Nutrición Hospitalaria

Trabajo Original

Effects of intravenous fluid overload on caloric and protein deficit in critically ill patients

Efectos de la sobrecarga de líquidos por vía intravenosa en el déficit calórico y proteico en pacientes críticamente enfermos

Suzana Souza Arantes[1], João Manoel Silva Jr[2], José Eduardo de Aguilar-Nascimento[3] and Diana Borges Dock-Nascimento[4]

[1]Nutrition. Centro Universitario de Varzea Grande (UNIVAG). Cuiabá, Mato Grosso. Brazil. [2]Physics. Institute for Medical Assistance for State-Level Government Employees (IAMSPE). São Paulo, Brazil. [3]Graduate Program in Health Sciences. Federal University of Mato Grosso (UFMT). Cuiabá, Mato Grosso. Brazil. Brazilian Society of Parenteral and Enteral Nutrition (BRASPEN, SBNPE). UNIVAG Medical School. Várzea Grande, Mato Grosso. Brazil. [4]Department of Food and Nutrition and Health Sciences Postgraduate Course. Federal University of Mato Grosso (UFMT). Cuiabá, Mato Grosso. Brazil

Abstract

Introduction: intravenous fluid overload may lead to dysmotility that may impair early enteral nutrition delivery in critically ill patients.

Objectives: this study aimed to compare the volume of intravenous fluids (IF) with the occurrence of caloric and protein deficits in Intensive Care Unit (ICU) patients.

Methods: this cohort study included critically ill patients with mechanical ventilation and receiving early enteral nutrition (target: 25-30 kcal/kg/day and 1.25-2.0 g of protein/kg/day). Over the first five days the volume of IF infused and caloric/protein deficits were calculated.

Results: eighty-six critically ill patients (SAPS III score: 62 ± 10) with a mean age of 68 (18-91) years were enrolled. Patients received a median of 2,969 (920-5,960) ml/day of IF, which corresponded to a median of 41.6 (17.0-88.2) ml/kg/day and 10.7 (3.31-21.45) g of sodium/day. All patients had a caloric deficit (mean: 1,812 ± 850 kcal over five days) and in 23 (27%) this deficit exceeded 480 kcal/day. The mean protein deficit was 94.6 ± 5.9 g over five days, and 34 patients (40%) had more than 20 g of deficit/day. Patients with caloric deficit greater than 480 kcal/day received approximately 1.5 l of IF and 10 g of NaCl more than the other patients. Similarly, patients with protein deficit greater than 20 g/day received approximately 3 l of IF and 25 g of NaCl more than the other patients. Mortality was greater in patients with critical protein deficit (69% *vs* 41.1%; p = 0.01).

Conclusion: in critically ill patients receiving enteral nutrition, the volume of intravenous fluids infused affected nutrition delivery and increased caloric and protein deficits.

Key words:

Critical care. Intravenous fluid. Enteral nutrition. Caloric deficit. Protein deficit.

Resumen

Introducción: la sobrecarga de líquidos por vía intravenosa puede provocar dismotilidad que puede afectar el suministro de nutrición enteral temprana en pacientes críticos.

Objetivos: este estudio tuvo como objetivo comparar el volumen de líquidos por vía intravenosa (IF) con la aparición de déficit calórico y proteico en pacientes de la Unidad de Cuidados Intensivos (UCI).

Métodos: este estudio de cohorte incluyó a pacientes críticamente enfermos con ventilación mecánica que recibían nutrición enteral temprana (*target*: 25-30 kcal/kg/día y 1,25-2,0 g de proteína/kg/día. Durante los primeros cinco días calculamos el volumen de IF y el déficit calórico/proteico.

