.25-35.99)⁽¹⁶⁾.

Beneficial effects in terms of LOS, days on IMV and costs, but not so on mortality, have been previously described in patients who received EEN. These differences may be explained by the definition used for EEN. Definitions are as broad as feeding within the first 24 hours or up to 72 hours of IMV. Farina et al., for exam-

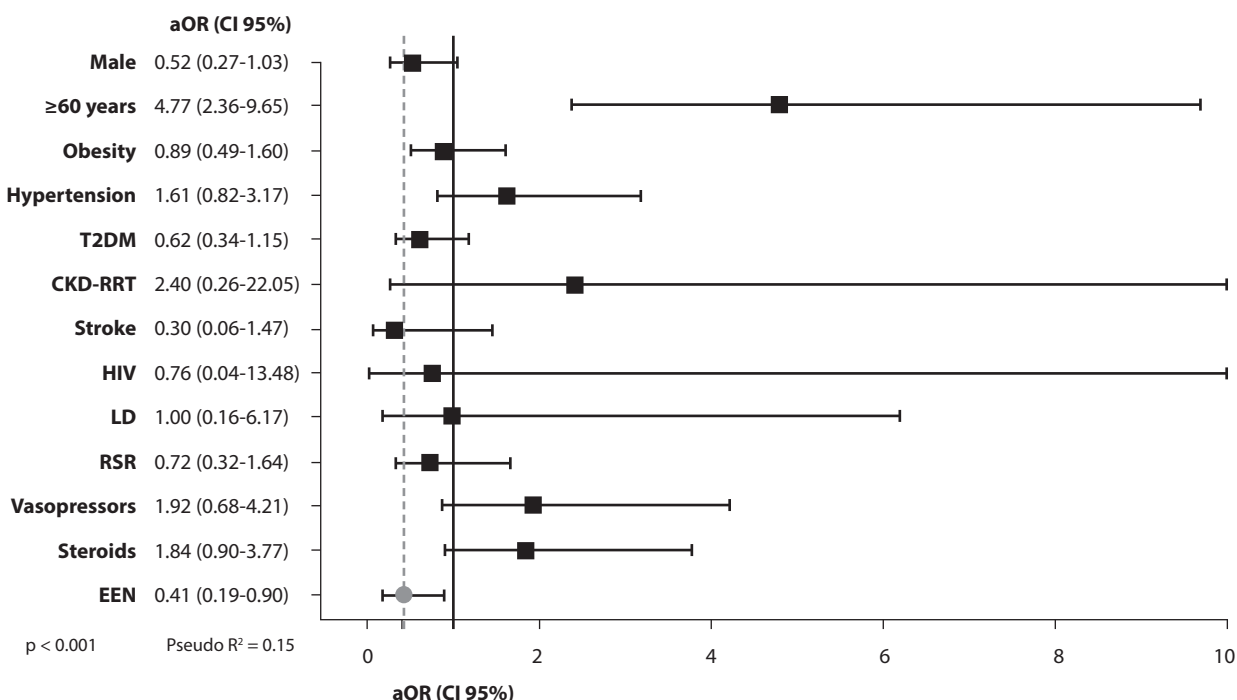


Figure 2. Early Enteral Nutrition effect on mortality. Forest Plot of adjusted odds ratios (aOR), multivariate analysis. Age 60 or older (≥ 60 years). CKD-RRT: Chronic Kidney Disease with Renal Replacement Therapy; EEN: Early Enteral Nutrition; HIV: Human Immunodeficiency Virus; LD: Liver Disease; RSR: Refeeding syndrome risk; T2DM: Type 2 Diabetes Mellitus.

