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Original article

Proportions of prognostic scoring models among ICU patients receiving enteral nutrition

Seyed Mohammad Hosein Mousavi Jazayeri[1], *Alireza Ostadrahimi*[2], *Shahryar Hashemzadeh*[3], *Abdolrasoul Safaiyan*[4], *Firouz Salehpour*[5], *Meisam Barati*[2], *Fatemeh Azizi-Soleiman*[6]

[1] Nutrition and Metabolic Disease Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran; [2] Nutrition Research Center, Faculty of Nutrition, Tabriz University of Medical Sciences, Tabriz, Iran; [3] Department of General and Thoracic Surgery, Tabriz University of Medical Sciences, Tabriz, Iran; [4] Road Traffic Injury Research Center, Department of Biostatics and Epidemiology, Tabriz University of Medical Sciences, Tabriz, Iran - E-mail: safaiyana@tbzmed.ac.ir; [5] Department of Neurosurgery, Tabriz University of Medical Sciences, Tabriz; [6] School of Health, Arak University of Medical Sciences, Arak, Iran

Summary. *Background:* The present study was designed to define the proportions of effective factors associated with feeding among intensive care unit (ICU) patients in predicting the Simplified Acute Physiology Score II (SAPS II) and Sequential Organ Failure Assessment (SOFA). *Material and Methods:* In a double blinded, randomized clinical trial, 32 critically ill patients were randomly assigned to one of four groups: early-opened, delayed-open, early-closed, and delayed-closed enteral nutrition (EN). SAPS II and SOFA were calculated on day 1, 3, 5 and 7 and the contribution rates of different variables were determined. *Results:* The proportion of time of the provision of EN (Early vs. Delayed) and system for the delivery (Open vs. Closed) in determining SAPS II was 48% and 3% respectively. The proportion of time of the provision of enteral feeding in defining SOFA was 14%. Age and gender had no impact on determining SOFA. Proportion of system for the delivery of EN and time in defining SOFA was 47% and 24%, respectively. *Conclusion:* Time of the provision of EN is the most effective factor in determining SAPS II and SOFA in critically ill patients admitted in ICU, rather than the system of delivery. *Clinical Relevancy Statement:* Intensive care units (ICU) scales play important roles in decision making and are consisted of well-known factors. We found that other factors like early administration of enteral nutrition (EN) and type of formula are also crucial in predicting the score of these scales. This finding is clinically relevant for guiding health care staff to make the best decision for choosing an efficient time and system for delivery of EN.

Key words: Enteral Nutrition, Simplified Acute Physiology Score**,** Intensive Care Units, Trauma

Introduction

Life expectancy has increased in the past half century due to significant advances in healthcare prevention, diagnosis and treatment approaches (1). Information derivable from validated intensive care units (ICU) scales, which measure the severity of illness in the ICUs has increased. (2) These scales play an increasingly important role in decision making and could facilitate evidence-based rationing of limited healthcare resources in the future (1). Commonly used ICU prognostic scoring models include the Simplified Acute Physiology Score II (SAPS II) and Acute Physiology and Chronic Health Evaluation II (APACHE II) (3). These scoring systems are rather complex, with a number of factors incorporated in the calculations, including physiological parameters (1, 4). The SAPS II and APACHE II prognostic models are the most commonly used scoring systems for critically ill patients admitted to the ICU (5) and measure severity of illness by a numeric score based on physiological variables selected because of their impact on mortality: the sicker the patient, the more deranged the values and the higher the score (2). In addition, SAPS II is designed for predicting outcome in ICU patients. It was developed in the 80s and a revised version was introduced in 1993 (6). The SAPS II system predicts mortality and morbidity well, but also seems more suitable for ICU patients (4). The Sequential Organ Failure Assessment (SOFA) score makes possible the prediction of organ dysfunction over six organ systems (7), in addition to recognizing the severity of their dysfunctions: respiratory, coagulation, liver, cardiovascular, renal, and neurological systems. Since its introduction, the SOFA score has also been used for predicting mortality, although it was not developed for this purpose. The SOFA score could be useful in providing therapeutic decision making and guiding resource allocation (7-9). Nutrition support is therefore considered to be an essential component in the management of critically ill patients. According to American and European clinical practice guidelines, the enteral route is preferred for delivering early nutrition support (10, 11). Time of the provision of EN and system for its delivery are two important factors affecting outcomes in critically ill patients. We have just reported about the preferability of standard enteral feeding over hospital-prepared blended formula (12). In addition, it has been found that early enteral nutrition (EN) has an important effect on Tumor Necrosis Factor-α (TNF-α) and high sensitive C-Reactive Protein (hs-CRP) levels (13) among patients admitted to ICU. However, it remains a debatable issue which factor has the biggest effect on those scores. The present study was therefore conducted to determine the parameters that can influence dynamic changes of SAPS II and SOFA scores in critically ill patients.

