Optimal Nutritional Factors Influencing the Duration of Mechanical Ventilation among Critically ill Adults in the Intensive Care Unit

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Abstract: Background: Malnutrition is associated with a complication problem affecting critically ill patients throughout the trajectory of their illness and which may increase the duration of hospitalization and mechanical ventilation and mortality. To explore nutritional factors impact on the duration of mechanical ventilation in critically ill patients. Methods: In this single-center, prospective observational study in a critical care unit. The sample of the study consisting of a total of 100 critically ill patients who were included in the regression analyzed by purposive sampling, performed to address the research objectives. The data were collected for each patient who participated in the study for 2 consecutive days with SGA, Dyspnea assessment form, APACHE II, and time to initial EN on the 24 hours of hospital admitted and the daily calories target requirement on the seven days. Results: At the end of monitoring, the nutrition status, time to initial EN, and calories, target requirements were moderate positive statistically significant related to the duration of mechanical ventilation (R = 0.54, R = 0.30, R= 0.40, p < 0.05). However, age, the severity of illness, and dyspnea scales were not related to the duration of mechanical ventilation (p> 0.05). Therefore, nutrition status and calory target requirements could be a predictor of the duration of mechanical ventilation. The predictive power was 28.0 percent of variance (R2 = 0.28, P < 0.01). Conclusion: The finding supports which assessment of the nutritional status and calory target requirement within 7 days revealed with reducing the duration of mechanical ventilation in critically ill patients.

Keywords: cohort study; critical care; enteral feeding; mechanical ventilation; nutritional status

1. Introduction

Critically ill patients usually have major organ failure; or dysfunctional respiratory, or circulation systems [1,2]. In life-threatening conditions, the body would respond by inflammatory stimulating systems due to hypermetabolic and hypercatabolic response and determine the malnutrition [3,4]. Critically ill patients' energy and protein stores decrease because of hypercatabolism and this may lead to increased infection complications, delayed recovery or wound healing, prolonged duration of hospitalization, and mechanical ventilation [5]. Although, the prevalence of malnutrition is revealed with a high proportion of critically ill with chronic disease of 40% to 60%, consequently there are changes in systematic functions [6], such as   loss of lean body mass, also diaphragmatic muscle mass and impairment of the respiratory muscle function accompanied by a reduction in lung capacity, risk of depletion of fat or protein reserves, diaphragm muscle

weakness, reducing the ability to wean from mechanical ventilation and increasing admission time to over 5 days, which results in increased morbidity and mortality [7,8].

Moreover, critically ill patients should start enteral nutrition support within 24-48 hours admission or after resuscitation was recommended by the American Society of Parenteral and Enteral Nutrition (ASPEN) [4] in order to maintain the systemic immune functions and structure of major organ [9]. A literature review of the nutritional support has shown that critically ill patients 75.6% of receive adequate protein and 61.2% of meet the requirements of energy within the first 7 day of admission which may improve their respiratory function and structure and it would be increased the ability to weaning the mechanical ventilation [10].

Previous studies show malnutrition survival rate relates to many factors, such as age, severity of illness, underlying disease, digestive system, medication, clinical treatment, and other therapies. Patients should receive more than 80% of energy and protein intake within 72 hours [11], however, 60% receive late nutritional treatment and 42% of them have malnutrition [12]. Furthermore, all critically ill patients admitted to ICU should have their nutritional status assessed to identify malnutritional and nutritional risk and monitor nutrition status so to start EN as soon as possible, this may help predict of the duration of mechanical ventilation in critically ill patients [13]. The association between nutritional status and calory target has not been adequately shown in critically ill patients. Therefore, the purpose of this study was to determine nutritional factors and calory target as a predictor of the duration of mechanical ventilation in critically ill patients.

2. Materials and Methods

2.1. Study site
This prospective cohort study was conducted between January 2019 to October 2019 in a medical-surgical intensive care unit at the Tertiary Hospital in Thailand.

2.2. Study population
Inclusion criteria
All patients who received the EN, who invasive mechanical ventilator after hemodynamic stable within 6 hours were included.
Exclusion criteria
Patients who terminated the EN or palliative care

2.3. Data collection
The following data were collected:
(a)   Demographic data: aged > 18 years of age, gender, underlying disease and diagnosis on admission to ICU, the date of initiation of invasive mechanical ventilation, length of mechanical ventilation in days and initiation EN in hours.
(b)   The data assessment for first 24 hours and then assessed every 7 days of admission to ICU: APACHE II, Dyspnea scales, Nutrition status, and Calory targets requirement in hours.