Table 3. Causes of delayed enteral nutrition

	Day 1 (n = 180)	Day 2 (n = 125)
Hemodynamic instability	42.8% (77)	55.2% (69)
Metabolic acidosis	26.7% (48)	33.6% (42)
Lack of access	14.4% (26)	1.6% (2)
Unjustified reasons	16.1% (29)	8.8% (11)
GI intolerance	–	0.8% (1)

GI: Gastrointestinal.

ple, defined EEN as the provision of enteral nutrition within the first 24 hours of IMV. On the other hand, Haines defined EEN as initiating nutrition feeding within the first 3 days of IMV^(4,17). ASPEN guidelines define EEN as the provision of enteral feeding in the first 12 hours of IMV or within 36 hours of admission to the ICU⁽¹⁾.

Benefits of enteral nutrition in critically ill patients with COVID-19 may be due to maintenance of gut

integrity, stress modulation, and disease severity attenuation⁽¹⁵⁾. Similar evidence has been found in critically ill patients who did not have COVID-19. Minnelli et al. hypothesized that timing of nutrition delivery may be crucial as enteral nutrition not only provides macro and micronutrients, but also helps to sustain gut integrity through blood flow stimulation in intraepithelial cells⁽¹⁸⁾. Also, enteral nutrition, even at a trophic rate, maintains gut integrity in the intestinal villi by preserving tight junctions. Nutrient interaction with mucosal cells and with gut-associated lymphoid tissue (GALT) may play a role in immune functions⁽¹⁹⁾.

Pardo et al. found an increase in mortality when EEN was used in critically ill patients⁽²⁰⁾. They included in their study patients with multiple organ failure, a factor that has been found to be associated with worse prognosis⁽²¹⁾. In studies that have not found differences in mortality with EEN, medical-nutrition therapy (MNT) was not guided by a nutritional support team⁽¹⁷⁾.

We found an independent association between age 60 or greater and in-hospital mortality. These results are consistent with previously published research⁽²²⁾. Association between mortality and male sex, obesity, T2DM or HTN was not found in this cohort, even

though these characteristics have been previously reported as risk factors for mortality. Nevertheless, all our patients already presented severe COVID-19.

Similar to our findings, reports show that 60% to 70% of all patients receive EEN^(3,4,6,13,17,23). Causes of DEN include the use of vasopressor agents, even at low doses, provider fear of aspiration in prone position, and obesity^(3,4,9,14). However, evidence suggests that EEN is possible and should be started at stable or decreasing doses of vasopressors and in prone position^(1,8,24).

One of the main strengths in this study is the large sample size. Also, MNT was guided by a dietitian specialized in clinical nutrition. However, this study has some limitations, including the fact that no information on vaccination was collected. As evidence shows, the benefit of the vaccine relies on preventing disease transmission and, above all, severe forms of COVID-19. Given that this study included critically ill ventilated patients, it is to be expected that the effect of vaccination would not be as reported in literature. There are also limitations inherent to the retrospective nature of this study. Additionally, steroid use was not associated with increased mortality in this cohort. This could be explained by the fact that patients with refractory shock were treated with hydrocortisone. Finally, we did not consider outcomes that could worsen risk of death, such as acute kidney injury and secondary infections. Additional research is needed.

In conclusion, EEN is associated with a lower mortality risk in critically ill patients with COVID-19. Additional studies are necessary to further clarify the effects of early enteral feeding on patient outcomes.

KEY POINTS

- Early enteral nutrition was associated with reduced mortality in critically ill patients with COVID-19.
- Early enteral nutrition was achieved in 74% of our patients.
- Most common causes for delayed enteral nutrition in critically ill patients with COVID-19 were hemodynamic instability, metabolic acidosis, and lack of feeding access.

Acknowledgments

The authors thank all the included patients and their families, physicians, nurses, and staff, especially Natalia Marin-Schlamme, Diego Oswaldo Moreira-Cardenas, Victor Gabriel Hernandez-Garcia, Mario Ivan De La Cruz-Lara and Linda Muñoz-Garcia. We are profoun-

dly grateful to Dr. Bernardo Martinez-Guerra and Dr. Ivan Osuna-Padilla for their invaluable help in the development of this paper.