Resultados: ochenta y seis pacientes críticamente enfermos (SAPS III: 62 ± 10) con una edad media de 68 (18-91) años fueron estudiados. Los pacientes recibieron una mediana de 2.969 (920-5.960) ml/día de IF, que correspondió a una mediana de 41,6 (17,0-88,2) ml/kg/día y a 10,7 (3,31-21,45) g de sodio/día. Todos los pacientes tenían déficit calórico (media: 1.812 ± 850 kcal en cinco días) y en 23 (27%) este déficit excedía las 480 kcal/día. El déficit medio de proteínas fue de 94,6 ± 5,9 g en cinco días y 34 pacientes (40%) tuvieron más de 20 g de déficit/día. Los pacientes con un déficit calórico superior a 480 kcal/día recibieron aproximadamente 1,5 l de IF y 10 g de NaCl más que los otros pacientes. De forma similar, los pacientes con un déficit de proteínas mayor de 20 g/día recibieron aproximadamente 3 l de IF y 25 g de NaCl más que los otros pacientes. La mortalidad fue mayor en pacientes con déficit proteico crítico (69% *vs.* 41,1%; p = 0,01).

Conclusión: en pacientes críticamente enfermos que reciben nutrición enteral, el volumen de líquidos intravenosos infundidos afecta el suministro de nutrición y aumenta el déficit de calorías y proteínas.

Palabras clave:

Cuidados intensivos. Líquidos intravenosos. Nutrición enteral. Déficit calórico. Déficit de proteínas.

Correspondence:

Diana Borges Dock-Nascimento. Department of Food and Nutrition and Health Sciences Postgraduate Course. Federal University of Mato Grosso (UFMT). Av. Fernando Corrêa da Costa, 2367. Bairro Boa Esperança. 78060-900 Cuiabá, Mato Grosso. Brazil e-mail: dianadock@hotmail.com

INTRODUCTION

Patients with systemic inflammatory responses experience intense catabolism that aggravates their clinical and nutritional status, and the consequences of these events are high complication and mortality rates (1,2). The optimization of intravenous fluid management and nutritional intake is fundamental in the care of critically ill patients. The objective of intravenous fluid therapy is to maintain adequate intravascular volume and prevent tissue hypoperfusion and organ dysfunction (3,4). However, continued and repeated infusion of fluids results in edema, electrolyte imbalance, and inadequate weight gain, all of which contribute to worse outcomes including increase of mortality (5-7). In addition, patients also receive fluids through diluents, medications, nutrition, and maintenance fluids (8). Therefore, similar to other medications, fluids have qualitative and quantitative adverse effects (9,10).

Strategies to prevent fluid overload are beneficial after hemodynamic stability (11). Enteral nutrition is one of the recommended methods for feeding critically ill patients (12). Enteral nutrition provision and fluid therapy should be balanced as continuous fluid infusion may lead to edema of the mesentery and intestinal wall, which results in dysmotility, vomiting, and ileus, all of which compromise the provision of enteral nutrition (13). According to the guidelines of the Surviving Sepsis Campaign (14), patients with septic shock should receive fluid resuscitation with an initial administration of 30 ml of fluid/kg of body weight. In line with this recommendation, the British Consensus Guidelines on Intravenous Fluid Therapy for Adult Surgical Patients suggests a more restrictive fluid volume (15,16).

Because no study has assessed the relationship between fluid administration and enteral nutrition infusion, the present study aimed to evaluate the effect of intravenous fluid administration on caloric and protein deficits in critically ill patients on mechanical ventilation and exclusively receiving enteral nutrition.

MATERIAL AND METHODS

This prospective cohort study was conducted between June 2014 and December 2015 in a tertiary hospital. The study was approved by the Human Research Ethics Committee of the Júlio Müller Hospital and was conducted according to the 1975 Declaration of Helsinki, revised in 2000. The relatives or guardians of the included patients provided informed consent, if the own patient could not sign the term.

INCLUSION AND EXCLUSION CRITERIA

The study included consecutive critically ill non-surgical patients who were admitted for a minimum of five days for clinical treatment, who were on mechanical ventilation in the intensive care unit (ICU), and who received exclusive enteral nutrition. The study excluded pregnant patients, patients with late introduction to enteral feeding (> 48 h after admission), patients who received parenteral nutrition associated or not to enteral nutrition, and patients who died within the first five days of hospitalization.

