Journal of Integrative Oncology
ISSN: 2329-6771
Filho et al., J Integr Oncol 2016, 5:1
DOI: 10.4172/2329-6771.1000156
Research Article
Open Access

Main Barriers in Control of Energy-Protein Deficit in Critical Oncologic Patient at Nutritional Risk

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Abstract

Introduction: The Nutrition Risk in Critically ill (NUTRIC) score is a specific tool for assessing the nutritional risk in the Intensive Care Unit (ICU). Under these conditions, it is extremely important to monitor Enteral Nutrition Therapy and identify main barriers in the control of energy-protein deficit.

Objective: To identify main barriers to control the energy-protein deficit in critically ill patients at nutritional risk, on enteral nutrition (EN) and on mechanical ventilation (MV).

Methods: Prospective, observational, descriptive study was conducted in an ICU in 2015. Patients >19 years of age on MV and underwent EN for >72 hours. The data collected were NUTRIC score, Subjective Global Assessment (SGA), Cachexia Syndrome, APACHE II, SOFA, ICU time, MV and EN times and main barriers for pausing EN. The protein-calorie deficit was compiled into total days of EN.

Results: Total of 62 patients, 22 were excluded, 40 analyzed. The scores were NUTRIC 7 (+0.7), APACHE 26 (+5.2), SOFA 11.5 (+2.2), Body Mass Index 23.2 (+6.2) kg/m², 47% malnourished (SGA B+C), 70% cachexia syndrome and mortality rate of 52.5%. Among these patients, 77.5% underwent early EN and percentage of volume prescribed infused was 89%. It was observed total deficit of -296 (+339) calories and -28 (IQ -58:-2.95) g/protein. Main barriers for pausing EN were extubation 38%, hemodynamic instability 29%, tracheostomy, diarrhea and vomiting, both 6.5%. There was a statistically significant difference between calorie ($p<0.003$) and protein ($p<0.002$) deficits in the subgroups of adult patients compared to malnourished elderly patients with cachexia syndrome: -358.9 (+305) calories and -33 (+14.24) g/protein; -91.6 (+190) calories and -18.8 (+7.96) g/protein, respectively.

Conclusion: The main barriers in control of energy-protein deficit in critical oncologic patient at nutritional risk on EN and on MV were extubation and hemodynamic instability.

Keywords: Enteral nutrition; Critically ill patient; Malnutrition; Cancer

Introduction

The prevalence of nutritional risk in cancer patients is high [1], Oliveira Filho et al. [2], after evaluating 551 cancer patients found a prevalence of 63% nutritional risk and these 57% were malnourished. Brazilian nutrition survey, a multicenter study involving 4000 hospitalized patients showed that 48.1% patients were malnourished, and these 12.5% were severely malnourished. In this study, the presence of malnutrition was related to the age of ≥ 60, length of stay in hospital and the presence of infection or cancer [1].

Fontes et al. [3], evaluated 185 critically ill patients and observed 54% malnutrition. According to the Subjective Global Assessment (SGA), 41% classified as moderately malnourished (SGA B) and 12.4% with severe malnutrition (SGA C) [3]. The Nutrition Risk in Critically ill (NUTRIC) is considered the best tool for assessing nutritional risk in the Intensive Care Unit (ICU) [4-6]. Critically ill patients on mechanical ventilation (MV) quickly developed malnutrition or aggravated a preexisting condition due to metabolic/oxidative stress associated with the inflammatory response and the constant catabolism [7-9].

Under these conditions, the implementation and rigorous monitoring of enteral nutrition therapy (ENT) is extremely important in order to avoid possible calorie-protein deficit and exacerbate malnutrition [6]. The ENT is also considered, the preferred route when the gastrointestinal tract is structurally intact and functioning [6,8,10]. The nutrient supply through the digestive system assists in maintaining the architecture and intestinal microbiota, modulates the intestinal immune system and it is associated with lower incidence of infectious complications in surgical patients when compared to parenteral nutrition therapy [6,10].