2.4. Setting and Sample
Critically ill patients with invasive mechanical ventilation were selected from a medical-surgical intensive care unit at the Tertiary Hospital in Kalasin, Thailand and recruited by purposive sampling. The research was conducted between January 2019 to October 2019. This study used the G*Power computer program (version 3.1) [14] to calculate the sample size. A total of 110 participants were selected and 10 out of participants were excluded as they were palliative care and terminate EN, therefore, the final number of participants was 100.

2.5. Study instrument

Daily calories target requirement was used the Harris Benedict equation x 1.0-1.3 and 1.0-2.0 gm/kg body weight to calculate the calories target requirement in first 24 hours after ICU admission and was assessed every 7 days. Cronbach's alpha coefficient was .84 for the pilot and .86 for the main study.

Disease severity assessment form was used the APACHE II, which was developed by Knaus, et al. [15] to determine during the initial 24 hours after ICU admission. The scale consisted of 12 potential physiologic measures and the score will be 0 to 71, as if the APACHE II scores of 25 and over indicated more than 50% risk of mortality. Cronbach's alpha coefficient was .86 for the pilot and .93 for the main study.

Dyspnea Scales form was used the Dyspnea Visual Analogue Scale [DVAS] [16] for dyspnea scales within 24 hours after invasive mechanical ventilator and hemodynamic stable and the score min-max from 0 to 100 with higher scores determining severe dyspnea. Cronbach's alpha coefficient was .82 for the pilot and .84 for the main study.

Nutritional status was used the Subjective Global Assessment (SGA) [17] to classify patients' nutrition status: well nourished (A), moderately malnourished (B), or severely malnourished (C) and the score min-max from 0 to 11. Cronbach's alpha coefficient was .84 for the pilot and .86 for the main study.

2.6. Outcome

The primary outcome was the duration of mechanical ventilation in days.

2.7. Data analysis

The data were analyzed using SPSS, version 22.0, statistical program (IBM Corp., Armonk, NY, USA). Descriptive statistics, such as number, percentage, mean, and standard deviation, were used to analyze the participants' demographics. The Pearson's product moment correlation coefficient was used to analyze the relationship of nutritional factors and daily calories target requirement variables with the duration of mechanical ventilation. The multiple regression analysis with the stepwise method was used to assess the nutritional factors and daily calory target requirement variables as predictors on the duration of mechanical ventilation. For all analyses, $P < 0.05$ was considered significant.

3. Results

3.1. Characteristics of the participants

One hundred and forty of the critically ill patients admitted to the ICU between January 2019 to March 2020 during this period, 110 were eligible and 100 were enrolled and 10 were excluded. Completed data were available on 100 patients and were analyzed (Table 1). Illustrates the enrollment flow chart. One hundred of the eligible participants, to describe the demographic and clinical characteristics of the participants which 76% men and the median age of the participants was 61.79 (min-max = 20-94 years, SD = 16.99). A vast number of participants was admitted for medical illness, particularly for cardiovascular disease, 40%. Fifty-two percent were severe in risk of malnutrition (mean=7.81, SD = 1.61), 67% were severity of illness (mean = 43.24, SD= 20.20), 69 % were severe dyspnea (min-max = 70-100, mean = 95.0, SD = 9.10), 57% were started EN within 6 h (min-max = 1-24 h, mean = 7.40, SD = 5.40), 89% had daily calorie target requirement within 24-48 h of admitted to ICU (min-max= 14-72 h, mean = 31.15, SD = 7.20) and 86% had length of mechanical ventilation within 40 days, as most of them had a mechanical ventilation around 5 to 20 days (min-max= 1-40 days, mean = 7.70, SD= 5.80) (Table 2).

3.2. Nutritional factors and calories target requirements related to duration of mechanical ventilation

The nutritional factors included nutrition status, age, severity of illness, dyspnea scale, and time to initial EN. The data were analyzed by The Pearson's product moment correlation coefficient. As the result, the present study was shown that the nutrition status,

time to initial EN and calories target requirements were moderate positive statistically significant related to the duration of mechanical ventilation (R = 0.54, R = 0.30, R= 0.40, p < 0.05) as well as the age, severity of illness and dyspnea scales no significant difference with duration of mechanical ventilation (Table 3).