Material and Methods

This double blinded, randomized clinical trial was conducted in the surgical ICU of the Emam Reza Hospital, Tabriz University of Medical Science (TUMS), Tabriz, Iran. Over 8 months, all patients admitted to the ICU were screened for study eligibility. Inclusion criteria were as follows: age of 18 – 65 years, a predicted stay in the ICU of more than 72 hours, APACHE II score (14) on admission of over 20, amenability to enteral feeding, no obstruction in the gastrointestinal (GI) tract, no GI bleeding, normal kidney function, and EN tolerance. Patients were excluded if they did not fulfill the follow-up period, received anti-inflammatory drugs or corticosteroids before admission, had GI bleeding or enteral feeding intolerance during the study period, were hemodynamically unstable, immunosuppressed, had chronic organ failure, previous organ transplantation, were pregnant, received massive blood transfusion, their post-cardiopulmonary resuscitation status was unknown, or follow-up was lost owing to hospital transfer. A total of 32 patients were included in the study and randomly assigned to one of four treatment groups as follows: (a) continuous early closed enteral feeding within 24-48 hours of admission to the ICU; (b) continuous delayed closed enteral feeding started after 48 hours admission to the ICU; (c) continuous early open enteral feeding within 24-48 hours of admission to the ICU; and (d) continuous delayed open enteral feeding started after 48 hours admission to the ICU. Computer-generated random numbers were utilized for randomization. Enteral products had identical opaque packaging with no differences in appearance, texture, or smell. Investigators and health care providers were blinded to treatment allocation. As categorized by others (15), closed enteral feeding consisted of industrialized, sterile and liquid enteral formulas packed in bags ready to be administered. Open enteral feeding was characterized by being produced in a restricted and specific area in which industrialized powder nutrients are mixed. All subjects had received EN by means of a modern continuous enteral feeding pump (16) consonant with the level of accuracy and features required in current markets (17). Early EN was defined as set out in guidelines (18, 19). Study patients were respectively followed-up until they had completed a follow-up of 7 days.

Measurements

For all patients, SAPS II scores were calculated as defined in the original literatures, as was the risk of death according to the published logistic equations (20), as well as SOFA. SAPS II and SOFA were evaluated on 1^{st}, 3^{rd}, 5^{th} and 7^{th} day of ICU admission. The SAPS II includes 12 physiology variables, age, type of admission and three underlying disease variables (6). The SOFA score is the sum of the scores of six variables, each representing an organ system: respiratory, cardiovascular, hepatic, coagulation, renal and neurological; graded from 0 to 4 according to the degree of organ dysfunction or failure (21).

Ethical issues

The research followed the tenets of the Declaration of Helsinki; written informed consent was obtained from patients or their kin. The study protocol was approved by the Tabriz University of Medical Sciences ethics committee (Code: 92205).

Statistical methods

The influential variables were adjusted between systems for the delivery of formula (Open and Closed) and time of the provision of EN (Early and Delayed) on the 1st day. Normality of variables was tested using Q-Q plot; then Mauchly's W test was checked to identify a covariance matrix of data, and finally repeated measures ANCOVA was performed using Minitab Software version 17. Holm-Sidak was used for post-hoc comparisons. We used the following ANCOVA formula:

$$VDV = \theta_{Time} + \theta_{Formula} + \theta_{Method} + \theta_{Method*Formula} + \theta_{ID(Method,Formula)} + \beta_{Gender} + \beta_{Age} + Error$$

VDV were used for SAPS II and SOFA, separately. The results include P-values for comparing multi and univariates. The first P-value ($P\text{-value}_{time}$) is for comparing variations in four times of intervention, the second P-value ($P\text{-value}_{formula}$) is for comparing the Open and Closed groups, the third P-value – ($P\text{-value}_{Method}$) is for comparing the Early and Delayed groups, and the fourth P-value ($P\text{-value}_{Method*Formula}$) is for comparing interactions of Open and Closed groups with Early and Delayed groups. $P\text{-value}_{Gender}$ and $P\text{-value}_{age}$ were used for controlling gender and age as confounding variables, respectively. The level of significance was set at 0.05 and all results were expressed as Mean±SEM (standard error of mean).

