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Malnutrition in Critical Ill Patients and Its Relation to Outcome

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Abstract

Malnutrition, specifically in hospitalized patients, is considered a major clinical problem worldwide. A large percentage of patients experience a decline in nutrition status throughout their hospitalization. Although major efforts have been made to prevent and treat malnutrition in hospitalized patients, studies still show that the problem is recurrent. The adverse health outcomes of malnutrition are serious and life-threatening and result in increased risk of infection, hospital length of stay (LOS), mortality rate, and healthcare costs. The provision of artificial nutrition for critically ill patients is of great importance as many are unable to maintain their own nutritional needs. The administration of either enteral nutrition (EN), parenteral nutrition (PN), or both has become a daily practice in intensive care units. Despite this, many patients remain undernourished or even malnourished and it estimated that the incidence of malnutrition in intensive care patients could be as high as 50%. The reasons by which patients become or remain undernourished are multifactorial and range from physiological to iatrogenic. In order to lessen the catabolic state, which results from the hypermetabolism associated with critical illness, prompt and adequate nutritional support must be delivered. It is essential that members of the multidisciplinary team caring for critically ill patients are aware of the importance of nutrition and the deleterious effects of malnutrition to achieve the best possible outcome for patients.

Keywords: Malnutrition, Critical Ill, EN, PN, NRS Score, Nutric Score

Full-length article **Corresponding Author*, e-mail: *Ahmedelbahrawy28@gmail.com*

1. Introduction

Nutritional support in critically ill patients is very important to support the patient during the period of stress to preserve the lean body mass, maintain the immune function and avoid metabolic complications [1]. An appropriate nutritional support is indispensable to critically ill patients, who are almost at hypermetabolic state of their clinical condition such as trauma, sepsis, and major surgery [2]. Malnutrition is commonly encountered in critically ill patients. The incidence in critically ill patients had been reported ranging from 38% to 78% in intensive care unit, which is associated with the patients' increased morbidity, mortality, and hospital- related cost [3]. Heyland et al. developed a screening tool for critically ill patients. Previous screening tools implicated all critically ill patients in high-risk category and no screening tool studied exclusively in critically ill population.

Heyland et al. in a prospective observational multicenter study, data were collected, and a multivariable model was developed. The authors selected the parameters based on a conceptual model of malnutrition in critically ill including inflammatory markers; severity illness scores, and developed the scoring system. The NUTRIC score was able to discriminate critically ill patients who will benefit from aggressive protein energy provision. This was the first screening tool that validated and developed in critically ill patients. The score can be easily calculated with parameters measured in daily care of critically ill patients. Addition of IL-6 marker called as modified NUTRIC score by the authors. However, the addition of IL-6 did not improve the discriminative ability of the score; hence, the authors suggest using the score also when IL-6 values are not available [4]. The A.S.P.E.N./society of critical care medicine guidelines suggest using either NRS 2002 or NUTRIC for nutritional screening in critically ill patients.

The NUTRIC score is more useful in critically ill patients as it developed in critically ill patients and recent food intake and weight change, which is difficult to obtain in ICU patients were not included. Limitations of the NUTRIC score were that it did not include nutritional parameters and also micronutrient deficiencies were not included [5]. The NUTRIC score still not prospectively tested in a randomized control trial. The NUTRIC score performed better as compared to the MUST score in critically ill patients. Comparative studies between NUTRIC and NRS 2002 scores showed inconsistent results. In one retrospective study, NRS 2002 showed higher sensitivity and specificity for the diagnosis of malnutrition when compared to NUTRIC score, while another retrospective study by Canales et al. found that NUTRIC score was superior to NRS 2002 for assessing malnutrition risk. An observational study by Coltman et al. found that NUTRIC score was no different to routine screening. In a recent observational study, NUTRIC score was also able identify high-risk critically ill COVID-19 patients [6].

1.1. Nutritional Assessment

Nutritional assessment is a formal assessment of the nutritional status of a patient by a trained healthcare professional usually a dietician, and results in nutrition-related diagnosis. Once a patient identified as at risk from the screening tools detailed, nutritional assessment should be performed. Indian Society of Critical Care Medicine practice guidelines for nutrition in critically ill patients recommend the nutritional assessment by Subjective Global Assessment (SGA). Assessment by anthropometry like body mass index (BMI) is difficult to measure in critical care setting. Measurement of serum albumin, transferrin, and prealbumin is not reliable in critically ill patients [6].