3.3. Nutritional factors and calories target requirements as predictors of the duration of mechanical ventilation

The result showed that nutrition status and calory target requirements could predict the duration of mechanical ventilation as the predictive power was 28.3 percent of the variance ($R^2 = 0.30$, p< 0.001). Therefore, nutrition status as the best predictor of the duration of mechanical ventilation (Beta = 0.59, p< 0.001) (Table 4).
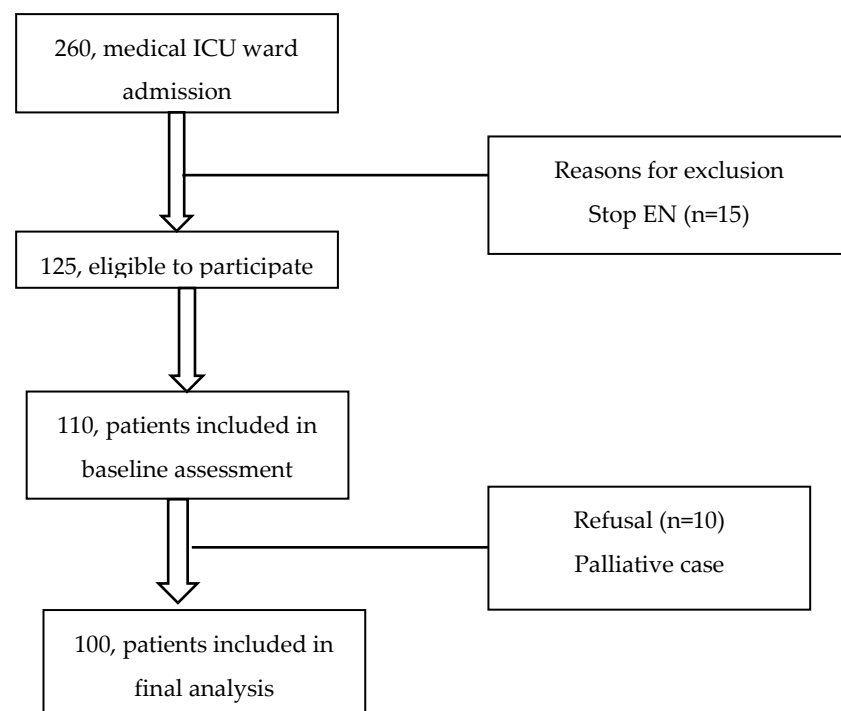
Figure 1. Study participant's flow chart in hospitals.

Table 1. This is a table. Tables should be placed in the main text near to the first time they are cited.

Characteristic data	Frequency	Percentages (%)
Gender		
Male	76	76
Female	24	24
Age (years)		
≤31	4	4
31-45	16	16
46-60	28	28
≥61	52	52
Diagnosis		
Cardiovascular disease	40	40
Respiratory disease	30	30
Kidney disease	21	21
Neurological disease	7	7
Gastrointestinal disease	2	2

Table 2. Mean scores for the demographic characteristics of critically ill patients.

Variables	Min	Max	Mean	SD
Age (years)	20	94	61.80	17
Nutrition status	3	7	7.81	1.61
Severity of illness	24	70	43.23	20.20
Dyspnea scales	70	100	94.8	9.04
Time to initial EN (hour)	1	24	7.41	5.40
Calories target requirements (hour)	14	72	31.20	7.20
Duration of mechanical ventilation (day)	1	40	7.70	5.80

Table3. Associated factors between the nutrition factors and duration of mechanical ventilation

Nutritional Factors	Duration of mechanical ventilation	
	R-value	p value
Nutrition status	0.54	<0.001
Age	0.10	0.40
Severity of Illness	0.10	0.54
Dyspnea scales	0.10	0.10
Time to initial EN	0.30	<0.001
Calories target requirements	0.40	<0.001

Table 4. The result of sequential multiple regression for predicting duration of mechanical ventilation (*N*=100)

Predictor	R	R^2	Adjust R^2	b	Beta	t	p value
Constant (a) = -190.11							
Nutrition status	0.53	0.28	0.28	50.35	0.58	6.29	<0.001
Calories target requirements	0.59	0.34	0.33	8.01	0.26	3.15	<0.001