INSTITUTIONAL NUTRITIONAL THERAPY PROTOCOL

Enteral feeding was initiated within 24 h after hemodynamic stability was reached and after the confirmation of the feeding tube position in the X-ray. Caloric and protein requirements were calculated according to the guidelines from the European Society for Parenteral and Enteral Nutrition (12). The targets were 25-30 kcal/kg of body weight and 1.25-2.0 g of protein/kg of body weight. The goal was to reach the targets on the third or fourth day of the nutrition regimen. To achieve this goal, either one-third or one-fourth of the calculated daily enteral feeding requirements was prescribed per day.

DEMOGRAPHIC, CLINICAL, NUTRITIONAL, BIOCHEMICAL AND MORTALITY-RELATED DATA

Age, sex, body weight, and nutritional status during the first 24 h of hospitalization were recorded. The illness severity score was determined using the Simplified Acute Physiology Score 3 (SAPS 3) in the ICU. The five-day caloric and protein requirements and deficits were calculated. Levels of C-reactive protein (mg/l), albumin (g/dl), lactate (mg/dl), and serum glucose (mg/dl) were measured daily. The serum albumin level was dichotomized into ≥ 3.5 g/dl or < 3.5 g/dl. Mortality at 28 days and length of hospital stay were recorded. Each patient's nutritional status was evaluated using the Subjective Global Assessment (SGA), which divides patients into the categories of SGA A (eutrophic), SGA B (at risk of malnutrition or moderate malnutrition), or SGA C (severe malnutrition).

CALORIC AND PROTEIN DEFICITS

Caloric and protein deficits were calculated on the fifth day of hospitalization. These calculations determined the difference between the prescribed amounts of calories and protein and the amount received over the course of the five days. All prescriptions of calories and protein followed the guidelines cited above (12). For statistical analysis, the patients were divided into two groups according to caloric and protein deficits: a) those with a caloric deficit (i.e., ≥ 480 kcal/day) and/or with a critical protein deficit (i.e., ≥ 20 g of protein/day); and b) those with no caloric deficit and/or critical protein deficit (deficits which did not reach the aforementioned levels). These parameters were based on a previous study (17) that showed that these limits of caloric and protein deficits are significantly sensitive for predicting the risk of mortality.

VOLUME OF INTRAVENOUS FLUIDS AND SODIUM

The volumes of intravenous fluids administered to the patients during the first five days of hospitalization were recorded. These fluids included crystalloid fluids (0.9% saline solution; simple Ringer's solution, lactated Ringer's solution, or glucose solution), colloid fluids of any type, distilled water/drug diluting solution, medications, and blood or blood products. In addition, the total volumes of sodium infused intravenously on the first day and over the five days of hospitalization were calculated using the information on the products' leaflets.

PRIMARY ENDPOINT

The primary endpoint consisted in comparing the volume of intravenous fluids received by patients with or without caloric and/or protein deficits (according to the previously described limits). The volumes of sodium and sodium chloride administered to the two groups of patients were also compared.

STATISTICAL ANALYSIS

Continuous variables were initially analyzed using Levene's test to assess homogeneity, followed by the Kolmogorov-Smirnov test to determine normality. Student's t-test was used to compare continuous variables. Dichotomous variables were compared using the Fisher's exact test or the Chi-square test with Yates' correction. Data are expressed as mean ± standard deviation or as median and minimum-maximum. Statistical significance was set at 5% ($p < 0.05$). Statistical Package for the Social Sciences, version 17.0 (IBM Corp., Armonk, NY) was used to analyze the data.

RESULTS

Eighty-six patients hospitalized for a minimum of five days and on mechanical ventilation and on exclusively enteral therapy were prospectively studied. The patients' data are shown in table I. Mortality was 41.9% (n = 36) and median SAPS 3 score was 63 (interquartile range: 52.7-79).