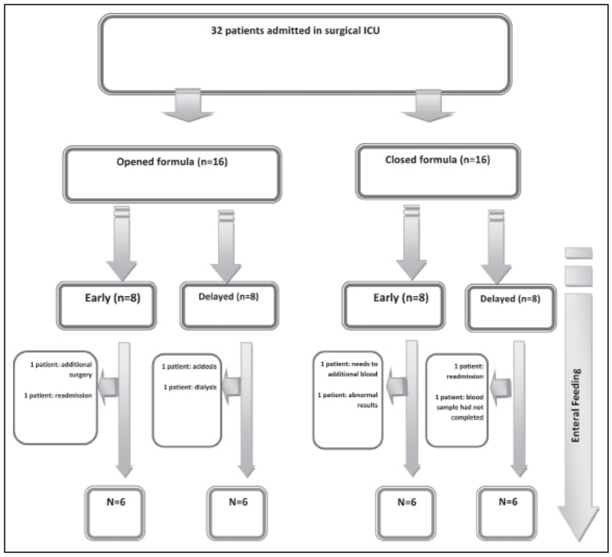

Figure 1. The flow chart of patients' enrollment and disposition

Results

Of the 32 patients, 24 participants completed the study period. The reasons of withdrawal were as follows: additional surgery, readmission, acidosis, dialysis, additional blood transfusion, abnormal results, and incomplete blood sample (Figure 1). There were no significant differences between the groups regarding their gender and age (Table 1). As presented in Table 2, mean SAPS II scores had no significant difference between the Open and Closed formula (P=0.131). The mean SAPS II score was lower in the Early group compared to the Delayed group. Figure 2 shows that the effective proportion of time of the provision of EN (Early vs. Delayed) on SAPS II was 48%. Age and gender did not have any

Table 1. Demographic characters of patients

		Open formula		Closed formula		PV
		Early (n=6)	Delayed (n=6)	Early (n=6)	Delayed (n=6)	
Gender	**Male**	3(%50)	4(%66.67)	3(%50)	2(%33.33)	0.303
	Female	3(%50)	2(%33.33)	3(%50)	4(%66.67)	
Age		38.8±2.82	34.8±2.82	33.1±2.75	36.9±2.73	0.462
Disease	**Trauma**	6 (%100)	5 (%83.33)	5 (%83.33)	5 (%83.33)	--
	Multiple Trauma	0	1 (%16.66)	1 (%16.66)	1 (%16.66)	
Place of feeding	**From Nose**	6 (%100)	5 (%83.33)	6 (%100)	5 (%83.33)	--
	From Gut	0	1 (%16.66)	0	1 (%16.66)	

P-Value reported by Cochran's and Mantek-Haenszel test

Table 2. Modifications in SAPS II and SOFA

Formula		Open		Closed		Open VS. Closed Formula	Early VS. Delayed	Interaction	Time	Gender
Feeding Time		Early	Delayed	Early	Delayed					
Variable	Date	X̄ ± SE	X̄ ± SE	X̄ ± SE	X̄ ± SE					
	1	45±1.44	41.17±0.31	42.5±0.76	41.33±0.33					
	3	46±0.97	48.67±0.21	47±0.86	48.5±0.22					
SAPS II	5	44.59±0.2	47.67±0.84	42±0	47.33±0.33	0.131	0.000	0.032	0.000	0.168
	7	41.17±0.79	44.76±0.17	40.33±0.42	44.67±0.49					
	Pv	0.020	0.000	0.000	0.000					
	1	4.95±0.12	4.82±0.16	5.32±0.06	4.96±0.13					
	3	5.22±0.13	5.4±0.13	5.4±0.05	5.39±0.1					
SOFA	5	6.19±0.16	7.03±0.1	5.49±0.07	5.77±0.09	0.000	0.000	0.011	0.000	0.440
	7	6.12±0.08	6.75±0.05	4.9±0.1	5.45±0.12					
	Pv	0.000	0.000	0.000	0.000					
Lawley-Hotelling Test						0.000	0.000	0.007	0.000	0.313

confounding effect. The proportion of system for the delivery of formula (Open vs. Closed) and time on SAPS II were 3% and 27%, respectively. The effects of time of the provision of EN (Early vs. Delayed) (Pv=0.000) and time (Pv=0.000) were significant on levels of SAPS II. Levels of SAPS II were statistically higher in Delayed enteral feeding than in those who received Earlier feeding (Pv=0.000). The Holm-Sidak test showed that levels of SAPS II were lower on the 1st day (Pv=0.008), 3rd day (Pv=0.005), 5th day (Pv=0.000), and 7th day (Pv=0.000) in those who received Earlier EN compared to the Delayed group. Figure 3 presents the modification in SAPS II levels based on the four groups.

