

Effect of Tubular Feeding with the Measurement of Gastric Residual Volume on Ventilator Associated Pneumonia

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Background: Several measures have been taken to prevent the onset of ventilator-associated pneumonia (VAP), one of which is measuring the gastric residual volume. The purpose of this study is to compare the effect of two tube feeding methods with and without gastric residual volume measurement on VAP.

Materials and Methods: This clinical trial was performed on the study population of patients with endotracheal tubes hospitalized in Intensive Care Units 1 and 2 of Golestan hospital, Ahvaz, Iran. Overall, 70 patients who met the inclusion criteria were randomly divided into groups 1 and 2. Groups 1 and 2 were fed with and without measuring gastric residual volume, respectively. The incidence of pneumonia was assessed using the Modified Clinical Pulmonary Infection Score prior to the intervention and on the fifth day post-intervention. The data were analyzed by the SPSS software version 22.

Results: The incidence of VAP was 9.12% in the group with gastric residual volume measurement and 7.14% in the other group. There was no significant difference between the two groups ($P=0.827$) regarding VAP prevalence.

Conclusion: Monitoring gastric residual volume requires aspiration and repeated measurements of gastric contents, resulting in increased nursing workload. Moreover, if the gastric residual volume is high, the patient will be deprived of calorie intake and subjected to malnutrition. As a result, removing the monitoring of gastric residual volume from the care setting and focusing on interventions proven to reduce VAP can be more helpful.

Key words: Gastric residual volume; Intensive care unit; Tube feeding; Ventilator-associated pneumonia

INTRODUCTION

Ventilator-associated pneumonia (VAP) is one of the subgroups of hospital pneumonia that refers to the development of pneumonia after the insertion of an artificial airway. It is the second most commonly reported infectious disease in the Intensive Care Unit (ICU) in the United States. The risk of VAP in critical patients connected to a ventilator for at least 24 h increases 6-21 times (1). In an epidemiologic study on hospital pneumonia, its incidence has been reported to be 10%-20%

in several studies, and it even can rise to 80% in patients under mechanical ventilation (1, 2).

In a study by Charles et al., the incidence of VAP had a range of 13-51 per 1,000 ventilation days, and the mortality rate was reported to be 24%-76% (3). In another investigation by Kalanuria et al., the mortality rate was reported as 33%-55% (1). The importance of VAP is due to certain complications that occur in patients. It has been noted that 8%-28% of the complications in patients with mechanical ventilation are associated with VAP. According

to the literature, patients with VAP stay in the ICU 4.3-13 days longer than others (1). The statistics released in North America in 2010 reported that an average cost of \$76,730 is estimated for each patient diagnosed with VAP. Evidence suggests that the prevalence of this infection in our country is greater than that of developed countries (4). Despite advances in the diagnosis and treatment of diseases, the risk, cost, mortality rate, and pathogens associated with hospital pneumonia, in particular VAP, have remained unacceptably high (5). The factors creating VAP are divided into two avoidable and unavoidable types. The patient-related unavoidable factors include male gender, underlying pulmonary diseases, coma, brain damage, and multiple organ disorder. The unavoidable factors associated with therapeutic actions entail neurosurgery, intracranial pressure control, re-intubation, and transition out of the ICU. The avoidable factors encompassed the prevention of gastrointestinal ulcers, supine position, gastric tube feeding, subglottic aspiration disorder, tracheostomy, and the tracheostomy cuff pressure less than 20 cm H₂O (3).

The avoidable factors are more important than avoidable variables in nursing because they can be avoided by modifying nursing interventions. Among the avoidable factors in recent years, feeding via nasogastric tube has attracted the attention of researchers around the world. One of the reasons for this attraction is that nutrition is one of the primary physiological needs of humans. Among the patients whose nutritional status is undergoing extensive changes are admitted to the intensive units, especially the ICU (6). Malnutrition is also a common problem in the patients hospitalized in these wards. Studies show that the malnutrition rate in these patients is 30%-55% (7).

Patients admitted to the ICU cannot satisfy their nutritional needs. Therefore, an artificial feeding method is required, including enteral feeding and venous feeding. In the survey conducted by Scurlock and Mechanick, the preference and fewer complications of tube feeding compared to the intravenous method have been proven (8). The benefits of this method include maintaining the

natural process of absorbing calories in the body, preventing gastrointestinal adhesion, and maintaining the balance of normal flora in the gastrointestinal tract (8-11).