Nevertheless, the benefits of enteral nutrition prescription can only be achieved if there is a systematic control of calorie-protein deficit [6]. In addition, it is also necessary to identify the main barriers that negatively impact the energy deficit in ICU patients. Studies show that the origin of complications of the gastrointestinal tract such as abdominal distension, vomiting and diarrhea are the main reasons for pausing EN [6], however, the main barriers in control calorie-protein deficit in critical cancer patients at nutritional risk and on ventilation remain modestly described in the literature.

Objective

To identify main barriers to control the energy-protein deficit in

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Received January 18, 2016; **Accepted** February 08, 2016; **Published** February 10, 2016

Citation: Filho RSO, Tamburrino AC, Trevisani VS, Rosa VM (2016) Main Barriers in Control of Energy-Protein Deficit in Critical Oncologic Patient at Nutritional Risk. J Integr Oncol 5: 156. doi:10.4172/2329-6771.1000156

critical oncologic patients at nutritional risk (NUTRIC score ≥ 6), on ENT and on MV.

Methods

This prospective, observational and descriptive study was conducted in an adult ICU of a public hospital, a reference in assistance to cancer patients in the city of São Paulo (SP) – Brazil. Demographic and clinical characteristics of the patients were collected through electronic medical records between January and August 2015.

Cancer patient, > 19 years of age, on MV, underwent exclusive ENT for at least 72 hours and at nutritional risk (NUTRIC ≥ 6) were included. Patients with < 19 years of age, without nutritional risk (NUTRIC <6), Parenteral Nutrition Therapy (PNT), mixed nutritional therapy (ENT and PNT), in palliative care and those who did not include the criteria mentioned above were excluded. The collected variables were NUTRIC score [4-6], SGA [11], Cachexia Syndrome according to Fearon et al. [12], APACHE II, SOFA, ICU time, MV and ENT times and reasons for pausing ENT.

Estimates of dietary requirements were individualized, according to the clinical condition of the patient. To calculate caloric [6] needs, it was used 25 – 30 kcal/kg, for protein [6] needs 1.2-1.5 g protein/kg of body weight and for obese patients (Body Mass Index - BMI ≥ 30 kg/m²) it was used Penn State [13] formula to the calorie and protein requirements, according to American Society for Parenteral and Enteral Nutrition (ASPEN) [14].

The enteral diets were administered continuously with infusion pumps for approximately 20 hours, and the remaining 4 hours were reserved for the performance of other medical procedures, physiotherapy, exams and the administration of medication.

From the day the EN was initiated until extubation or patient death, the data regarding the infused EN volume, factors associated with EN interruption such as exams, procedures and gastrointestinal tolerance were collected daily. The assessment of gastrointestinal tolerance was based on a clinical evaluation of the occurrence of abdominal distension or vomiting and periodic checking of the gastric residuals (≥ 200 ml) and diarrhea (≥ 3 liquid stools per day) according to institutional protocol. After the data collection, the percentage of adequacy for calories and protein was calculated using the ratio of the amount of calories and proteins administered and the respective amounts prescribed daily. Subsequently, the mean percentage of adequacy was calculated for each patient and the mean adequacy of the sample.

The identification of the main barriers responsible for EN pause in hours and consequently the caloric-protein deficit was performed after consulting the daily electronic medical record of each patient.

The statistical analysis was performed using the STATA program. The Kolmogorov-Smirnov test was used to assess the sample normality. When the quantitative variable had a normal distribution, the mean and standard deviation were used. Otherwise, the median and interquartile ranges were used. To compare the qualitative variables, the chi-square test was used. To compare the quantitative variables, Student's t-test for normally distributed variables or the Mann-Whitney test for the other variables were adopted. For all of the tests, p values ($p < 0.05$) were considered significantly different.

