Lesson learnt from the COVID-19 pandemic. Analysis of nutritional aspect of critically ill patients treated in intensive care unit — single-centre, retrospective study

Lekcja z pandemii COVID-19. Analiza wybranych aspektów interwencji żywieniowych u pacjentów leczonych na oddziale intensywnej terapii — badanie retrospektywne, jednośrodkowe

Paweł Kutnik

II Department of Anesthesiology and Intensive Care, Lublin, Poland

Correspondence address:
lek. Paweł Kutnik
II Department of Anesthesiology and Intensive Care, Lublin, Poland
ul. Staszica 16, 20–081, Lublin
e-mail: pe.kutnik@gmail.com

Postępy Żywienia Klinicznego
2024, tom 19, 26–31

DOI: 10.5603/pżk.99236

ISSN 1896–3706

e-ISSN 2956–9249

ABSTRACT

Background: The patient overload brought about by the COVID-19 pandemic challenged the capacity healthcare system. The virus causes respiratory symptoms, including cough and dyspnea as well as loss of taste and smell. These symptoms can lead to reduced food intake and, in severe cases, may result in malnutrition, which is one of the important challenges among hospitalized patients.

Methods: This was a retrospective study assessing the nutritional aspects of the Intensive Care Unit (ICU) COVID-19 patients with the primary aim of analysing preadmission data and ICU stay data with the occurrence of refeeding syndrome.

Results: Out of 165 patients included in the study, 110 (66.6%) developed refeeding syndrome. The only discriminating factor of developing refeeding syndrome in this study was phosphate levels at the admission (p = 0.0001). In the study, 69 out of 165 (41.8%) patients had enteral access present at admission to ICU. All 165 patients received enteral nutrition during ICU stay at median day 1 (1–1). 38 (23%) additionally received parenteral nutrition (PN). The indications for PN were appropriate protein delivery during continuous renal replacement therapy in 30 out of 38 patients (78.9%) and persistent enteral nutrition intolerance in 8 out of 38 patients (21.1%).

Conclusion: In conclusion, monitoring for refeeding syndrome should be implemented in all patients with malnutrition risk. Nutritional education and establishing internal protocols regarding nutritional intervention could provide better care for patients. Further studies that monitor the nutritional status of ICU patients could greatly improve nutritional interventions in critically ill patients.

Key words: refeeding, nutrition in ICU, COVID-19 nutrition

STRESZCZENIE

Wstęp: Przeciążenie systemów opieki zdrowotnej spowodowane pandemią COVID-19 stanowiło wyzwanie dla wydolności i jakości procesu leczenia. Wirus SARS-COV-2 wywoływał objawy ze strony układu oddechowego, w tym kaszel i duszność, a także utratę smaku i węchu. Objawy te mogły prowadzić do zmniejszonego spożycia pokarmu, a w ciężkich przypadkach do niedożywienia, będącego jednym z wyzwań w leczeniu pacjentów.

Metody: Było to jednoośrodkowe badanie retrospektywne, w którym oceniano aspekty żywieniowe pacjentów z COVID-19 na Oddziale Intensywnej Terapii (OIT). Głównym celem badania była korelacja danych przed przyjęciem do szpitala oraz danych dotyczących pobytu na OIT z wystąpieniem zespołu ponownego żywienia.

Wyniki: Spośród 165 pacjentów włączonych do badania u 110 (66,6%) rozwinął się zespół ponownego odżywienia. Jedynym czynnikiem przy przyjęciu identyfikującym ryzyko rozwoju zespołu ponownego odżywienia w tym badaniu był poziom fosforanów (p = 0,0001). W badaniu 69 pacjentów (41,8%) miało dostęp dojelitowy obecny przy przyjęciu w OIT. Wszyscy pacjenci leczeni w OIT w trakcie badania (165) otrzymywali żywienie dojelitowe od 1. dnia (1–1); 38 pacjentów (23%) otrzymało dodatkowo żywienie pozajelitowe (PN). Wskazaniami do PN było odpowiednie dostarczanie białka podczas ciągłej terapii nerkozastępczej (30 sposród 38 pacjentów) (78,9%) oraz utrzymująca się nietolerancja żywienia dojelitowego u 8 spośród 38 pacjentów (21,1%).

Wnioski: Podsumowując, monitorowanie zespołu ponownego żywienia należy wdrożyć u wszystkich pacjentów z ryzykiem niedożywienia. Edukacja żywieniowa i ustanowienie wewnętrznych protokołów dotyczących interwencji żywieniowych może zapewnić lepszą opiekę nad pacjentami. Dalsze badania, które monitorują stan odżywienia pacjentów w OIT, mogą znacznie poprawić interwencje żywieniowe u pacjentów w stanie krytycznym.