1.1.1. Subjective Global Assessment

It is a subjective nutritional assessment tool initially developed for post-gastrointestinal surgery patients. The tool was later studied in critically ill patients. The SGA scale includes parameters to assess subcutaneous fat, muscle wasting, fluid retention, weight change, recent food intake, gastrointestinal symptoms, and functional capacity. Subjective Global Assessment class C includes severe malnutrition, SGA class B includes moderate malnutrition, and SGA class A includes no malnutrition [7]. In a meta-analysis of studies of use of SGA in critically ill patients, SGA was more favorable than other assessment tools and SGA grade B and C had poor outcomes. Subjective Global Assessment is simple and easy to assess at the bedside and is cost-effective. The main limitations of SGA were that severity of illness were not included, assessment of weight and food history in critically ill patients was difficult, changes in SGA grade takes a long time usually many days [8].

Besides the subjective assessment, it is also important to assess the gastrointestinal tract with gastric residual volumes to assess the nutritional status in critically ill patients. Other methods studied were use of computed tomography (CT) scan to assess the muscle mass, as CT scan is cumbersome use of ultrasonography assessment of quadriceps muscle thickness has been studied. Ultrasonography is a simple, noninvasive, bedside tool to assess muscle mass. It can be performed serially and detect short-term changes. A prospective study by Rodrigues et al. assessed quadriceps and rectus femoris muscle thickness using ultrasonography and the reduction in muscle mass correlated with severe malnutrition. Ultrasonographic assessment of muscle mass needs further validation and is a useful future tool. Bioelectrical impedance is another tool used to measure fat free mass; however, the fluid electrolyte imbalance in critically ill patients affects the measurements taken [9].

1.1.2. Practical Implications of Nutritional Assessment in Critically Ill Patients

Nutrition assessment and prescription in critically ill patients is often ignored world over. International guidelines recommend that every patient should be screened for malnutrition within 24–48 hours of ICU admission, as many of these patients are at a risk or may have malnutrition at admission to ICU due to the underlying severity of the illness [7]. Malnutrition and muscle wasting set in early during the ICU stay because of the imbalance between energy and protein requirements and intake. A trained nutrition expert or a dietician is not necessary to identify patients who are, or at risk of malnutrition. Nutrition assessment starts with a good patient history and physical examination for emaciation and loss of muscle mass. However, loss of muscle function may occur much before loss of muscle mass, which may go unnoticed in an obese or fluid retained critically ill patient, unless actively screened. Anthropometric measurements like patient's weight in ICU is technically difficult and may fluctuate widely due to fluid shifts during the ICU stay [10]. The NUTRIC score is an easy screening tool, which can be used at the bedside. If found at risk the patient should be assessed in detail by a nutritionist/dietician or by the treating clinician if nutritionist is not available. Nutritional assessment should be performed using the SGA tool. The SGA although validated in critically ill patients has its limitations; to obtain the necessary anthropometric measurements and muscle function assessment in a sedated patient may be near impossible.Nutrition screening and assessment should be a continuous process for all hospitalized patients so as to intervene early with necessary protein and energy supplementation [7].

1.2. Complications of malnutrition in ICU patients

1.2.1. Airway-related consequences of malnutrition

Tracheostomy complications

- Malnutrition leads to the development of premature age-related changes in the trachea [10]. In other words, you may be thirty with an eighty-year-old trachea.
- Delayed healing of the tracheostomy wound results from protein malnutrition
- Breakdown of the wound, and the need to up-size the tube as the patient loses weight
- Greater risk of periprocedural complications (e g. puncture of the posterior wall)
- Greater risk of tracheal cartilage damage, as the malnourished trachea is less elastic

1.2.2. Respiratory consequences of malnutrition

Respiratory muscles wasting

- In patients who are at ~ 70% of their ideal, body mass, the diaphragmatic muscular mass reduced by 43%.
- Half of this reduction is due to thinning of the diaphragm, and half is due to loss of its length.
- Intercostal and accessory muscles are also wasted

1.2.3. Decreased capacity to compensate for respiratory disease

- There is a diminished ability to compensate for an acute increase in demand: there is decreased respiratory muscle bulk, and respiratory muscle fatigue occurs with less effort.
- Thus, these patients are more susceptible to respiratory failure.
- This is illustrated in the increased propensity of malnourished COPD patients to undergo mechanical ventilation, as compared to their well-nourished counterparts [11].