Authorship declaration

All authors participated equally in the design, acquisition, analysis, and interpretation of the data and drafting and critical review of the manuscript, and agreed with the final version of the project.

Conflict of interest

The authors had no disclosures to declare.

Funding

No funding was received for this study.

References

1. Martindale R, Patel JJ, Taylor B, Arabi YM, Warren M, McClave SA. Nutrition Therapy in Critically Ill Patients With Coronavirus Disease. *JPEN*. 2020;44(7):1174–84. doi: 10.1002/jpen.1930
2. Reintam Blaser A, Starkopf J, Alhazzani W, Berger MM, Casaer MP, Deane AM, et al. Early enteral nutrition in critically ill patients: ESICM clinical practice guidelines. *Intensive Care Med*. 2017;43(3):380-98. doi: 10.1007/s00134-016-4665-0
3. Tian F, Heighes PT, Allingstrup MJ, Doig GS. Early enteral nutrition provided within 24 hours of ICU admission: A meta-analysis of randomized controlled trials. *Crit Care Med*. 2018;46(7):1049-56. doi: 10.1097/CCM.0000000000003152
4. Haines K, Parker V, Ohnuma T, Krishnamoorthy V, Raghunathan K, Sulo S, et al. Role of Early Enteral Nutrition in Mechanically Ventilated COVID-19 Patients. *Crit Care Explor*. 2022;4(4):e0683. doi: 10.1097/CCE.0000000000000683
5. Terblanche E, Bear D. Critical Care Specialist Group of the BDA guidance on management of nutrition and dietetic services during the COVID-19 pandemic [Internet]. BDA; 2020 [cited on December 20, 2022]. Available from: <https://www.bda.uk.com/uploads/assets/f5215258-7a34-4426-83620ba89f87c638/63decf82-db85-41d7-b5a6caba-be757a4a2/CCSG-Guidance-for-COVID-19-Formatted.pdf>
6. Osuna IA, González S, Rodríguez NC. El nutricionista/dietista como agente de cambio en la unidad de cuidados intensivos. *Rev Nutr Clín Metab*. 2022;6(2). doi: 10.35454/rncm.v6n2.455
7. Wu Z, McGoogan JM. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases from the Chinese Center for Disease Control and