Słowa kluczowe: zespół ponownego odżywienia, żywienie na OIT, żywienie po COVID-19

INTRODUCTION

The patient overload brought about by the COVID-19 pandemic challenged the capacity of health providers and the healthcare system as a whole. The virus causes respiratory symptoms, including cough and dyspnea as well as loss of taste and smell [1, 2]. These symptoms can lead to reduced food intake and, in severe cases, may result in malnutrition, which is one of the important challenges among hospitalized patients [3]. In 2020, expert statements were published to help healthcare providers identify, monitor, and treat those at risk of COVID-19-related malnutrition [4]. The majority of these statements were based on evidence from earlier studies that formed the basis for previous European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines. The statements included recommendations for mild, moderate, and severe courses of COVID-19, with strategies for both noninvasive and invasive respiratory support in intensive care units (ICU). They listed indications and requirements for oral, enteral (EN), and parenteral nutrition (PN) and outlined potential complications.

At the Regional Extracorporeal Membrane Oxygenation (ECMO) Centre, admitted were the most severe cases of COVID, who often required both mechanical ventilation and advanced life support techniques [5]. In critically ill COVID-19 patients, nutritional difficulties have been reported, including a high risk of malnutrition, a high rate of occurrence of refeeding syndrome, and nutritional intolerance [6]. Responding to nutritional issues played a major role in the treatment of critically ill patients. Gathering and sharing data regarding nutritional interventions among critically ill patients is an interest of many researchers. With the pandemic ending, conclusions should be drawn to improve patient care in the future.

Thus, in this study the nutritional aspects of the ICU COVID-19 patients were assessed with the primary aim of the study being to analyse preadmission data, and ICU stay data with the occurrence of refeeding syndrome.

METHODS

This was a single-centre, retrospective study approved by the local ethics committee at the Medical University of Lublin (KE-0254/14/01/2024) performed with adherence to the Declaration of Helsinki and Good Clinical Practice. Due to the retrospective nature of the study, the need for informed consent was waived. Patients' data was collected from tertiary hospital digital database screening for patients diagnosed with COVID-19 and treated in the ICU.

Included were patients aged 16–80 who were admitted to the ICU for COVID-19 treatment between November 2020 and January 2022. Patients whose hospital stays were shorter than four days and patients who did not require advanced respiratory support, including mechanical ventilation, non-invasive ventilation (NIV), and high-flow nasal oxygenation therapy (HFNOT) were excluded, as well as patients with missing data related to the parameters measured in this study.

General information was gathered at the admission point, including age, height, weight, body mass index (BMI), gender, date of COVID-19 positive test, date of admission to the centre, duration of the stay in the centre, presence of enteral access at the time of admission (nasogastric or nasojejunal tubes), need for noradrenaline infusion upon admission, and admissions serum levels of: phosphates (mmol/L normal range: 0.84–1.45), albumin (g/dL; normal range: 3.5–5.2), and total protein(g/dL normal range: 6.4–8.3).

The study included data regarding patients' stay in ICU including duration of ICU stay, the number of days that patients received enteral nutrition (EN) or parenteral nutrition (PN), which day of patient stay EN or PN was introduced, and the prevalence of EN or PN as a nutrition strategy during patient stays (defined as the number of days patients received EN or PN divided by the number of days patients stayed in the centre; for PN, included were only patients qualified for PN. Additionally, collected were laboratory measurements of the lowest serum phosphates, the last measures of albumin and total protein during ICU stay.

The primary aim of the study was to analyse preadmission data, and ICU stays data with the occurrence of the refeeding syndrome (defined as refeeding hypophosphatemia of < 0.65 mmol/L or a drop of at least 0.16 mmol/L after the introduction of the nutritional intervention).

Secondary aims of the study included:

1. Factors assessment associated with the prevalence of enteral access at the admission.
2. Correlation of preadmission and ICU stay data with the need for PN intervention, implementation of continuous renal replacement therapy (CRRT), and ICU mortality.
3. Evaluation of above events on how they changed albumin and total protein levels during ICU stay by calculating the change between admission levels and the last measured levels of serum albumin and total protein (defined as the admission levels minus the last measured levels).