- Respiratory muscle loss results in a greater propensity towards hypercapnic respiratory failure, and in a decreased capacity to compensate for metabolic acidosis.

1.2.4. Decreased ventilatory drive

- Nutritional depletion affects the CNS respiratory drive center.
- Nutrient-restricted volunteers (on 550kcal/day) had a 58% reduced ventilatory response to hypoxia.

1.2.5. Poor spirometry

- The vital capacity was reduced by 37% from expected normal values in malnourished individuals who did not have respiratory disease
- In these people, maximum inspiratory and expiratory pressures also reduced by 63% when compared to healthy age-matched controls.

1.2.6. Structural changes of lung tissue

- Lungs of rats starved to lose 40% of their total body weight demonstrated emphysema-like changes [12].
- There was also a decrease in the surfactant properties of the surfactant

1.2.7. Prolonged ventilator weaning

- Decreased muscle mass and easier fatigue gives rises to poorer response in spontaneous breathing trials; these people tire faster and require either shorter trials, or a slower decremental wean of pressure support.
- Duration of ventilation correlates with the severity of nutritional depletion

1.2.8. Blunted respiratory immune defenses

- Impaired regeneration of respiratory epithelium.
- Decreased alveolar macrophage activity and number [13].
- Decreased levels of IgA in the respiratory secretions.
- Thus, increased incidence and severity of respiratory tract infections.

1.2.9. Circulatory consequences of malnutrition

- ***Cardiac muscle atrophy and reduced left ventricular function***
- Cardiac mass is lost in proportion to body mass [14]
- This is mainly due to LV wall thinning
- Intrinsic properties of the myocardium usually maintained.
- In severe marasmic kwashiorkor, circulatory failure with high vascular resistance is seen [15].

1.2.10. Bradycardia, hypotension, and decreased cardiac output

- Decreased whole-body metabolic rate tends to result in decreased demand on the myocardium.
- The energy-conserving adaptations to prolonged starvation include the following cardiac changes:
  - Bradycardia
  - Hypotension
  - Decreased cardiac contractility
- This results in a decreased capacity to compensate for increased demand, e g. Septic shock state.

1.2.11. Consequences of micronutrient depletion, e g. Beri Beri

- Key micronutrients involved in cardiac metabolism are coenzyme Q10, l-carnitine, thiamine, and amino acids, including taurine [16].
- The depletion of thiamine may give rise to a high output cardiac failure state (wet Beri Beri).

1.2.12. Endocrine and electrolyte consequences of malnutrition

- ***Depression of hypothalamic and pituitary function***
- Nonessential metabolic activities suppressed, e.g. gonadotropins and other reproductive hormone secretion is impaired.
- In starvation, menstruation is suspended and amenorrhea develops.
- Thyroid function is depressed; the patients trend to hypothermia.
- Adrenal function is depressed, and though not clinically hypo- adrenal the patient has diminished adrenal reserve and may more easily develop the relative adrenal insufficiency of critical illness.

1.3. Effects of malnutrition on the function of other organ systems

1.3.1. Increased mortality in malnourished renal failure patients

- Malnourished patients have increased mortality when they develop acute renal failure, particularly when it is in association with septic or cardiogenic shock [17].
- Hemodialysis patients are at risk of malnutrition because they suffer a constant amino acid loss via the circuit
- CRRT is particularly good at removing water-soluble vitamins

1.3.2. Gastrointestinal consequences of malnutrition

- Poor healing of anastomotic joins
- Poor barrier function of the gut
- Increased propensity to gastric ulceration (and decreased rate of gastric ulcer healing)

1.3.3. Hematological consequences of malnutrition

- Decreased hematopoiesis.
  - Iron deficiency
  - Hematinic vitamin deficiency
- Structurally abnormal cells (e g. the macrocytosis of B12 depletion)
- Diminished synthesis of clotting factors

1.3.4. Immunological consequences of malnutrition

- Decreased immune cell number and function
- Decreased wound healing
- Decreased phagocytosis
- Decreased synthesis of complement proteins
- Decreased synthesis of immunoglobulin