4. Discussion

In this prospective study of critically ill patients on mechanical ventilation, our studied found a significantly an association between nutrition status, time to initial EN and calory target requirements on admission and duration of mechanical ventilation. Nutritional factors that could be predicted by the duration of mechanical ventilation is nutrition status and calories target requirements as well as nutrition status is a best predictor in the meantime. As a result of this present study, a malnourished in one score may require longer duration time for mechanical ventilation about 50.34 days. However, the timing of initiating of EN which quicker than 1 hour might be decreased because of the duration of mechanical ventilation in 8 days. This study has delivered average daily amounts of early full energy EN within 7 days and initial EN within 48 hours as followed the guidelines recommended. Moreover, more patients reached the calorie target in our study and this may be related to the fact that fully use of energy, EN might decrease the duration of mechanical ventilation [18-20].

Critically ill patients typically associated with hypermetabolic and hypercatabolic lead to increased loss of lean body mass, and these may induce malnutrition [19]. According to the American Society of Parenteral and Enteral Nutrition (ASPEN) we recommended that nutrition support therapy with early enteral nutrition should be started within 24-48 hours after ICU admission or when stable hemodynamic conditions after resuscitation, which received at least one vasopressor, and even in the absence of bowel

sound [1,21]. As recommended initial early enteral nutrition (EN) to support the functional integrity of the gut by maintaining structural integrity, especially respiratory muscle, also maintained by systemic immune function [22,23]. Critically ill patients who received daily calorie target requirement within first 7 days of hospitalization   which may help their respiratory muscle function improved, which would increase the ability to wean mechanical ventilation [24-26].

As a result of this present study showed nutrition status and calorie target requirements as predictors of a duration of mechanical ventilation. Therefore, assessment of nutrition status within 24 hours of arrival in the ICU for assessment of the risk of malnutrition and monitor in every 7 days as an importance to integrating nutritional support strategy for these populations. Moreover, the daily calories target requirement was a predictor of the duration of mechanical ventilation. Critically ill patients who are expected to be mechanically ventilated more than 72 hours may need 1,000 kcal/day or 30 g protein/day or 1.2 – 1.5 g/kg/BW/day or 25-kc/kg/day estimated nutrition requirements to reduce the duration of mechanical ventilation and mortality [20,27,28]. Likewise, Koontalay, et al. [29] reported critically ill patients prescribed early EN accrued significantly reduced duration of mechanical ventilation in comparison with those receiving standard care. Khalid, et al. [30] also reported that the beneficial effect of early EN was associated with decreased duration of mechanical ventilation and hospital mortality. Additionally, previous studies suggested that EN supports intestinal structure and function, preventing the increased permeability, bacteria translocation, and consequent systemic inflammation seen with gut obstructed. Early EN has been shown to decrease infection, complications and shorten of hospitalization and mortality [4].

In the present study, age, severity of illness, dyspnea scales, and time to initial EN were not predictors as nutrition factors of the duration of mechanical ventilation. As a result, to predictor of the duration of mechanical ventilation in critically ill patients is associated with several factors such as residual gastric volume, interrupted feeding, feeding formulas [27]. Recently study, Honda, Freitas, Stanich, Mazza, Castro, Nascente, Bafi, Azevedo and Machado [5] reported the achievement of daily calorie goals was inadequate and the main factors associated with the use and dosage of midazolam and the number of nurses available.

4.1. Study Limitations

There were several limitations of the present study. The first limitation was the sample size. Additionally, this study was conducted in a single hospital with medical surgical critical care unit, thus, the findings might not reflect other critical care units. Furthermore, the factors predicting selection were not extensive and lack of outcome assessment such as patients' morbidity or mortality.

5. Conclusions

The findings from the present study have shown that assessment of nutritional status is essential procedure for critically ill patients. Critically ill patients who receive enteral nutrition should be monitoring a daily calorie target requirement in every 7 days, to provide a nutritional support strategy to decrease the duration of mechanical ventilation in critically ill patients. Nutritional supports are carried out with guidelines that decrease the duration of mechanical ventilation in critically ill patients by providing appropriate nutritional care support should be an assessment of nutritional status and performed start early EN after hemodynamic stable.

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Data Availability Statement: There are no additional data used to support the findings of this study can be made available from the corresponding author upon request. All the data other than which are mentioned in the article already. The obtained data and materials were used only for the present study and are available only to the researchers who participated in the study project.