Statistical data was collected using Microsoft Excel spreadsheets (Microsoft, Redmond, WA, USA). Categorical variables were presented as numbers and frequencies and analysed using the Chi-square test. Continuous variables were tested for normal distribution using the Kolmogorov-Smirnov, Lilliefors, and Shapiro-Wilk tests. Normally distributed continuous variables are presented as means and standard deviations of the mean and were analysed using Student's t-test. Non-normally distributed variables are presented as medians and interquartile ranges (IQRs) and were analysed using the Mann-Whitney U test. All statistical calculations were performed using Statistica 14.0 (StatSoft Inc., Tulsa, OK, USA).

RESULTS

228 patients were screened and 165 met the inclusion criteria, of whom 70.3% were male. Of the patients included in the study, 90.3% were transferred to the study centre from other hospitals. The patients' mean age was 51 years, and the mean BMI was 32.5 kg/m^2. Detailed data regarding preadmission and ICU data from the entire study population is presented in Table 1.

Table 1. Study population preadmission and ICU stay data

	Study population (n = 165)
Preadmission data	
Days from positive COVID-19 test to admission to the centre [days, IQR]	8 (4–11)
Admission phosphates [mmol/L, IQR]	1.28 (0.98–1.57)
Admission total protein [g/dL, SD]	5.31 ± 0.69
Admission albumin [g/dL, SD]	2.73 ± 0.49
Prevalence of enteral access at admission [n, %]	69 (41.8)
Noradrenalin infusion upon admission [n, %]	64 (38.8)
ICU stay data	
Duration of stay in the centre [days]	12 (8.5–18)
Prevalence of patients receiving EN [n, %]	165 (100)
Day of starting EN [days, IQR]	1 (1–1)
Prevalence of EN as a nutrition strategy during patient stay (%, IQR)	100 (90–100)
Prevalence of patients receiving PN [n, %]	38 (23)
Day of starting PN [days, IQR]	9 (6–12)
Prevalence of PN as a nutrition strategy during patient stay (%, IQR)	32.8 (20–53.3)
Lowest phosphates [mmol/L, IQR]	0.75 (0.6–0.88)
Last measure total protein [g/dL, SD]	5.07 ± 0.74
Last measured albumin [g/dL, SD]	2.3 ± 0.5

IQR — interquartile range; SD — standard deviation; EN — enteral nutrition; PN — parenteral nutrition; CRRT — continuous renal replacement therapy

Refeeding syndrome

Refeeding syndrome defined as hypophosphatemia occurred in 110 patients in this study (66.6%). The refeeding syndrome analysis is presented in Table 2.

Enteral access at admission

Patients admitted to the centre with enteral access showed a statistically longer mean time between the date of positive COVID-19 test and admission to the centre than

Table 2. Comparison of patients with and without refeeding syndrome

	Patients with refeeding syndrome (n = 110)	Patients without refeeding syndrome (n = 55)	P-value
Age [years, SD]	49.7 ± 12.3	53.3 ± 12.7	0.08
BMI [kg/m^2, SD]	32.4 ± 6.5	32.6 ± 5.3	0.81
Days from positive COVID-19 test to admission to the centre [days, IQR]	8 (5–11)	8 (4–12)	0.89
Admission phosphates [mmol/L, IQR]	1.23 (0.91–1.44)	1.42 (1.11–1.84)	0.0001
Admission total protein [g/dL, SD]	5.26 ± 0.73	5.41 ± 0.62	0.2
Admission albumin [g/dL, SD]	2.69 ± 0.48	2.81 ± 0.47	0.14
Prevalence of enteral access at admission [n, %]	21 (38.2)	48 (43.6)	0.5
Lowest phosphates [mmol/l, IQR]	0.63 (0.53–0.75)	0.95 (0.87–1.21)	<0.0001
Last measure total protein [g/dL, SD]	5.12 ± 0.75	4.97 ± 0.71	0.27
Last measured albumin [g/dL, SD]	2.31 ± 0.48	2.30 ± 0.54	0.89
Prevalence of patients receiving PN [n, %]	13 (23.6)	25 (22.7)	0.65
CRRT [n, %]	17 (15.5)	25 (45.5)	0.0003
Mortality [n, %]	85 (77.3)	43 (78.1)	0.89

IQR — interquartile range; SD — standard deviation; PN — parenteral nutrition; CRRT — continuous renal replacement therapy patients without enteral access (median 7 days (IQR: 4–11) vs. median 9 days (IQR: 6–13), p = 0.02). The absence of enteral access upon admission was not associated with mortality (76.6% vs. 81.1%, p = 0.48) and the need for noradrenaline infusion upon admission (36.2% vs. 43.5%, p = 0.35). No statistical difference was observed between patients admitted with and without enteral access in terms of admission laboratory parameters [i.e., serum total protein (p = 0.43), serum albumin (p = 0.35), and serum phosphates (p = 0.23)].