Hiura et al. [18] found that malnutrition using various definitions has previously been associated with increased hospital length of stay (LOS) and in-hospital mortality rates. A recent retrospective study by Hudson et al found that among patients diagnosed with severe malnutrition using the Academy of Nutrition and Dietetics/ American Society of Parenteral and Enteral Nutrition (AND/ASPEN) criteria (n = 3907), 30-day hospital readmission rates, hospital LOS, and in-hospital mortality rates were significantly increased [19]. Among critically ill patients assessed by the AND/ASPEN criteria in the intensive care unit (ICU) (n = 327), Ceniccola et al showed that patients with malnutrition had significantly increased mortality rates compared with patients without malnutrition [20]. Most studies that have explored the effects of malnutrition on LOS or mortality have had small sample sizes, were conducted internationally, or have used other validated screening tools [21-24]. By validating these characteristics in larger hospital settings, we can demonstrate the importance of standardizing the data collection process and begin to elucidate relevant diseases or conditions associated with malnutrition.

Table 1. Nutritional risk screening 2002 [4]

Nutritional status	Score	Stress metabolism (severity of disease)	Score
None	0	None	0
Moderate	2	Moderate stress metabolism	2
Weight loss >5% in 2 months		Patient is bedridden due to illness	
BMI 18.5–20.5 kg/m^2 AND		Highly increased protein requirement	
Reduced general condition		Stroke, hematologic cancer, severe pneumonia, extended abdominal surgery	
OR			
25–50% of the normal food intake in the last week			
Severe	3	Severe stress metabolism	3
Weight loss >5% in 1 month		Patient is critically ill (intensive care unit)	
OR		Very strongly increased protein requirement can only be achieved with parenteral nutrition	
BMI <18.5 kg/m^2 AND reduced general condition		APACHE II >10, bone marrow transplantation, head traumas	
OR			
0–25% of the normal food intake in the last week			

Total (A) Total (B)
Age = <70 years: 0 pt, ≥70 years: 1 pt
Total = (A) + (B) + Age
≥3 points: Patient is at nutritional risk. Nutritional care plan to be set up, <3 points: Repeat screening weekly

Table 2. NUTRIC scoring system: if IL-6 available [7]

Sum of points	Category	Explanation
6–10	High score	• Associated with worse clinical outcomes (mortality, ventilation).
		• These patients are the most likely to benefit from aggressive nutrition therapy.
0–5	Low score	• These patients have a low malnutrition risk.

Table 3. NUTRIC scoring system: If no IL-6 available*[7]

Sum of points	Category	Explanation
5–9	High score	• Associated with worse clinical outcomes (mortality, ventilation).
		• These patients are the most likely to benefit from aggressive nutrition therapy.
0–4	Low score	• These patients have a low malnutrition risk.

Koontalay et al. [25] show that the nutritional status, time to initial EN, and calorie target requirement within 7 days of admission are associated with the mechanical ventilation duration in the critical patients. Therefore, it can used to develop guidelines reducing the mechanical ventilation duration and to promote the ventilator halting for critical patients. The critical illness steadily increases hypermetabolism as protein and fats in muscle tend to decrease, especially the diaphragm resulting in muscle atrophy, fatigue movement, difficult breathing and extended mechanical ventilation [26-27]**.** The American Society of Parenteral and Enteral Nutrition (ASPEN) recommended that ICU patients should start enteral nutrition (EN) support within 24 to 48 hours of admission or after resuscitation [27] in order to maintain systemic immune functions and structure of major organs [28]. Accordingly, the American Society of Parenteral and Enteral Nutrition (ASPEN) recommended that 75.6% of patients receive adequate protein and 61.2% meet energy requirements within the first 7 days of admission.

It can improve their respiratory function, structure, increase weaning ability [29] and reduce mechanical ventilator duration [30]. It has been discovered that nutrition importantly supports critical patient recovery by affecting treatment outcome and mechanical ventilator duration [31]. Factors correlated with nutritional conditions for critical patients using ventilator have been studied, however, it is not applied. Therefore, this study purposely focuses on factors influencing the mechanical ventilators duration for critical patients. The selected factors include malnutrition, age, disease severity, dyspnea scale, initial EN time, and targeted calorie requirement [32]. It could be defined as a guideline in mechanical ventilation for critical patients leading to ventilator availability and reduced admission duration [32].