Metheny stated that tube feeding, in addition to its various benefits, has some side effects, such as vomiting, diarrhea, dumping syndrome, hyperglycemia, electrolyte disturbances, and aspiration (12). Much evidence indicates that most patients admitted to the ICU who use tube feeding and also undergo mechanical ventilation experience aspiration at least once during their feeding days (13). Moreover, delayed gastric emptying is one of the common problems of ICU patients fed by tube feeding. Delayed gastric emptying occurs in 50%-60% of the patients undergoing mechanical ventilation, leading to an increased risk of regurgitation of the stomach contents, aspiration, VAP, delay in achieving nutritional goals, malnutrition, and gavage intolerance (14).

Different methods are used for assessing nutritional tolerance. One of the most important recommendations is to check gastric residual volume (GRV) before feeding each time. Measuring GRV is generally used as an indicator of tube feeding tolerance in patients, and it is defined as the volume that can be aspirated from the stomach before intestinal feeding. The acceptable GRV is 100-200 cc. If the residual volume is more than this, the contents should be returned to the stomach, and feeding should be delayed for 1-2 h. Feeding intolerance is a marker of high GRV, which is a risk factor for aspiration. On the other hand, it can be said that the measurement of GRV is still considered as a feeding standard in textbooks, and if the correct principles are followed, the risk of aspiration will decrease (15).

In spite of the standardization of GRV measurement, the inappropriateness of this method and its complications, as well as the ineffectiveness of measuring the residual volume on the incidence of VAP, have been mentioned in the review, interventional, and prospective studies (16-19). In a clinical trial conducted by Reignier et al., the results showed that measuring GRV for adult patients is ineffective in preventing VAP development, compared to not measuring it and requires further investigation (16).

Moreover, Li et al., in a review in 2014, reported after analyzing 59 published articles that measuring GRV before enteral feeding in premature infants causes digestive and nutritional complications (17).

Despite the standards, some studies have shown that measuring GRV causes complications, such as reducing the volume of enteral feeding and the nutritional requirements of the patient and thereby diminishing calorie intake (16-18). In addition, decreased average energy received by patients due to interruptions during the measurement of GRV (20), increased incidence of intolerance in patients (17), as well as digestive and nutritional disturbances in premature infants (17, 19) have been observed. Some studies showed that not measuring GRV is ineffective in raising the incidence of VAP and reduces the complications caused by the method of GRV measurement (16-20). A recent challenging question for the nursing community is how tube feeding with GRV measurement affects the prevalence of VAP, compared to tube feeding without measuring GRV (8, 9, 12, 15-20). Research in this area is limited, and researchers have recommended further studies. Therefore, it was decided to design and conduct a study to compare the effects of two tube feeding methods, with and without measuring the GRV, on VAP.

MATERIALS AND METHODS

The present clinical trial was performed on the study population of all patients with mechanical ventilation admitted to the ICUs 1 and 2 of Golestan hospital, Ahvaz, Iran, from April 2018 to October 2018. Feeding by tube was carried out using the bolus feeding method. Based on the results of Reignier et al. (16) and considering $\beta=0.8$, $\alpha=0.05$, $P1=15.8\%$, $P2=47.4\%$, 70 samples were selected according to the inclusion criteria and were then assigned randomly to two groups of with and without GRV measurement using the method of six blocks. This research was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences with the ethics code of 1396.945 IR.AJUMS.REC and was registered as IRCT20170118032029N3 at the Iranian Registry of Clinical Trials.

The inclusion criteria were hospitalization in the ICU, not having renal failure, being at least 18 years old, being connected to the ventilator, being allowed to use tube feeding through the nasogastric tube for 24-48 h after intubation, not having undergone nasogastric tube insertion over four days before the study, the absence of pneumonia prior to the study, no history of abdominal surgery in recent months, no history of any surgery or bleeding in the esophagus, stomach, duodenum, or pancreas, and not being pregnant. The exclusion criteria encompassed patient discharge, patient transition, change in the type of feeding, and severe gastrointestinal complications, such as intolerance, vomiting, diarrhea, and gastrointestinal bleeding.