Parenteral nutrition

The two identified indications for PN were appropriate total protein delivery during CRRT in 30 out of 38 patients (78.9%) and persistent enteral nutrition intolerance in 8 out of 38 patients (21.1%). Patients receiving PN had a statistically longer median stay at the centre than patients without PN (median 15 days (IQR: 10–21) vs. 11 days (IQR: 8–16), p = 0.003. They also presented with lower last measured serum albumin but not lower last measured total protein (2.04 ± 0.48 vs. 2.39 ± 0.48, p = 0.0003; 4.99 ± 0.65 vs. 5.1 ± 0.76, p = 0.43, respectively). The implementation of PN did not affect the change between admission and last measured serum albumin (p = 0.21), and total protein (p = 0.74).

Continuous renal replacement therapy

The CRRT was implemented in 42 (25.5%) of all study patients. Patients undergoing CRRT had decreased last measured albumin and total protein in comparison to patients without CRRT (2.04 ± 0.52 vs. 2.38 ± 0.47, p = 0.0005; 5.07 ± 0.69 vs. 5.06 ± 0.79 p = 0.63). No statistically significant change of admission and last measured albumin (p = 0.1), or total protein (p = 0.64) was found between patients with and without CRRT. Patients requiring CRRT also presented with higher admission phosphate levels (1.48 (IQR: 1.15–1.95) vs. 1.21 (QR: 0.95–1.43), p = 0.0001), as well as higher lowest measured phosphate during ICU stay (0.86 (IQR: 0.75–1.12) vs. 0.7 (IQR: 0.57–0.84), p = 0.0001).

Mortality

The general mortality of all patients was 77.6% (128/165). No significant nutritional predictors of mortality were found upon admission. It was observed that mortality was associated with a decreased value in the last measured serum total protein and albumin levels in comparison to survivors (4.98 ± 0.67 vs. 5.38 ± 0.86, p = 0.005, and 2.24 ± 0.47 vs. 2.53 ± 0.54, p = 0.002, respectively). The change between admission and last measured serum albumin was also significantly smaller in survivors (0.27 ± 0.61 vs. 0.57 ± 0.69, p = 0.02). Survivors also spent more days in the centre (median 18 days (IQR: 11–27) vs. 11 days (IQR: 8–16), p = 0.0005). Use of PN was similar in both survivors and nonsurvivors (22.2% vs. 30.6%, p = 0.88).

DISCUSSION

The results of this study highlight some of the challenges of treating COVID-19 patients in ICU settings. Due to the nature of the study ICU, during COVID-19, it acted as one of the main extracorporeal membrane oxygenation centres in the country; thus, over 90% of all admissions to the centre came from other hospitals.

Due to the nature of the admitted patients, the authors were unable to perform nutritional screening. However, they found a median of eight days from patients' positive COVID-19 test to admission to the centre with symptoms such as coughing, dyspnoea, and loss of taste and smell, all of which affect food consumption, as well as a lack of enteral access, suggesting a high risk for malnutrition among the study population. In the present study, 66.6% of patients met the hypophosphate refeeding syndrome criteria. A previous study reported a high risk of refeeding syndrome among COVID-19 patients, reaching up to 82% of all critically ill cases and developing in 36% of patients [7]. In the present cohort, the occurrence of refeeding syndrome was almost two times higher than in the aforementioned study, which supports the theory of inadequate nutritional interventions in the preadmission period. Lower, but still within normal range, admission phosphate levels were the only predictive factor of developing refeeding syndrome in patients from the present study. All other measured in this study factors, such as admission albumin and total protein serum levels, or duration of COVID-19, did not predict the development of refeeding syndrome. This further confirms that after the introduction of nutritional intervention for the patients with malnutrition risk, careful monitoring for development of refeeding syndrome should be implemented. And the standard laboratory markers of malnutrition including albumin and total protein levels can be implemented in elective patients, but not in acute phases of severe diseases [8].

Patients undergoing CRRT had a statistically significant lower percentage of identified incidents of refeeding syndrome. This phenomenon is most likely not associated with the better nutritional status of patients with renal failure but rather with the diagnostic criteria of refeeding syndrome, which include electrolyte imbalance caused by renal insufficiency. The diagnostic criteria for and the management of refeeding syndrome in patients undergoing CRRT, as well as its impact, remain elusive due to a lack of high-quality evidence. It is reasonable to assume that similar precautions should be taken to prevent potential harm caused by overfeeding malnourished patients undergoing CRRT.