INFUSION OF INTRAVENOUS FLUIDS AND SODIUM

The patients received 2,969 (range: 920-5,958) ml of intravenous fluid/day in the first five days, which is equivalent to 41.6 (range: 17.0-88.2) m/kg/day. On the first day, 3,015 (range: 1,195-9,280) ml/day and 44.4 (range: 16-168) ml/kg/day of intravenous fluids were administered. During this period, the patients received 134 (range: 41-268) ml of sodium chloride/day and 10.7 (range: 3.3-21.4) g of sodium/day. Sixty-five

Table I. Demographic, clinical, nutritional and biochemical data of the patients

Variable	Median	Range
Age (years)	68	18-91
Sex (n; %)		
Female	47	54.7
Male	39	45.3
Weight (kg)	70	40-130
Malnourished (n; %)	22	25.6
SAPS 3	63	29-94
Length of hospital stay (days)	21	5-202
Death (n; %)	50	58.8%
Caloric requirements (kcal)	1,750	1,000-2,500
Protein requirements (g)	95	48-165
Caloric deficit (kcal)	1,635	146.5-4,215
Protein deficit (g)	87	6.5-251
CRP (mg/l)	125	17-323
Albumin (g/dl)	2.9	1.5-4.8
Lactate (mg/dl)	24	10-68
Glucose (mg/dl)	182	94-353

SAPS 3: Simplified Acute Physiology Score 3; CRP: C-reactive protein. Data expressed as median, minimum-maximum, or number of cases and percentage.

patients (76.5%) received more than 30 ml of fluid/kg of body weight/day over the five days.

INFUSION OF ENTERAL NUTRITION

Enteral nutrition was initiated up to 48 h after admission in all patients. The mean percentage of enteral feeding infusion during the first five days was 67 ± 19.8% of the prescribed volume. Only 24.4% of the patients (n = 21) received ≥ 80% enteral feeding and 20.9% (n = 18) received < 50% enteral feeding in the first five days of hospitalization.

CALORIC AND PROTEIN DEFICITS

All patients exhibited caloric deficits, with the mean of 1,812 ± 850 calories over five days and 362 ± 170 kcal/day. Similarly, all patients had protein deficits (mean: 94.6 ± 45.9 g over five days and 18.9 ± 9.2 g/day). Twenty-three patients (27.0%) exhibited critical caloric deficits (≥ 480 kcal/day) and 34 (40%) exhibited critical protein deficits (≥ 20 g per day). Mortality was greater in patients with critical protein deficit (69% *vs* 41.1%; p = 0.01) but did not differ in patients with critical caloric deficit (58.7% *vs* 56.5%; p = 0.85) compared to patients without critical deficits.

Table II shows the comparison between the volume of intravenous fluids, sodium chloride, and sodium infused to patients and the extent of their caloric deficits. Table III shows the comparison between these infused fluids and the extent of the patients' protein deficits. Critical protein deficits and critical caloric deficits were associated with a higher volume of infused fluids, sodium, and sodium chloride (p < 0.01 in all comparisons).

CLINICAL AND LABORATORY VARIABLES AND INTRAVENOUS FLUID

Tables IV and V show the comparison between the clinical, demographic, and laboratory variables and the extent of caloric and protein deficits, respectively. The level of serum albumin was significantly lower in patients with critical caloric deficits than in those without. There was no difference in the clinical and biochemical results between the patients with and those without critical protein deficits (Table V).

DISCUSSION

The findings of this study indicate that excessive infusion of intravenous fluids and sodium is associated with caloric and protein deficits in critically ill patients receiving exclusive enteral nutrition. A positive fluid balance of fluids in critically ill patients may disturb gastrointestinal function by causing edema of the intestinal wall, gastroparesis, and ileus, all of which are associated with worse outcomes (1,18). Complications such as pulmonary edema, poor wound healing, and intestinal dysmotility can be reduced with fluid restriction (19,20).