References

[1] R.A. Hegazi, P.E. Wischmeyer. (2011). Clinical review: optimizing enteral nutrition for critically ill patients-a simple data-driven formula. Critical Care. 15: 1-11.

[2] E. Ridley, D. Gantner, V. Pellegrino. (2015). Nutrition therapy in critically ill patients-a review of current evidence for clinicians. Clinical Nutrition. 34(4): 565-571.

[3] C.C.H. Lew, R. Yandell, R.J. Fraser, A.P. Chua, M.F.F. Chong, M. Miller. (2017). Association between malnutrition and clinical outcomes in the intensive care unit: a systematic review. Journal of Parenteral and Enteral Nutrition. 41(5): 744-758.

[4] D.K. Heyland, R. Dhaliwal, X. Jiang, A.G. Day. (2011). Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. Critical Care. 15: 1-11.

[5] E. Reber, F. Gomes, M.F. Vasiloglou, P. Schuetz, Z. Stanga. (2019). Nutritional risk screening and assessment. Journal of clinical medicine. 8(7): 1065.

[6] C. Canales, A. Elsayes, D.D. Yeh, D. Belcher, A. Nakayama, C.M. McCarthy, N. Chokengarmwong, S.A. Quraishi. (2019). Nutrition risk in critically ill versus the nutritional risk screening 2002: are they comparable for assessing risk of malnutrition in critically ill patients? Journal of Parenteral and Enteral Nutrition. 43(1): 81-87.

[7] S.K. Narayan, K.K. Gudivada, B. Krishna. (2020). Assessment of nutritional status in the critically ill. Indian journal of critical care medicine: peer-reviewed, official publication of Indian Society of Critical Care Medicine. 24(Suppl 4): S152.

[8] Y. Mehta, J. Sunavala, K. Zirpe, N. Tyagi, S. Garg, S. Sinha, B. Shankar, S. Chakravarti, M. Sivakumar, S. Sahu. (2018). Practice guidelines for nutrition in critically ill patients: a relook for Indian scenario. Indian journal of critical care medicine: peer-reviewed, official publication of Indian Society of Critical Care Medicine. 22(4): 263.

[9] C.N. Rodrigues, J. Ribeiro Henrique, Á.R.S. Ferreira, M.I.T.D. Correia. (2021). Ultrasonography and other nutrition assessment methods to monitor the nutrition status of critically ill patients. Journal of Parenteral and Enteral Nutrition. 45(5): 982-990.

[10] N.M. Mehta, M.R. Corkins, B. Lyman, A. Malone, P.S. Goday, L. Carney, J.L. Monczka, S.W. Plogsted, W.F. Schwenk, A.S.f. Parenteral, E.N.B.o. Directors. (2013). Defining pediatric malnutrition: a paradigm shift toward etiology-related definitions. Journal of Parenteral and Enteral Nutrition. 37(4): 460-481.

[11] S. Bouma. (2017). Diagnosing pediatric malnutrition: paradigm shifts of etiology-related definitions and appraisal of the indicators. Nutrition in Clinical Practice. 32(1): 52-67.

[12] M.R. Corkins. (2017). Why is diagnosing pediatric malnutrition important? Nutrition in Clinical Practice. 32(1): 15-18.

[13] S. Moriguchi, S. Sone, Y. Kishino. (1983). Changes of alveolar macrophages in protein-deficient rats. The Journal of Nutrition. 113(1): 40-46.

[14] P.B. Alden, R.D. Madoff, T.J. Stahl, D.J. Lakatua, W.S. Ring, F.B. Cerra. (1987). Left ventricular function in malnutrition. American Journal of Physiology-Heart and Circulatory Physiology. 253(2): H380-H387.

[15] P. Viart. (1977). Hemodynamic findings in severe protein-calorie malnutrition. The American journal of clinical nutrition. 30(3): 334-348.

[16] V. Soukoulis, J.B. Dihu, M. Sole, S.D. Anker, J. Cleland, G.C. Fonarow, M. Metra, E. Pasini, T. Strzelczyk, H. Taegtmeyer. (2009). Micronutrient deficiencies: an unmet need in heart failure. Journal of the American College of Cardiology. 54(18): 1660-1673.