The tools used in this study included 1) a demographic questionnaire including questions about age, gender, diagnosis, the hospitalization date, and the date of entering the study, 2) a medical checklist about underlying diseases, taking medications, the date of inserting the nasogastric tube, tube size, the date of starting feeding, respiratory tube type and number, the amount of gavage solution, feeding duration, GRV, the times of vomiting, and 3) the standardized instrument of Modified Clinical Pulmonary Infection Score (MCPIS). The MCPIS has five clinical and laboratory factors, including temperature, white blood cell count, oxygenation, chest radiography, as well as the amount and purulence of tracheal tube secretion. Each item is scored as 0-2, and the total score has a range of 0-10. The diagnosis of VAP is based on a score of 6 or more (Table 1). The sensitivity and specificity of this tool in various studies are reported to be 65%-89.3% and 58%-100%, respectively (21-23).

The patients were included in the study based on the inclusion criteria, and MCPIS was completed for them initially. Afterwards, in the first group (the group with measured GRV), an intermittent tube feeding was performed according to the international guidelines by measuring the GRV. Based on the needs of patients and the doctor's prescription, in addition to kitchen food, a variety of Enetra Meal products were used thrice a day. The

gavage solution was poured into a dish and dissolved slowly. Before starting feeding, the head of the bed was slowly raised to 30-45 degrees and was kept in the same position for 30 min after feeding. The GRV was measured and recorded by the researcher or the assistant researcher pre-gavage by aspirating the stomach contents by a 60 mL syringe and returned to the stomach if it was less than 250 cc. If the residual volume was more than 250 mL, half of it was returned to the stomach based on the international guidelines, the remainder was discarded, and the doctor was informed about prescribing prokinetic agents. Feeding was stopped and then started with half of the previous amount and was continued according to the protocol (24).

Before feeding, the researcher ensured the correct placement of the nasogastric tube. The feeding volume was 200-300 mL every 3 h and at least seven times a day. The total daily feeding volume was calculated based on the calorie requirements of the patient by the physician, and standard dietary solutions were utilized. Each meal was served slowly and at least for 15 min. Before and after each feeding, the tube was washed with 30-50 cc of water or normal saline. Feeding intolerance was defined as vomiting, a residual volume of more than 250 mL, or both in this group. Vomiting was considered the excretion of stomach contents in the oropharyngeal region or out of the mouth with or without pressure (spontaneous regurgitation) and did not include the cases where regurgitation was due to the procedure.

The pressure of the tracheal tube cuff was measured twice a day. In order to measure the pressure inside the cuff, a pressure manometer with a cuff underneath was connected to the cuff in the trachea tube, and the researchers inflated the cuff. The manometer showed the pressure inside the cuff, and the pressure was adjusted in the range of 20-25 mmHg. In order to prevent the aspiration of subglottic secretions, mouthwash was performed every 6-8 h with chlorhexidine solution. All the above actions were carried out by the researcher and the research assistant supervised by the doctor. Furthermore, all nurses were trained regarding the correct implementation of the feeding protocol and the measurement of GRV. In the second group, tube feeding was started without the measurement of GRV. In this

group, tube feeding was performed similar to the first group, except that GRV was not measured before feeding, and feeding intolerance was defined only as vomiting. Other care procedures were completely carried out and supervised by the researcher and the research assistant.

Early-onset VAP develops within 48-96 h after endotracheal intubation. Consequently, on the fifth day, the MCPIS was completed again for all the patients to diagnose pneumonia. Regarding the importance of performing chest X-ray, chest radiography was performed applying the same device for all the patients, and all the radiographs were observed by the same physician. The complete blood count test was also performed with a similar device for all the patients. In order to implement the intervention, informed written consents were obtained from the companions of patients, and they were assured that they could exclude their patient from the study any time without affecting the treatment process of the patient. The information obtained from patients was confidential, and the results were announced in general.

Continuous variables are reported as mean \pm standard deviation (SD). Categorical data are expressed as numbers (percentages). The normality of continuous variables was examined using the Shapiro-Wilk W-test. Independent samples t-test was used to compare the mean age of the two groups. In addition, multiple regression analysis was applied for comparing the number of vomiting times in the groups adjusted for smoking status. Multivariable binary logistic regression analysis was performed to calculate the adjusted odds ratio of the relationship between the groups (i.e., intervention and control) and the VAP adjusted for smoking status. Statistical analysis was performed using the statistical software SPSS version 18.0.0. (SPSS Inc. Chicago, IL, USA).