In the present study, some patients received more than 80 ml of intravenous fluids/kg/day. This may have resulted in unrecorded gastrointestinal complications, which may have contributed to the caloric and protein deficits.

An increased mortality rate may be expected in patients who received aggressive fluid therapy (21). Since the publication of the early goal-directed therapy study (22), there have been significant changes in approaches to fluid resuscitation in case of critical

Table II. Comparison of the extent of caloric deficits and the infusion of intravenous fluids, sodium chloride and sodium

Variable	Critical caloric deficit (≥ 480 kcal/day) (n = 23)	Non-critical caloric deficit (< 480 kcal/day) (n = 62)	p
Fluids accumulated within five days (ml)	16,234 ± 4,816	14,908 ± 5,249	0.01
Fluids accumulated per day (ml)	3,246 ± 963	2,981 ± 1,049	0.01
Fluids accumulated on the first day (ml)	3,853 ± 1,611	3,225 ± 1,312	0.01
NaCl (g)	146 ± 43	134 ± 47	0.01
Na$^+$ (g)	58.4 ± 17.3	53.7 ± 18.9	0.01
Na$^+$ (g)/day	11.7 ± 3.4	10.7 ± 3.8	0.01

Data expressed as mean ± standard deviation.

Table III. Comparison of the extent of protein deficits and the infusion of intravenous fluids, sodium chloride and sodium

Variable	Critical protein deficit (≥ 20 g/day) (n = 34)	Non-critical protein deficit (< 20 g/day) (n = 51)	p
Fluids accumulated within five days (ml)	16,945 ± 4,717	14,147 ± 5,150	0.01
Fluids accumulated per day (ml)	3,389 ± 943	2,829 ± 1,030	0.01
Fluids accumulated on the first day (ml)	3,842 ± 1,649	3,100 ± 1,167	0.01
NaCl (g)	152 ± 42	127 ± 46	0.01
Na$^+$ (g)	61.0 ± 16.9	50.9 ± 18.5	0.01
Na$^+$ (g)/day	12.2 ± 3.4	10.2 ± 3.7	0.01

Data expressed as mean ± standard deviation

Table IV. Comparison of calorie deficits and patients' data

Variable	Critical caloric deficit (≥ 480 kcal/day) (n = 23)	Non-critical caloric deficit (< 480 kcal/day) (n = 62)	p
Sex (n; %)			0.09
Male	9 (19.1)	38 (80.2)	
Female	14 (35.9)	25 (64.1)	
Age (years)	62.8 ± 19.2	65.8 ± 16.2	0.47
Nutritional status (n; %)			0.40
Well nourished	19 (29.7)	45 (70.3)	
Malnourished	4 (18.2)	18 (81.8)	
SAPS 3	60.9 ± 13.7	66.0 ± 17.1	0.45
Lactate (mg/dl)	24.3 ± 10.9	23.5 ± 11.3	0.75
CRP (mg/l)	132.7 ± 84.3	122.9 ± 83.4	0.63
Serum albumin (g/dl)	2.69 ± 0.49	2.98 ± 0.56	0.03

SAPS 3: Simplified Acute Physiology Score 3; CRP: C-reactive protein. Data are expressed as mean ± standard deviation or number of cases and percentage.