SOFA was greater in the Open formula group in comparison to those who received Closed formula (PV=0.000), and its score was lower in the Early enteral group compared to the Delayed (PV=0.000) groups (Table 2). There was a significant interaction between the Closed vs. Open formula as well as the Early vs. Delayed groups. The proportion of time of the provision of EN (Early vs. Delayed) in predicting SOFA was 14%. Age and gender did not have any confounding effects regarding SOFA. The proportion of the system for the delivery of formula (Open vs. Closed) and time was 47% and 24%, respectively. The effects of the system for the delivery, time of the provision of EN (Early vs. Delayed), and time on SOFA were statistically signifi-

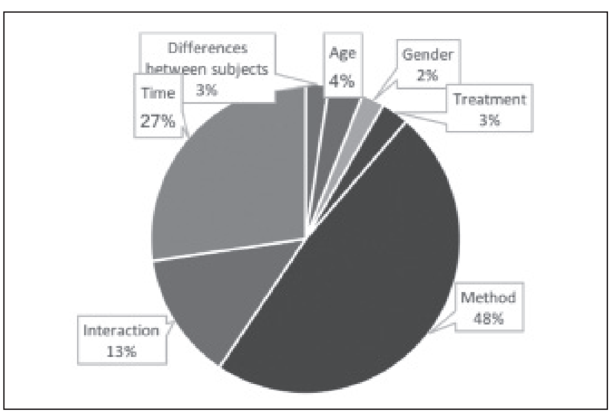

Figure 2. Proportion of effective factors on SAPS II

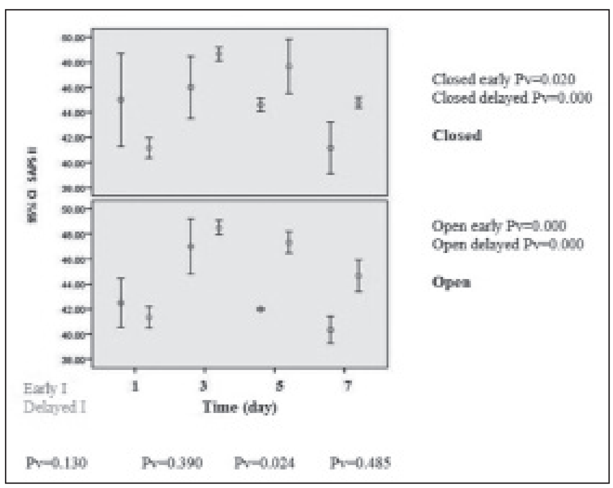

Figure 3. 95% Confidence Interval based on type of formula (Open VS. Closed) and method of feeding (Early VS. Delayed) in different dates

cant. The mean of SOFA was statistically higher in the Open group compared to those in the Closed formula (Pv=0.000). In addition, SOFA was statistically higher in the Delayed group compared to the Early formula (Pv=0.000). SOFA score increased from the 1st day until the 5th day, then decreased (Pv=0.000). Figure 5 presents the modification in SOFA levels based on the four groups. Based on the Holm-Sidak test results, levels of SOFA had a significant interaction on the 5th day (Pv=0.021). The Lawley-Hotelling test has confirmed for the findings related to SAPS II and SOFA (Table 2). The proportion of the system for the delivery of formula, time of the provision of EN, and time in predicting both SAPS II and SOFA scores were 33%, 27%, and 25%, respectively. Age and gender did not have any confounding effects (Figure 6).