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References

1. Mueller, C.; Compher, C.; Ellen, D.M.; Parenteral, A.S.f.; Directors, E.N.B.o. ASPEN clinical guidelines: nutrition screening, assessment, and intervention in adults. Journal of Parenteral and Enteral Nutrition 2011, 35, 16-24, doi:10.1177/0148607110389335.
2. Stewart, M.L. Interruptions in enteral nutrition delivery in critically ill patients and recommendations for clinical practice. Critical Care Nurse 2014, 34, 14-22, doi:10.4037/ccn2014243.
3. Doig, G.S.; Heighes, P.T.; Simpson, F.; Sweetman, E.A. Early enteral nutrition reduces mortality in trauma patients requiring intensive care: A meta-analysis of randomised controlled trials. Injury 2011, 42, 50-56, doi:10.1016/j.injury.2010.06.008.
4. Elamin, E.M.; Camporesi, E. Evidence-based nutritional support in the intensive care unit. International Anesthesiology Clinics 2009, 47.
5. Honda, C.K.Y.; Freitas, F.G.R.; Stanich, P.; Mazza, B.F.; Castro, I.; Nascente, A.P.M.; Bafi, A.T.; Azevedo, L.C.P.; Machado, F.R. Nurse to bed ratio and nutrition support in critically ill patients. American Journal of Critical Care 2013, 22, e71-e78, doi:10.4037/ajcc2013610.
6. O'Leary-Kelley, C.; Bawel-Brinkley, K. Nutrition support protocols: enhancing delivery of enteral nutrition. Critical Care Nurse 2017, 37, e15-e23, doi:10.4037/ccn2017650.
7. Puthucheary, Z.A.; Rawal, J.; McPhail, M.; Connolly, B.; Ratnayake, G.; Chan, P.; …; Montgomery, H.E. Acute skeletal muscle wasting in critical illness. JAMA 2013, 310, 1591-1600, doi:10.1001/jama.2013.278481.
8. VanBlarcom, A.; McCoy, M.A. New nutrition guidelines: Promoting enteral nutrition via a nutrition bundle. Critical Care Nurse 2018, 38, 46-52, doi:10.4037/ccn2018617.
9. Klaude, M.; Mori, M.; Tjäder, I.; Gustafsson, T.; Wernerman, J.; Rooyackers, O. Protein metabolism and gene expression in skeletal muscle of critically ill patients with sepsis. Clinical Science 2011, 122, 133-142, doi:10.1042/cs20110233.
10. 10.Sungur, G.; Sahin, H.; Tasci, S. The effects of implementing a nutritional support algorithm in critically ill medical patients. J Pak Med Assoc 2015, 65, 810-814.
11. 11.Santos, H.; Araújo, I. Impact of protein intake and nutritional status on the clinical outcome of critically ill patients. Revista Brasileira de terapia intensiva 2019, 31, 210-216, doi:10.5935/0103-507X.20190035.
12. 12.Sharada, M.; Vadivelan, M. Nutrition in critically ill patients. Journal, Indian Academy of Clinical Medicine 2014, 15, 205-209.
13. 13.Kahraman, B.B.; Ozdemir, L. The impact of abdominal massage administered to intubated and enterally fed patients on the development of ventilator-associated pneumonia: A randomized controlled study. International Journal of Nursing Studies 2015, 52, 519-524, doi:10.1016/j.ijnurstu.2014.11.001.
14. 14.Faul, F.; Erdfelder, E.; Buchner, A.; Lang, A.-G. Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. Behavior Research Methods 2009, 41, 1149-1160, doi:10.3758/BRM.41.4.1149.
15. 15.Knaus, W.A.; Draper, E.A.; Wagner, D.P.; Zimmerman, J.E. APACHE II: A severity of disease classification system. Crit Care Med 1985, 13, 818-829.
16. 16.Gift, A.G. Validation of a vertical visual analogue scale as a measure of clinical dyspnea. Rehabilitation Nursing 1989, 14, 323-325, doi:10.1002/j.2048-7940.1989.tb01129.x.
17. 17.Detsky, A.S.; McLaughlin, J.R.; Baker, J.P.; Johnston, N.; Whittaker, S.; Mendelson, R.A.; Jeejeebhoy, K.N. What is subjective global assessment of nutritional status? Journal of Parenteral and Enteral Nutrition 1987, 11, 8-13, doi:https://doi.org/10.1177/014860718701100108.