Table V. Comparison of the extent of protein deficits and the patients' data

Variable	Critical protein deficit (≥ 20 g/day) (n = 23)	Non-critical protein deficit (< 20 g/day) (n = 62)	p
Sex (n; %)			0.07
Male	14 (29.8)	33 (70.2)	
Female	20 (51.3)	19 (48.7)	
Age (years)	62.4 ± 18.0	66.8 ± 16.2	0.25
Nutritional status (n; %)			0.10
Well nourished	29 (45.3)	35 (54.7)	
Malnourished	5 (22.7)	17 (77.3)	
SAPS 3	64.2 ± 15.9	64.9 ± 16.9	0.92
Lactate (mg/dl)	22.6 ± 6.9	24.5 ± 13.3	0.48
CRP (mg/l)	119.8 ± 78.9	129.5 ± 87.1	0.60
Serum albumin (g/dl)	2.84 ± 0.52	2.94 ± 0.57	0.10

SAPS 3: Simplified Acute Physiology Score 3; CRP: C-reactive protein. Data are expressed as mean ± standard deviation or number of cases and percentage.

illness. Several studies have indicated that the conservative use of fluids is more beneficial than liberal use (23-25). In most cases, approximately 30 ml/kg/day is sufficient for maintenance.

In the present study, an infusion of more than 30 ml/kg/day was recorded in up to 75% of the patients, which may have contributed to the lower infusion of enteral nutrition and increased caloric and protein deficits. This present study confirmed a previous study in our ICU (17) relating protein deficit in critically ill patients receiving enteral nutrition to greater mortality. Several studies have shown that the mean percentage of infused enteral nutrition is 50% to 70% of the prescribed volume (2,26-28). The excessive administration of fluids and sodium may have a role with that. In this context, caloric and protein deficits result in increased mechanical ventilation-free days, and increased length of hospital stay; these deficits represent an independent factor for death (18,29). Moreover, when caloric and protein targets are met, the result is reduced mortality rates (30,31). The adequate infusion of proteins reduces protein catabolism by 50%, improves nitrogen balance (32), and reduces days on mechanical ventilation and (33) mortality (34). In the present study, the mean percentage of infused enteral nutrition was approximately 70% of the prescribed volume. Patients improve when the percentage of infused enteral nutrition is higher than 80 (35).

The results involving the total sodium volume administered to patients were very relevant. Sodium contributes to the occurrence of edema and anasarca. The infusion of saline solution is common but 0.9% sodium chloride is proven to be inadequate and "non-physiological" (36). Some patients receive up to ten times the adequate sodium volume (37) solely through the intravenous route, and sodium infused through enteral feeding needs to be added. According to a study, patients who receive more than 3 l of fluids and 154 mmol of sodium/day remain hospitalized for a longer period of time and exhibit delayed recovery of intestinal function (38).

The results of the present study show that the sodium volume may also have contributed to the observed caloric and protein deficits. Although the present study adds new data to the current literature on the topic, its limitations include the size and homogeneity of the sample. However, the overall results showed that overload of fluid infusion may impact the success of enteral nutrition infusion. These findings pave the way for further research on the topic. The current belief is that only gastrointestinal disorders and enteral nutrition formulation lead to enteral nutrition intolerance with subsequent caloric and protein deficits. To conclude, critical caloric and protein deficits are associated with a higher volume of fluids, sodium chloride, and sodium when these products are infused to critically ill patients on mechanical ventilation and receiving exclusively enteral nutrition.