RESULTS

We found that in the group without GRV measurement, one participant was excluded due to transfer to the general ward. In the group with GRV measurement, two individuals were excluded because of death as a result of advanced underlying diseases, namely metastatic cancer and stroke, one due to transfer to the general ward, and

one due to gavage intolerance. According to Table 2, there was no statistically significant difference between the two groups in terms of demographic and clinical variables ($P>0.05$), except for smoking status ($P=0.013$).

Concerning the incidence of VAP, the results showed that 9.12% and 7.14% in the groups with and without GRV measurement had VAP, respectively. The incidence of VAP

was not significantly different between the two groups ($P=0.827$) (Table 3). The mean \pm SD of vomiting frequency was 36.58 \pm 1.25 in the group with GRV measurement and 36.26 \pm 1.13 in the group without GRV measurement. Comparison of the two groups revealed no statistically significant difference between the two groups ($P=0.965$) (Table 4).

Table 1. Clinical Score of Pulmonary Infection

Criteria examined	Score of 0	Score of 1	Score of 2
Body temperature	36.5 to 38.5	38.5 to 38.9	36 > or > 39
WBC white blood cell count	4000-10000	> 11000 Or 4000 >	> 11000 Or 4000 >
The ratio of arterial blood oxygen to inhaled air oxygen Pao ₂ / Fio ₂	More than 240 or ARDS		Along with the formation of granulocyte 240 \geq or no ARDS
New or resistant infiltrates in chest radiography	No Infiltration	Diffused infiltration or patchy	Local and focal infiltration
Tracheal tube secretions	does not have	Non- supportive	Pussy

Table 2. Comparison of demographic and clinical variables in two groups with measuring gastric residual volume and without measurement

Demographic variables		Group with measurement Number (percent)	Group without measurement Number (percent)	p-value
Gender	Male	17 (54.8)	24 (70.6)	0.210
	Female	14 (44.2)	10 (29.4)	
Smoking	Have	12 (38.7)	24 (70.6)	0.013
	Does not have	19 (61.3)	10 (29.4)	
Cause of hospitalization	General surgery	8 (6/25)	14 (40.6)	0.554
	Neurosurgery	12 (38.4)	14 (34.8)	
	Care in intensive care unit	5 (16)	4 (11.6)	
	Cancer	5 (16)	2 (5.8)	
	Gynecological diseases	1 (3.2)	2 (5.8)	
Underlying disease	Does not have	14 (45.1)	19 (55.8)	0.852
	Cardiovascular disease	11 (35.4)	7 (20.3)	
	Respiratory diseases	1 (3.2)	2 (5.8)	
	Kidney Diseases	1 (3.2)	1 (2.9)	
	Endocrine diseases	3 (9.6)	3 (3.7)	
	Other diseases	1 (3.2)	2 (5.8)	
	6 and 6.5	3 (9.6)	0 (0)	
Endotracheal tube size	7 and 7.5	21 (67.2)	23 (67.6)	0.169
	8	7 (22.4)	11 (32.4)	
Age		Mean \pm SD 50.23 \pm 15.075	Mean \pm SD 49.38 \pm 19.117	0.845

Table 3. Comparison of the incidence of VAP in two groups of with and without measurement of GRV

	With measurement Number (percent)	Without measurement Number (percent)	Adjusted OR	p-value*
VAP				
Have	4 (9.12)	5 (7.14)	1.18 (0.26, 5.26)	0.827
Does not have	27 (1.87)	29 (3.85)		

*After adjustment for smoking status.

Table 4. Comparison of the number of vomiting in two groups of with and without measurement of GRV

	Group with measurement Mean± SD	Group without measurement Mean± SD	p-value*
Counts of vomiting	36.58±1.25	36.26±1.13	0.965

*After adjustment for smoking status.

DISCUSSION

Based on the results of the current study, measuring GRV has no significant effects on the prevention of VAP. This result is not consistent with the findings of Tablan et al., according to which measuring GRV was considered one of the most important recommendations for preventing VAP prior to each feeding (15). White et al. (2014) found the same result in their study and suggested measuring GRV every 4 h (in continuous feeding) and before each feeding (in intermittent feeding).

Reignier et al. (2013) aimed to investigate the impact of measuring or not measuring GRV in tube feeding on VAP incidence. These authors stated that not measuring GRV in adult patients could help prevent VAP development and requires further investigation (16). On the other hand, Li et al. (2014) conducted a meta-analysis on 59 papers and reported that measuring GRV prior to intestinal feeding causes digestive and nutritional complications. Furthermore, they stated that among all reviewed articles, the measurement of GRV in intestinal feeding is not confirmable, and this procedure is not evidence-based and may be harmful (17).