The majority of the patients in this study were mechanically ventilated at admission, while enteral access at admission was present in roughly 42% of cases. According to ESPEN guidelines, oral nutrition should be the first choice of nutritional intervention followed by enteral nutrition if oral nutrition is contraindicated or nonviable [9]. In the centre, the median for starting EN was day one, which makes the lack of enteral access upon admission difficult to explain. There has been discussion about EN patients receiving NIV or HFNOT support and the fact that placing nasogastric tubes often results in mask air leakage and air stomach dilatation, which affects ventilation and may potentially lead to vomiting [10]. However, the evidence regarding these issues remains scant, and after invasive mechanical ventilation was implemented in the patients, the enteral nutrition should be started unless it was contraindicated. Some situations that have been previously considered contraindications are no longer considered so; these include the use of vasopressors or neuromuscular blocking agents or prone position implementation [11]. A small number of patients who were admitted to the centre from ICUs in other hospitals and who already had enteral access may have been exposed to a lack of enteral nutrition protocols. In a study by Kim et al., implementation of such protocols increased the number of patients receiving EN within the first 24 hours of admission and significantly reduced the time that elapsed from admission to implementation of EN [12]. Overall, sites that have implemented nutritional protocols use more EN alone, better manage enteral mobility issues, and achieve better nutritional adequacy in comparison with sites without such protocols [13]. Constant education and encouragement to implement EN protocols could increase the number of patients receiving EN in the country.

Parenteral nutrition (PN) was used in 23% of the present study's patients, which is similar to a large study conducted in Italy [14]. The main causes for implementing PN were inadequate nutrient delivery during CRRT (78.9%) and enteral nutrition intolerance (21.1%). Despite use of parenteral nutrition mostly in CRRT patients they still had lower last measured albumin levels probably due to increased amino acid clearance, which increases the demand for protein intake. The implementation of PN did not affect mortality in the study patients. In this study, the potential complications of parenteral nutrition, such as central venous access infections, were not evaluated, due to multiple factors, including prolonged ICU stays, which could have altered the results.

This study did not find any significant nutritional factors that directly affected the mortality of the patients. A severe COVID-19 course has been associated with extremely high mortality in ICUs, reaching over 80% in some studies [15]. It is still unclear which major factors affected the survival rate of COVID-19 patients during the pandemic. Thus, it is rather unlikely that nutrition as a single factor is associated directly with mortality. However, it could be part of a multifactorial model that, despite multiple studies, has still not been determined almost two years after the pandemic. In the present study, despite similar nutritional interventions in survivors and non-survivors, total protein and albumin serum levels were statistically higher in survivors. This is in line with findings suggesting that both these parameters represent overall patient condition and not nutritional status in intensive care patients [16]. There is still. no nutritional marker that can be objectively measured by a laboratory test in the ICU. It is needed to combine daily physical examination, assessment of nutritional intervention, general laboratory testing, and the personal experience to assess patients' nutritional status in the ICU.

This study has some limitations. It was a retrospective, single-centre study of the most critically ill patients, who often required advanced life support techniques; thus, the results do not apply to all COVID-19 patients with severe illness. Proper nutritional screening could not be performed in mechanically ventilated patients at the time of admission, and there was no access to information about nutritional interventions from the referring centres. Due to a lack of computerized data, it was impossible to assess the nutritional provisions of the patients, which could be a factor in the occurrence of refeeding syndrome.

In conclusion, the COVID-19 pandemic was a challenging period that resulted in an overload of patients in many ICUs. Monitoring for refeeding syndrome should be implemented in all patients with malnutrition risk. Focus must be put on nutritional education as well as on establishing internal protocols regarding nutritional intervention to provide better care for patients, even in difficult times. Further studies that monitor the nutritional status of ICU patients could greatly improve nutritional interventions in critically ill patients.