FINANCIAL SUPPORT

REFERENCES

1. Giner M, Laviano A, Meguid MM, Gleason JR. In 1995, a correlation between malnutrition and poor outcome in critically ill patients still exists. Nutrition 1996;12(1):23-9.
2. Petros S, Engelmann L. Enteral nutrition delivery and energy expenditure in medical intensive care patients. Clin Nutr 2006;25(1):51-9.
3. Angus DC, Van der Poll T. Severe sepsis and septic shock. N Engl J Med 2013;369(9):840-51.
4. Packman MI, Rackow EC. Optimum left heart filling pressure during fluid resuscitation of patients with hypovolemic and septic shock. Crit Care Med 1983;11(3):165-9.
5. ARISE Investigators, ANZICS Clinical Trials Group, Peake SL, Delaney A, Bailey M, Bellomo R, et al. Goal-directed resuscitation for patients with early septic shock. N Engl J Med 2014;371(6):1496-506.
6. Rehm M, Hulde N, Kammerer T, Meidert AS, Hofmann-Kiefer K. State of the art in fluid and volume therapy: A user-friendly staged concept. Anaesthesist 2017;66(3):153-67. DOI: 10.1007/s00101-017-0272-x
7. Rosenberg AL, Dechert RE, Park PK, Bartlett RH; NIH NHLBI ARDS Network. Review of a large clinical series: association of cumulative fluid balance on outcome in acute lung injury: a retrospective review of the ARDS net tidal volume study cohort. J Intensive Care Med 2009;24(1):35-46. DOI:10.1177/0885066608329850
8. Silversides JA, Major E, Ferguson AJ, Mann EE, McAuley DF, Marshall JC, et al. Conservative fluid management or deresuscitation for patients with sepsis or acute respiratory distress syndrome following the resuscitation phase of critical illness: a systematic review and meta-analysis. Intensive Care Med 2017;43(2):155-70. DOI: 10.1007/s00134-016-4573-3
9. Boyd JH, Forbes J, Nakada T-A, Walley KR, Russell JA. Fluid resuscitation in septic shock: a positive fluid balance and elevated central venous pressure are associated with increased mortality. Crit Care Med 2011;39:259-65.
10. Raghunathan K, Murray PT, Beattie WS, Lobo DN, Myburgh J, Sladen R, et al. Choice of fluid in acute illness: what should be given? An international consensus. Br J Anaesth 2014;113(5):772-83. DOI: 10.1093/bja/aeu301
11. Hoste EA, Maitland K, Brudney CS, Mehta R, Vincent JL, Yates D, et al. ADQI XII Investigators Group. Four phases of intravenous fluid therapy: a conceptual model. Br J Anaesth 2014;113(5):740-7. DOI: 10.1093/bja/aeu300
12. Kreymann KG, Berger MM, Deutz NE, Hiesmayr M, Jolliet P, Kazandjiev G, et al; ESPEN (European Society for Parenteral and Enteral Nutrition). ESPEN Guidelines on Enteral Nutrition: Intensive Care. Clin Nutr 2006;25(2):210-23.
13. Lobo DN. Fluid, electrolytes and nutrition: physiological and clinical aspects. Proc Nutr Soc 2004;63(3):453-66.
14. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al.; Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med 2013;39(2):165-228.
15. Soni N. British Consensus Guidelines on Intravenous Fluid Therapy for Adult Surgical Patients (GIFTASUP): Cassandra's view. Anaesthesia 2009;64(3):235-8.
16. Woodcockm TE, Woodcock TM. Revised Starling equation and the glycocalyx model of transvascular fluid exchange: an improved paradigm for prescribing fluid therapy. Br J Anaesthesia 2012;108(3):384-94.
17. Siqueira-Paese MC, Dock-Nascimento DB, De Aguilar-Nascimento JE. Critical energy deficit and mortality in critically ill patients. Nutr Hosp 2016;33(3):253. DOI: 10.20960/nh.253
18. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. N Engl J Med 1999;340(6):448-54.
19. Brandstrup B, Tonnesen H, Beier-Holgersen R, Hjortsø E, Ørding H, Lindorff-Larsen K, et al. Effects of intravenous fluid restriction on postoperative complications: Comparison of two perioperative fluid regimens: a randomized assessor-blinded multicenter trial. Ann Surg 2003;238:641-8.
20. Lobo DN, Bostock KA, Neal KR, Perkins AC, Row-lands BJ, Allison SP. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomised controlled trial. Lancet 2002;359:1812-8.
21. Kelm DJ, Perrin JT, Cartin-Ceba R, Gajic O, Schenck L, Kennedy CC, et al. Fluid overload in patients with severe sepsis and septic shock treated with early goal-directed therapy is associated with increased acute need for fluid-related medical interventions and hospital death. Shock 2015;43:68-73.
22. Rivers EP, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345:1368-77.
23. Mitchell KH, Carlbom D, Caldwell E, Leary PJ, Himmelfarb J, Hough CL. Volume overload: prevalence, risk factors, and functional outcome in survivors of septic shock. Ann Am Thorac Soc 2015;12(12):1837-44. DOI: 10.1513/AnnalsATS.201504-187OC
24. Rehm M, Hulde N, Kammerer T, Meidert AS, Hofmann-Kiefer K. State of the art in fluid and volume therapy: a user-friendly staged concept. Anaesthesist 2017;66(3):153-67. DOI: 10.1007/s00101-017-0272-x
25. Glassford NJ, Myles P, Bellomo R. The Australian approach to perioperative fluid balance. Curr Opin Anaesthesiol 2012;25:102-10.
26. De Jonghe B, Appere-De-Vechi C, Fournier M, Tran B, Merrer J, Melchior JC, et al. A prospective survey of nutritional support practices in intensive care unit patients: what is prescribed? What is delivered? Crit Care Med 2001;29(1):8-12.
27. Heyland DK, Heyland RD, Cahill NE, Dhaliwal R, Day AG, Jiang X, et al. Creating a culture of clinical excellence in critical care nutrition: the 2008 "Best of the Best" award. JPEN J Parenter Enteral Nutr 2010;34(6):707-15.
28. Lee ZY, Barakatun-Nisak MY, Noor Airini I, Heyland DK. Enhanced protein-energy provision via the enteral route in critically ill patients (PEP uP Protocol): a review of evidence. Nutr Clin Pract 2016;31(1):68-79.
29. Villet S, Chiolero RL, Bollmann MD, Revelly JP, Cayeux RNMC, Delarue J, et al. Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients. Clin Nutr 2005;24(4):502-9.
30. Weijs PJ, Stapel SN, De Groot SD, Driessen RH, De Jong E, Girbes AR, et al. Optimal protein and energy nutrition decreases mortality in mechanically ventilated, critically ill patients: a prospective observational cohort study. JPEN J Parenter Enteral Nutr 2012;36(1):60-8. DOI: 10.1177/0148607111415109
31. Allingstrup MJ, Esmailzadeh N, Wilkens Knudsen A, Espersen K, Hartvig Jensen T, Wiis J, et al. Provision of protein and energy in relation to measured requirements in intensive care patients. Clin Nutr 2012;31(4):462-8. DOI: 10.1016/j.clnu.2011.12.006