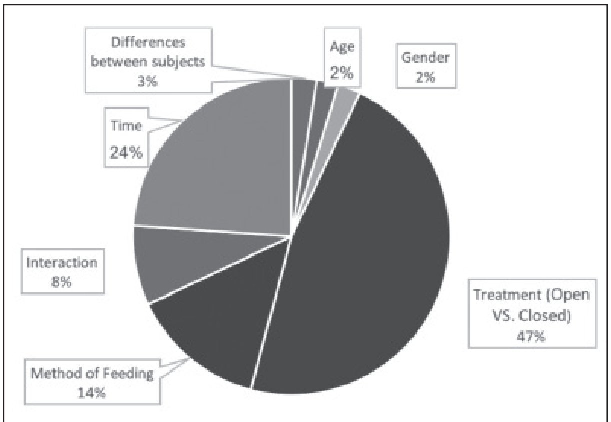

Figure 4. Proportion of effective factors on SOFA

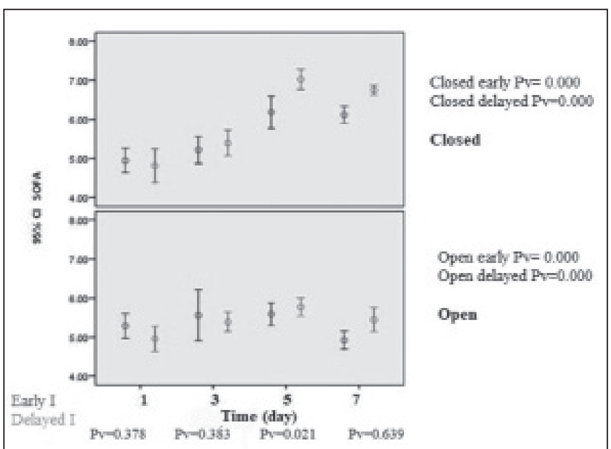

Figure 5. Confidence Interval SOFA based on type of formula (Open VS. Closed) and method of feeding (Early VS. Delayed) in different dates

Discussion

To the best of our knowledge, the present study is the first study in which the effective proportion of different factors was monitored in predicting SAPS II and SOFA among ICU patients. Our findings showed that SAPS II was significantly lower in those who received Early EN compared to the Delayed group. Time of the provision of EN (Early vs. Delayed) and time were the most effective factors affecting the levels of both SAPS II and SOFA. Although the proportion of the system for the delivery of formula was an important factor in defining the SOFA score, it was not a major factor for SAPS II. The SAPS II score provides a reliable prediction of mortality without having to specify a primary diagnosis. The variables in the SAPS II score are readily available and the calculation of the score is rapid (22). SAPS II had the highest accuracy in relation to severe purulent bacterial meningitis (23)and subjects with hematological malignancies (24). EN is possible in the majority of patients with severe hemodynamic failure, but usually results in hypocaloric feeding. EN should be considered in patients with careful abdominal and energy monitoring (25).

Here, it was found that early and closed EN could play more important roles in predicting the score of scales related to ICU patients' prognosis. This finding can help health care staff to make the best decision for choosing an efficient time and system for delivery of EN. Early EN has been related to less mortality, gut dysfunction, ventilator-associated pneumonia, and the duration of mechanical ventilation and ICU stay. Early EN is recommended to be initiated in major trauma