Conflict of interest: None declared.
Funding: None

REFERENCES

1. Dawson P, Rabold EM, Laws RL, et al. Loss of taste and smell as distinguishing symptoms of coronavirus disease 2019. Clin Infect Dis. 2021; 72(4): 682–685, doi: 10.1093/cid/ciaa799, indexed in Pubmed: 32562541.
2. Piwowarczyk P, Szczukocka M, Kutnik P, et al. Risk factors and outcomes for acute respiratory failure in coronavirus disease 2019: An observational cohort study. Adv Clin Exp Med. 2021; 30(2): 165–171, doi: 10.17219/acem/130603, indexed in Pubmed: 33382215.
3. Kutnik P, Wichowska O, Sysiak-Sławecka J, et al. Malnutrition risk in elective surgery patients and effectiveness of preoperative nutritional interventions at a pre-anaesthetic clinic: a 4-year apart, single-centre, observational study. Anaesthesiol Intensive Ther. 2023; 55(3): 179–185, doi: 10.5114/ait.2023.130632, indexed in Pubmed: 37728445.
4. Barazzoni R, Bischoff SC, Breda J, et al. endorsed by the ESPEN Council. ESPEN expert statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection. Clin Nutr. 2020; 39(6): 1631–1638, doi: 10.1016/j.clnu.2020.03.022, indexed in Pubmed: 32305181.
5. Kutnik P, Szczukocka M, Borys M, et al. Procalcitonin dynamics, lactates, and haemoglobin serum levels might be a useful predictive tool of mortality in patients undergoing veno-venous extracorporeal oxygenation membrane support. Single centre experience. Anaesthesiol Intensive Ther. 2019; 51(5): 343–347, doi: 10.5114/ait.2019.90235, indexed in Pubmed: 31893600.
6. Nguyen LT, Ta TV, Bui AnT, et al. Nutritional Status, Refeeding Syndrome and Some Associated Factors of Patients at COVID-19 Hospital in Vietnam. Nutrients. 2023; 15(7), doi: 10.3390/nu15071760, indexed in Pubmed: 37049600.
7. Vahdat Shariatpanahi Z, Vahdat Shariatpanahi M, Shahbazi E, et al. Refeeding syndrome and its related factors in critically Ill coronavirus

disease 2019 patients: A prospective cohort study. Front Nutr. 2022; 9: 830457, doi: 10.3389/fnut.2022.830457, indexed in Pubmed: 35479751.

8. Kutnik P, Bierut M, Rypulak E, et al. The use of the ERAS protocol in malnourished and properly nourished patients undergoing elective surgery: a questionnaire study. Anaesthesiol Intensive Ther. 2023; 55(5): 330–334, doi: 10.5114/ait.2023.134190, indexed in Pubmed: 38282499.
9. Singer P, Blaser AR, Berger MM, et al. ESPEN practical and partially revised guideline: Clinical nutrition in the intensive care unit. Clin Nutr. 2023; 42(9): 1671–1689, doi: 10.1016/j.clnu.2023.07.011, indexed in Pubmed: 37517372.
10. Leder SB, Siner JM, Bizzarro MJ, et al. Oral alimentation in neonatal and adult populations requiring high-flow oxygen via nasal cannula. Dysphagia. 2016; 31(2): 154–159, doi: 10.1007/s00455-015-9669-3, indexed in Pubmed: 26590570.
11. Wischmeyer PE. Overcoming challenges to enteral nutrition delivery in critical care. Curr Opin Crit Care. 2021; 27(2): 169–176, doi: 10.1097/MCC.0000000000000801, indexed in Pubmed: 33395086.
12. Kim SH, Park CM, Seo JM, et al. The impact of implementation of an enteral feeding protocol on the improvement of enteral nutrition in critically ill adults. Asia Pac J Clin Nutr. 2017; 26(1): 27–35, doi: 10.6133/apjcn.122015.01, indexed in Pubmed: 28049258.
13. Heyland DK, Cahill NE, Dhaliwal R, et al. Impact of enteral feeding protocols on enteral nutrition delivery: results of a multicenter observational study. JPEN J Parenter Enteral Nutr. 2010; 34(6): 675–684, doi: 10.1177/0148607110364843, indexed in Pubmed: 21097768.
14. Tetamo R, Fittipaldi C, Buono S, et al. Nutrition support for critically ill patients during the COVID-19 pandemic: the Italian SIAARTI survey. J Anesth Analg Crit Care. 2022; 2(1): 35, doi: 10.1186/s44158-022-00063-6, indexed in Pubmed: 37386650.
15. Lavrentieva A, Kaimakamis E, Voutsas V, et al. An observational study on factors associated with ICU mortality in Covid-19 patients and critical review of the literature. Sci Rep. 2023; 13(1): 7804, doi: 10.1038/s41598-023-34613-x, indexed in Pubmed: 37179397.
16. Singer P, Blaser AR, Berger MM, 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, indexed in Pubmed: 30348463.