18. 18. Moisey, L.L.; Mourtzakis, M.; Cotton, B.A.; Premji, T.; Heyland, D.K.; Wade, C.E.; Bulger, E.; Kozar, R.A.; for the, N.; Rehabilitation Investigators, C. Skeletal muscle predicts ventilator-free days, ICU-free days, and mortality in elderly ICU patients. Critical Care 2013, 17, R206, doi:10.1186/cc12901.

19. 19. McKendry, J.; Thomas, A.C.Q.; Phillips, S.M. Muscle mass loss in the older critically ill population: Potential therapeutic strategies. Nutrition in Clinical Practice 2020, 35, 607-616, doi:10.1002/ncp.10540.

20. 20. Kim, S.-H.; Park, C.-M.; Seo, J.-M.; Choi, M.; Lee, D.-S.; Chang, D.K.; Rha, M.; Yu, S.; Lee, S.; Kim, E. The impact of implementation of an enteral feeding protocol on the improvement of enteral nutrition in critically ill adults. Asia Pacific Journal of Clinical Nutrition 2017, 26, 27, doi:10.6133/apjcn.122015.01.

21. 21. McClave, S.A.; Taylor, B.E.; Martindale, R.G.; Warren, M.M.; Johnson, D.R.; Braunschweig, C.; McCarthy, M.S.; Davanos, E.; Rice, T.W.; Cresci, G.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, 159-211, doi:10.1177/0148607115621863.

22. 22. Reignier, J.; Mercier, E.; Le Gouge, A.; Boulain, T.; Desachy, A.; Bellec, F.; Clavel, M.; Frat, J.-P.; Plantefeve, G.; Quenot, J.-P.; 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, 249-256, doi:10.1001/jama.2012.196377.

23. 23. Rice, T.W.; Mogan, S.; Hays, M.A.; Bernard, G.R.; Jensen, G.L.; Wheeler, A.P. Randomized trial of initial trophic versus full-energy enteral nutrition in mechanically ventilated patients with acute respiratory failure. Crit Care Med 2011, 39, 967-974, doi:10.1097/CCM.0b013e31820a905a.

24. 24. Shen, Y.; Cheng, X.; Ying, M.; Zhang, W.; Jiang, X.; Du, K. Early low-energy versus high-energy enteral nutrition support in patients with traumatic intracerebral haemorrhage: Protocol for a randomised controlled trial. BMJ Open 2017, 7, e019199, doi:10.1136/bmjopen-2017-019199.

25. 25. Li, Q.; Zhang, Z.; Xie, B.; Ji, X.; Lu, J.; Jiang, R.; …; Sun, R. Effectiveness of enteral feeding protocol on clinical outcomes in critically ill patients: A before and after study. PLOS ONE 2017, 12, e0182393, doi:10.1371/journal.pone.0182393.

26. 26. Padar, M.; Uusvel, G.; Starkopf, L.; Starkopf, J.; Reintam Blaser, A. Implementation of enteral feeding protocol in an intensive care unit: Before-and-after study. World J Crit Care Med 2017, 6, 56-64, doi:10.5492/wjccm.v6.i1.56.

27. 27. Weijs, P.J.M.; Stapel, S.N.; de Groot, S.D.W.; Driessen, R.H.; de Jong, E.; Girbes, A.R.J.; Strack van Schijndel, R.J.M.; Beishuizen, A. Optimal protein and energy nutrition decreases mortality in mechanically ventilated, critically ill patients. Journal of Parenteral and Enteral Nutrition 2012, 36, 60-68, doi:10.1177/0148607111415109.

28. 28. Perman, M.I.; Ciapponi, A.; Franco, J.V.; Loudet, C.; Crivelli, A.; Garrote, V.; Perman, G. Prescribed hypocaloric nutrition support for critically-ill adults. Cochrane Database of Systematic Reviews 2018, doi:10.1002/14651858.CD007867.pub2.

29. 29. Koontalay, A.; Sangsaikaew, A.; Khamrassame, A. Effect of a clinical nursing practice guideline of enteral nutrition care on the duration of mechanical ventilator for critically ill patients. Asian Nursing Research 2020, 14, 17-23, doi:10.1016/j.anr.2019.12.001.

30. 30. Khalid, I.; Doshi, P.; DiGiovine, B. Early enteral nutrition and outcomes of critically ill patients treated with vasopressors and mechanical ventilation. American Journal of Critical Care 2010, 19, 261-268, doi:10.4037/ajcc2010197.