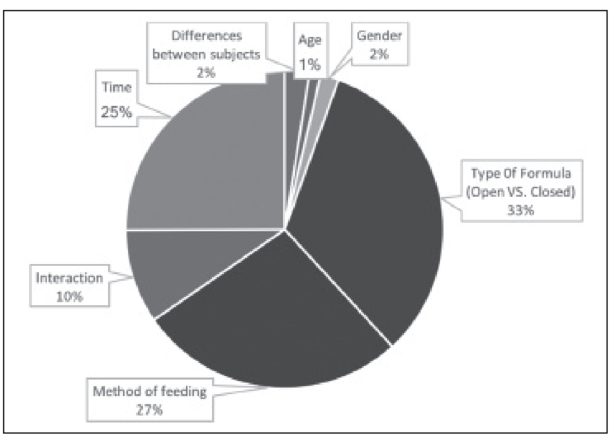

Figure 6. Effective factors on SAPS II and SOFA

patients, patients with major burns, and ICU patients. Here, we found that the SOFA score was significantly lower in patients receiving early EN. Kompan et al., have shown that starting early EN during the first 24 hours of hospitalization in ventilated multiply injured patients decreased upper digestive intolerance compared to delayed EN. The odds ratio of pneumonia was 7.2 in the delayed EN group vs. the other group. Similarly, the multiple organ dysfunction (MOD) score in multiply injured patients was lower in those who started EN early (26). A recent Retrospective Review (27) in mechanically ventilated patients with septic shock found an improvement in the length of intensive care unit stay (LOS) and the duration of mechanical ventilation (DOMV) in those receiving <600 kcal/d EN within 48 hours compared to those receiving no EN or ≥600 kcal/d within 48 hours. A meta-analysis (28) on 3 RCTs evaluating the benefits of early EN in trauma ICU patients showed that the rate of mortality was significantly lower; however the quality of the studies was inadequate. Based on the review by Yang et al., (29) there are some controversies with respect to the effect of early EN on gastrointestinal blood flow and perfusion in critically ill patients with hemodynamic instability. The effectiveness of early EN following thoracic surgery is also doubtful. It seems that the patient's condition is an important factor in predicting the outcomes. Our patients undergoing closed EN exhibited lower SOFA scores. Closed EN feeding systems provide some benefits over Open EN. As a result of preparing these formulas in a sterile environment, the risk of microbial contamination and consequent infection is lower. It is also time-saving in comparison to Open EN (30). There are also some disadvantages including costs (31), and change in medication administration route (32). Using Closed EN in patients vulnerable to infection is highly recommended. Despite the advantages of the closed TF, because of the greater proportion of the early EN approach in predicting scores related to physiological and organ dysfunction assessment, the use of this method is recommended. Economic analysis of supplying early EN to critically ill patients reported by Doig et al., (28) demonstrated that using this method can lower costs. This can be regarded as another proof of the efficiency of early EN.

Conclusion

The effective proportion of early administration of EN is much more important than the type of formula (Open vs. Closed). Therefore, early EN must be considered a priority for ICU patients.

Limitations

Limitations of the present study include the restricted sample size.

Acknowledgments

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References

1. Haq, A., et al., The Simplified Acute Physiology Score III Is Superior to the Simplified Acute Physiology Score II and Acute Physiology and Chronic Health Evaluation II in Predicting Surgical and ICU Mortality in the "Oldest Old". Curr Gerontol Geriatr Res, 2014. 2014: p. 934852.
2. Faruq, M.O., et al., A comparison of severity systems APACHE II and SAPS II in critically ill patients. Bangladesh Critical Care Journal, 2013. 1(1): p. 27-32.
3. Pittet, D., et al., Importance of pre-existing co-morbidities for prognosis of septicemia in critically ill patients. Intensive Care Med, 1993. 19(5): p. 265-72.
4. Thorsen, K., J.A. Soreide, and K. Soreide, Scoring systems for outcome prediction in patients with perforated peptic ulcer. Scand J Trauma Resusc Emerg Med, 2013. 21: p. 25.
5. Vassar, M.J., et al., Prediction of outcome in intensive care unit trauma patients: a multicenter study of Acute Physiology and Chronic Health Evaluation (APACHE), Trauma and Injury Severity Score (TRISS), and a 24-hour intensive care unit (ICU) point system. J Trauma, 1999. 47(2): p. 324-9.
6. Le Gall, J.R., S. Lemeshow, and F. Saulnier, A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. Jama, 1993. 270(24): p. 2957-63.
7. Ho, K., Combining sequential organ failure assessment (SOFA) score with acute physiology and chronic health