- Prevention. *JAMA*, 2020;323(13):1239-42. doi: 10.1001/jama.2020.2648
8. 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(1):48-79. doi: 10.1016/j.clnu.2018.08.037
 9. Chapple LAS, Fetterplace K, Asrani V, Burrell A, Cheng AC, Collins P, et al. Nutrition management for critically and acutely unwell hospitalised patients with coronavirus disease 2019 (COVID-19) in Australia and New Zealand. *Australian Critical Care*, 2020;33(5):399-406. doi: 10.1016/j.aucc.2020.06.002
 10. Rabito EI, Mialich MS, Martínez EZ, D García RW, Jr Jordao AA, Marchini JS, et al. Validation of predictive equations for weight and height using a metric tape validación de ecuaciones predictivas para el peso y talla utilizando cinta métrica Resumen. *Nutr Hosp*. 2008;23(6):614-8.
 11. Guzmán Hernández C, Reinoza Calderón G, Hernández Hernández RA. Estimación de la estatura a partir de la longitud de pierna medida con cinta métrica estimation of height from leg length measured with tape measure. *Nutr Hosp*. 2005;(5):358-63.
 12. Friedli N, Stanga Z, Culkin A, Crook M, Laviano A, Sobotka L, et al. Management and prevention of refeeding syndrome in medical inpatients: An evidence-based and consensus-supported algorithm. *Nutrition*. 2018;47:13-20. doi: 10.1016/j.nut.2017.09.007
 13. Ojo O, Ojo OO, Feng Q, Boateng J, Wang X, Brooke J, et al. The Effects of Enteral Nutrition in Critically Ill Patients with COVID-19: A Systematic Review and Meta-Analysis. *Nutrients*. 2022;14(5):11-20. doi: 10.3390/nu14051120
 14. Ortiz Martínez K, Ugarte Martínez P, Gaytán García CJ, Ruiz Álvarez M, Martínez Díaz BA, Aguirre Sánchez JS. Impacto de la nutrición enteral temprana en la mortalidad y días de estancia en la Unidad de Cuidados Intensivos. *Medicina Crítica*. 2022;36(8):496-9. doi: 10.35366/109169
 15. Chawla GS, Fazzari MJ, Baron SW, Assa A, Mohrmann L, Chekuri S, et al. Early Enteral Nutrition Reduces In-Hospital Mortality of Critically Ill COVID-19 Patients. *Nutrients*, 2022;14(5):1120. doi: 10.3390/nu14051120
 16. Chin Han LC, Shi Ng P, Wah Wong K, Hon Puah S, Duan Qi LC, Kayambu G, et al. Nutrition support practices for critically ill patients with severe acute respiratory syndrome coronavirus-2: A multicentre observational study in Singapore. *Ann Acad Med Singap*. 2022;51(6):329-340. doi: 10.47102/annals-acadmedsg.202231
 17. Farina N, Nordbeck S, Montgomery M, Cordwin L, Blar F, Cherry-Bukowiec J, et al. Early Enteral Nutrition in Mechanically Ventilated Patients With COVID-19 Infection. *Nutr Clin Pract*. 2021;36(2):440-448. doi: 10.1002/ncp.10629
 18. Minnelli N, Gibbs L, Larrivee J, Sahu KK. Challenges of Maintaining Optimal Nutrition Status in COVID-19 Patients in Intensive Care Settings. *J Parenter Enter Nutr*. 2020;44(8):1439-1446. doi: 10.1002/jpen.1996
 19. Szefer J, Kruszewski WJ, Buczek T. Enteral feeding and its impact on the gut immune system and intestinal mucosal barrier. *Przegląd Gastroenterol*. 2015;10(2):71-77. doi: 10.5114/pg.2015.48997
 20. Pardo E, Lescot T, Preiser J-C, Massanet P, Pons A, Jaber S, et al. Association between NET early nutrition support and 28-day mortality in critically ill patients: The Frans Prospective Nutrition Cohort Study. *Critical Care*. 2023;27(1):7. doi: 10.1186/s13054-022-04298-1
 21. Mokhtari T, Hassani F, Ghaffari N, Ebrahimi B, Yarahmadi A, Hassanzadeh G. COVID-19 and multiorgan failure: A narrative review on potential mechanisms. *J Mol Histol*, 2020;51(6):613-628. doi: 10.1007/s10735-020-09915-3
 22. Dadras O, SeyedAlinaghi SA, Karimi A, Shamsabadi A, Qaderi K, Ramezani M, et al. Covid-19 mortality and its predictors in the elderly: A systematic review. *Health Science Reports*. 2022;5(3):e657. doi: 10.1002/hsr2.657
 23. Karayiannis D, Kakavas S, Sarri A, Giannopoulou V, Liakopoulou C, Jahaj E, et al. Does Route of Full Feeding Affect Outcome among Ventilated Critically Ill COVID-19 Patients: A Prospective Observational Study. *Nutrients*, 2021;14(1):153. doi: 10.3390/nu14010153
 24. BDA Critical Care Specialist Group COVID-19 Best Practice Guidance: Feeding Patients on Critical Care Units in the Prone Position (awake and sedated) [Internet]. BDA; 2020 [cited on December 20, 2022]. Available from: <https://www.bda.uk.com/uploads/assets/3f487dea-81e4-4277-bf1def44abc075bd/e319c889-23a3-4c7c-ab49e5efc9d82f91/201209-CCSG-BP-Guidance-for-Prone-Enteral-Feeding-Formatted-v2.pdf>