[17] L.E. Carter, G. Shoyele, S. Southon, A. Farmer, R. Persad, V.C. Mazurak, M.K. BrunetWood. (2020). Screening for pediatric malnutrition at hospital admission: which screening tool is best? Nutrition in Clinical Practice. 35(5): 951-958.

[18] G. Hiura, B. Lebwohl, D.S. Seres. (2020). Malnutrition diagnosis in critically ill patients using 2012 Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition standardized diagnostic characteristics is associated with longer hospital and intensive care unit length of stay and increased in-hospital mortality. Journal of Parenteral and Enteral Nutrition. 44(2): 256-264.

[19] L. Hudson, J. Chittams, C. Griffith, C. Compher. (2018). Malnutrition identified by Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition is associated with more 30-day readmissions, greater hospital mortality, and longer hospital stays: a retrospective analysis of nutrition assessment data in a major medical center. Journal of Parenteral and Enteral Nutrition. 42(5): 892-897.

[20] G.D. Ceniccola, T. Holanda, R. Pequeno, V. Mendonça, A. Oliveira, L. Carvalho, I. de Brito-Ashurst, W. Araujo. (2018). Relevance of AND-ASPEN criteria of malnutrition to predict hospital mortality in critically ill patients: A prospective study. Journal of critical care. 44: 398-403.

[21] M.N. Thomas, J. Kufeldt, U. Kisser, H.-M. Hornung, J. Hoffmann, M. Andraschko, J. Werner, P. Rittler. (2016). Effects of malnutrition on complication rates, length of hospital stay, and revenue in elective surgical patients in the G-DRG-system. Nutrition. 32(2): 249-254.

[22] P.P. Verghese, A.S. Mathai, V. Abraham, P. Kaur. (2018). Assessment of malnutrition and enteral feeding practices in the critically ill: A single-centre observational study. Indian Journal of Anaesthesia. 62(1): 29-35.

[23] E.A. Cano-Torres, L.E. Simental-Mendía, L.A. Morales-Garza, J.M. Ramos-Delgado, M.M. Reyes-Gonzalez, V.M. Sánchez-Nava, A.d.J. Barragán-Berlanga, I. Rangel-Rodríguez, F. Guerrero-Romero. (2017). Impact of nutritional intervention on length of hospital stay and mortality among hospitalized patients with malnutrition: a clinical randomized controlled trial. Journal of the American College of Nutrition. 36(4): 235-239.

[24] C. Mosquera, N.J. Koutlas, K.C. Edwards, A. Strickland, N.A. Vohra, E.E. Zervos, T.L. Fitzgerald. (2016). Impact of malnutrition on gastrointestinal surgical patients. Journal of Surgical Research. 205(1): 95-101.

[25] A. Koontalay, W. Suksatan, J.M. Sadang, K. Prabsangob. (2021). Optimal nutritional factors influencing the duration of mechanical ventilation among adult patients with critical illnesses in an intensive care unit. Journal of Multidisciplinary Healthcare. 1385-1393.

[26] G.S. Doig, P.T. Heighes, F. Simpson, E.A. Sweetman. (2011). Early enteral nutrition reduces mortality in trauma patients requiring intensive care: a meta-analysis of randomised controlled trials. Injury. 42(1): 50-56.

[27] E.M. Elamin, E. Camporesi. (2009). Evidence-based nutritional support in the intensive care unit. International Anesthesiology Clinics. 47(1): 121-138.

[28] M. Klaude, M. Mori, I. Tjäder, T. Gustafsson, J. Wernerman, O. Rooyackers. (2012). Protein metabolism and gene expression in skeletal muscle of critically ill patients with sepsis. Clinical science. 122(3): 133-142.

[29] G. Sungur, H. Sahin, S. Tasci. (2015). The effects of implementing a nutritional support algorithm in critically ill medical patients. JPMA. The Journal of the Pakistan Medical Association. 65(8): 810-814.

[30] H.V.D.d. Santos, I.S.d. Araújo. (2019). Impact of protein intake and nutritional status on the clinical outcome of critically ill patients. Revista Brasileira de terapia intensiva. 31: 210-216.

[31] M. Sharada, M. Vadivelan. (2014). Nutrition in critically ill patients. J Indian Acad Clin Med. 15(3-4): 205e9.

[32] B.B. Kahraman, L. Ozdemir. (2015). 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. 52(2): 519-524.