evaluation (APACHE) II score to predict hospital mortality of critically ill patients. Anaesthesia and intensive care, 2007. 35(4): p. 515-521.
8. LOPES FERREIRA, F., et al., Serial evaluation of the SOFA score to predict outcome in critically ill patients. JAMA, the journal of the American Medical Association, 2001. 286(14): p. 1754-1758.
9. Gerent, A., et al., Base deficit and SOFA score are predictive factors of early acute kidney injury in oncologic surgical patients. Critical Care, 2015. 19(Suppl 1): p. P297.
10. McClave, S.A., et al., Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). JPEN J Parenter Enteral Nutr, 2016. 40(2): p. 159-211.
11. K.G. Kreymann, M.M.B., N.E.P. Deutz, M. Hiesmayr, P. Jolliet, G. Kazandjiev, G. Nitenberg, G. van den Berghe, J. Wernerman, DGEM: C. Ebner, W. Hartl, C. Heymann, C. Spies, ESPEN Guidelines on Enteral Nutrition: Intensive care. Clinical Nutrition, 2006. 25: p. 210–223.
12. Jazayeri, S.M.H.M., et al., Standard enteral feeding improves nutritional status compared with hospital-prepared blended formula among Intensive Care Unit (ICU) patients. Progress in Nutrition, 2016. 18(1): p. 22-25.
13. Jazayeri, S.M.H.M., et al., Effects of four different enteral feeding methods on tumor Necrosis Factor-α (TNF-α) and high sensitive C-Reactive Protein (hs-CRP) in critically Ill Patients: double blinded, randomized controlled trial. Progress in Nutrition, 2016. 18(3): p. 236-241.
14. Xiao-Yu Zhou , S.-Q.B., Hong-Lin Chen, Song-Shi Ni, Comparing the APACHE II and the CPIS scores in predicting 30-day 3 mortality in patients with ventilator-associated pneumonia. Int J Infect Dis, 2014.
15. Silva, S.M., et al., Open versus closed enteral nutrition systems for critically ill adults: is there a difference? Rev Assoc Med Bras, 2012. 58(2): p. 229-33.
16. Joey Enteral Feed and Flush Pump with Pole Clamp, Progammable (product brochure). 2012, Covidien llc: Mansfield, MA.
17. White, H. and L. King, Enteral feeding pumps: efficacy, safety, and patient acceptability. Med Devices (Auckl), 2014. 7: p. 291-8.
18. McClave, S.A., et al., Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). JPEN J Parenter Enteral Nutr, 2009. 33(3): p. 277-316.
19. Dhaliwal, R., et al., The Canadian critical care nutrition guidelines in 2013: an update on current recommendations and implementation strategies. Nutr Clin Pract, 2014. 29(1): p. 29-43.
20. Park, S.K., et al., Acute Physiology and Chronic Health Evaluation II and Simplified Acute Physiology Score II in predicting hospital mortality of neurosurgical intensive care unit patients. J Korean Med Sci, 2009. 24(3): p. 420-6.
21. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med, 1992. 20(6): p. 864-74.
22. Prakash, P., K. Krishna, and D. Bhatia, Usefulness of SAPS II Scoring System as an Early Predictor of Outcome in ICU Patients. JIACM, 2006. 7(3): p. 202-5.
23. Pietraszek-Grzywaczewska, I., et al., Predictive value of the APACHE II, SAPS II, SOFA and GCS scoring systems in patients with severe purulent bacterial meningitis. Anaesthesiology intensive therapy, 2016.
24. Sawicka, W., et al., The effectiveness of the APACHE II, SAPS II and SOFA prognostic scoring systems in patients with haematological malignancies in the intensive care unit. Anaesthesiol Intensive Ther, 2014. 46(3): p. 166-170.
25. Berger, M.M., et al., Enteral nutrition in critically ill patients with severe hemodynamic failure after cardiopulmonary bypass. Clinical Nutrition, 2005. 24(1): p. 124-132.
26. Kompan, L., et al., Effects of early enteral nutrition on intestinal permeability and the development of multiple organ failure after multiple injury. Intensive care medicine, 1999. 25(2): p. 157-161.
27. Patel, J.J., et al., Early Trophic Enteral Nutrition Is Associated With Improved Outcomes in Mechanically Ventilated Patients With Septic Shock A Retrospective Review. Journal of intensive care medicine, 2014: p. 0885066614554887.
28. Doig, G.S., et al., Early enteral nutrition reduces mortality in trauma patients requiring intensive care: a meta-analysis of randomised controlled trials. Injury, 2011. 42(1): p. 50-56.
29. Yang, S., et al., Early Enteral Nutrition in Critically Ill Patients With Hemodynamic Instability An Evidence-Based Review and Practical Advice. Nutrition in Clinical Practice, 2014. 29(1): p. 90-96.
30. Vanek, V.W., Closed versus open enteral delivery systems: a quality improvement study. Nutrition in Clinical Practice, 2000. 15(5): p. 234-243.
31. Phillips, W., B. Roman, and K. Glassman, Economic impact of switching from an open to a closed enteral nutrition feeding system in an acute care setting. Nutrition in Clinical Practice, 2013: p. 0884533613489712.
32. Gunnell, S., et al., Converting to a Closed Enteral Feeding System in a Pediatric Hospital. ICAN: Infant, Child, & Adolescent Nutrition, 2011. 3(5): p. 296-299.

Correspondence:
Abdolrasoul Safaiyan
Road Traffic Injury Research Center, Department of Biostatics and Epidemiology, Tabriz University of Medical Sciences, Tabriz, Iran - E-mail: safaiyana@tbzmed.ac.ir