There might be various explanations for this disagreement between studies. Some investigations have argued that measuring GRV causes complications, such as reducing the volume of enteral feeding and nutritional requirements of the patient's body and thereby diminishing calorie intake (16-18), decreasing the average

energy received by the patient due to the interruptions during GRV measurement (20), augmenting the likelihood of intolerance in patients (17), as well as digestive and nutritional disturbances (17, 19). Moreover, some studies showed that not measuring GRV is ineffective in increasing the incidence of VAP and reduces the complications caused by the method of measuring GRV (16-20).

Therefore, according to our findings, removing GRV monitoring from standard care may have beneficial effects. First, high levels of GRV often lead to the interruption of enteral feeding, which in turn causes poor nutrition, along with the elevated rates of harm and mortality (25, 26). Recent data challenge the influences of low calorie intake on mortality during primary enteral feeding rather than high-energy enteral feeding in patients undergoing mechanical ventilation with acute respiratory failure (27). Second, different pathological mechanisms can be involved in the occurrence of VAP. Consequently, other types of preventive care related to these mechanisms are recommended (28, 29). The acceptability and effectiveness of care are at their best when all the interventions in the care setting are considered (29). Monitoring GRV requires aspiration and repeated measurements of gastric contents, resulting in a high workload of nurses. Omitting GRV monitoring from the care setting may allow increased focus on the interventions that have been proven to reduce the risk of VAP (28). Differences in the skills and performance of nurses regarding tube feeding and tube

feeding care were the limitations of the present research. It was attempted to reduce their impact on findings by practicing skills under the researcher's supervision and monitoring the performance of nurses.

CONCLUSION

The findings of the present investigation revealed no significant difference in the incidence of VAP between the groups with and without GRV measurement. Therefore, it might be possible to remove GRV monitoring from the standard care of patients with critical conditions under mechanical ventilation. However, before recommending widespread use, it is necessary to conduct similar studies with larger sample size and more extended intervention periods.

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Conflict of interest

The authors declare no conflict of interest.

REFERENCES

1. Kalanuria AA, Ziai W, Mirski M. Ventilator-associated pneumonia in the ICU. *Crit Care* 2014;18(2):208.
2. Giard M, Lepape A, Allaouchiche B, Guerin C, Lehot JJ, Robert MO, et al. Early- and late-onset ventilator-associated pneumonia acquired in the intensive care unit: comparison of risk factors. *J Crit Care* 2008;23(1):27-33.
3. Charles MP, Kali A, Easow JM, Joseph NM, Ravishankar M, Srinivasan S, et al. Ventilator-associated pneumonia. *Australas Med J* 2014;7(8):334-44.
4. Hekmatafshar M, Bardigorchaei A, Amin GH, Vakili MA, Eshginia S, Sanagoo A. The effect of a ginger extract on gastric residual volume among mechanically ventilated patients who hospitalized in intensive care unit. *Journal of Urmia Nursing & Midwifery Faculty* 2012;10(3): 1-9.
5. Restrepo MI, Anzueto A, Arroliga AC, Afessa B, Atkinson MJ, Ho NJ, et al. Economic burden of ventilator-associated pneumonia based on total resource utilization. *Infect Control Hosp Epidemiol* 2010;31(5):509-15.
6. Fremont RD, Rice TW. How soon should we start interventional feeding in the ICU? *Curr Opin Gastroenterol* 2014;30(2):178-81.
7. Heydari A, Emami Zeydi A. Is gastric residual volume monitoring in critically ill patients receiving mechanical ventilation an evidence-based practice? *Indian J Crit Care Med* 2014;18(4):259-60.
8. Scurlock C, Mechanick JI. Early nutrition support in the intensive care unit: a US perspective. *Curr Opin Clin Nutr Metab Care* 2008;11(2):152-5.
9. White H, King L. Enteral feeding pumps: efficacy, safety, and patient acceptability. *Med Devices (Auckl)* 2014;7:291-8.
10. Hejazi N, Mazloom Z, Zand F, Rezaianzadeh A, Amini A. Nutritional Assessment in Critically Ill Patients. *Iran J Med Sci* 2016;41(3):171-9.
11. Shpata V, Ohri I, Nurka T, Prendushi X. The prevalence and consequences of malnutrition risk in elderly Albanian intensive care unit patients. *Clin Interv Aging* 2015;10:481-6.
12. Metheny NA. Preventing respiratory complications of tube feedings: evidence-based practice. *Am J Crit Care* 2006;15(4):360-9.
13. Longo DL, Jameson JL, Kasper D. Harrison's Principles of Internal Medicine: Volume 2. Macgraw-Hill; 2011.
14. Kamali M, Farsi Z, Zareiyani A. The effect of body change position on gastric residual volume in patients undergoing mechanical ventilation in the intensive care units of a military hospital. *Military Caring Sciences* 2017;4(2):111-9.
15. Tablan OC, Anderson LJ, Besser R, Bridges C, Hajjeh R; CDC; Healthcare Infection Control Practices Advisory Committee. Guidelines for preventing health-care--associated pneumonia, 2003: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. *MMWR Recomm Rep* 2004;53(RR-3):1-36.