32. Ishibashi N, Plank LD, Sando K, Hill GL. Optimal protein requirements during the first 2 weeks after the onset of critical illness. Crit Care Med 1998;26(9):1529-35.

33. Trials N, Wiedemann HP, Wheeler AP, Bernard GR, Thompson BT, Hayden D, et al. Comparison of two fluid-management strategies in acute lung injury. N Engl J Med 2006;354:2564-75.

34. Weijs PJ, Looijaard WG, Beishuizen A, Girbes AR, Oudemans-van Straaten HM. Early high protein intake is associated with low mortality and energy overfeeding with high mortality in non-septic mechanically ventilated critically ill patients. Crit Care 2014;18(6):701. DOI: 10.1186/s13054-014-0701-z

35. Wei X, Day AG, Ouellette-Kuntz H, Heyland DK. The association between nutritional adequacy and long-term outcomes in critically ill patients requiring prolonged mechanical ventilation: a multicenter cohort study. Crit Care Med 2015;43(8):1569-79. DOI: 10.1097/CCM.0000000000001000

36. Allison S. Fluid, electrolytes and nutrition. Clin Med (Lond) 2004;4(6):573-8.

37. World Health Organization (WHO). Healthy ageing profiles. Guidance for producing local health profiles of older people: report of OMS consultation. Geneva: WHO; 2006.

38. Lobo DN, Bostock KA, Neal KR, Perkins AC, Rowlands BJ, Allison SP. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomised controlled trial. Lancet 2002;359(9320):1812-8.