16. Reignier J, Mercier E, Le Gouge A, Boulain T, Desachy A, Bellec F, et al. Effect of not monitoring residual gastric volume on risk of ventilator-associated pneumonia in adults receiving mechanical ventilation and early enteral feeding: a randomized controlled trial. *JAMA* 2013;309(3):249-56.
17. Li YF, Lin HC, Torrazza RM, Parker L, Talaga E, Neu J. Gastric residual evaluation in preterm neonates: a useful monitoring technique or a hindrance? *Pediatr Neonatol* 2014;55(5):335-40.
18. Poulard F, Dimet J, Martin-Lefevre L, Bontemps F, Fiancette M, Clementi E, et al. Impact of not measuring residual gastric volume in mechanically ventilated patients receiving early enteral feeding: a prospective before-after study. *JPEN J Parenter Enteral Nutr* 2010;34(2):125-30.
19. Torrazza RM, Parker LA, Li Y, Talaga E, Shuster J, Neu J. The value of routine evaluation of gastric residuals in very low birth weight infants. *J Perinatol* 2015;35(1):57-60.
20. O'Leary-Kelley CM, Puntillo KA, Barr J, Stotts N, Douglas MK. Nutritional adequacy in patients receiving mechanical ventilation who are fed enterally. *Am J Crit Care* 2005;14(3):222-31.
21. Papazian L, Thomas P, Garbe L, Guignon I, Thirion X, Charrel J, et al. Bronchoscopic or blind sampling techniques for the diagnosis of ventilator-associated pneumonia. *Am J Respir Crit Care Med* 1995;152(6 Pt 1):1982-91.
22. Pelosi P, Barassi A, Severgnini P, Gomiero B, Finazzi S, Merlini G, et al. Prognostic role of clinical and laboratory criteria to identify early ventilator-associated pneumonia in brain injury. *Chest* 2008;134(1):101-8.
23. Shan J, Chen HL, Zhu JH. Diagnostic accuracy of clinical pulmonary infection score for ventilator-associated pneumonia: a meta-analysis. *Respir Care* 2011;56(8):1087-94.
24. Kreymann KG, Berger MM, Deutz NE, Hiesmayr M, Jolliet P, Kazandjiev G, et al. ESPEN Guidelines on Enteral Nutrition: Intensive care. *Clin Nutr* 2006;25(2):210-23.
25. Villet S, Chiolero RL, Bollmann MD, Revelly JP, Cayeux R N MC, 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.
26. Rubinson L, Diette GB, Song X, Brower RG, Krishnan JA. Low caloric intake is associated with nosocomial bloodstream infections in patients in the medical intensive care unit. *Crit Care Med* 2004;32(2):350-7.
27. National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network, Rice TW, Wheeler AP, Thompson BT, Steingrub J, Hite RD, Moss M, Morris A, Dong N, Rock P. Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial. *JAMA* 2012;307(8):795-803.
28. Rello J, Afonso E, Lisboa T, Ricart M, Balsera B, Rovira A, et al. A care bundle approach for prevention of ventilator-associated pneumonia. *Clin Microbiol Infect* 2013;19(4):363-9.
29. Rello J, Lode H, Cornaglia G, Masterton R; VAP Care Bundle Contributors. A European care bundle for prevention of ventilator-associated pneumonia. *Intensive Care Med* 2010;36(5):773-80.