Results

Total of 62 patients, 22 were excluded, 40 analyzed, mean age 64.65 (± 10.3) years, 65% were ≥ 60 years, 8.5 (± 2.8) days in ICU, 8 (± 2.8) days on MV, 7 (IQ 4:11) days on ENT and 52% were male. The main ICU diagnoses were septic shock 62% and 22% sepsis and the most frequent cancer diagnoses were Lung 22.5% and Gastrointestinal 20%. Furthermore, other results were observed such as APACHE score 26 (± 5.2), SOFA 11.5 (± 2.2) and mortality rate of 52.5%. In addition, the inflammatory profile was observed a mean of C-reactive protein 162.31 (± 114) mg/dL, while for Lactate, a marker of tissue perfusion, it was seen 24.4 (± 10.11) mg/dL. All described in Table 1.

In relation to nutritional status, all patients had nutritional risk at ICU admission with NUTRIC score 7 (± 0.7), BMI [15] 23.2 (± 6.2) kg/m², 15% were obese (BMI ≥ 30 kg/m²), 47% were malnutrition moderate and severe (SGA B+C), 70% had cachexia syndrome, 26% pre cachexia, 64% cachexia and 10% refractory cachexia (Table 2).

The ENT was prescribed 31.7 (± 19.7) hours after ICU admission, with early-onset in 77.5% patients, the nutritional goal was achieved 61.2 (± 30.1) hours, the prescribed for calories and proteins was 22 (± 5.1) kcal/kg, 0.9 (± 0.2) g/kg, respectively, while the administered was 19.67 (± 5.79) kcal/kg and 0.8 (± 0.24) g protein/kg. Besides that, it was found 92% of adequacy of prescribed infused for calories, 91.9% for proteins and 89.1% for volume of ENT (Table 3).

In all patients analyzed, it were observed deficit of -296 (± 339) calories and -28 (IQ -58:-2.95) g/protein. After subdividing the sample between adults and malnourished elderly and with cachexia syndrome, there was a statistically significant difference between calorie (p <

Total of patients (n)	62
Total of patients analyzed (n)	40
Male (%)	52
Age (years)	64.65 (± 10.3)
Elderly (≥ 60 years) (%)	65
Mortality (%)	52.5
Lung cancer (%)	22.5
GI tract cancer (%)	20
Septic Shock (%)	62
Sepsis (%)	22
APACHE II	26 (± 5.2)
SOFA *score*	11.5 (± 2.2)
ICU time (days)	8.5 (± 2.8)
MV time (days)	8 (± 2.8)
C-reactive protein (mg/dL)	162.31(± 114)
Lactate (mg/dL)	24.4 (± 10.11)

GI: Gastrointestinal, ICU: Intensive Care Unit, MV: Mechanical Ventilation.

Table 1: Demographic and clinical profiles of patients undergoing enteral nutrition therapy.

NUTRIC *score*	7 (± 0.7)
Mean BMI (Kg/m²)	23.2 (± 6.2)
Obesity (%)	15
SGA (Malnutrition moderate and severe) (%)	47
Cachexia syndrome (%)	70
- Pre cachexia (%)	26
- Cachexia (%)	64
- Refractory Cachexia (%)	10

Cachexia Syndrome according to Fearon et al. [12] Malnutrition according to OPAS, 2002 to patients ≥60 years. BMI: Body Mass Index, NUTRIC: Nutrition Risk in Critically ill, SGA: Subjective Global Assessment.

Table 2: Characteristics of nutritional status in patients on enteral nutrition.

Variables	Values
Duration of ENT (days)	7.1 (± 2.8)
Time of initiation ENT (hours)	31.7 (± 19.7)
Time to reach the nutritional goal (hours)	61.2 (± 30.1)
Mean prescribed calories (kcal/kg)	22 (± 5.1)
Mean prescribed proteins (g/kg)	0.9 (± 0.2)
Mean administered calories (kcal/kg)	19.67 (± 5.79)
Mean administered proteins (g/kg)	0.8 (± 0.24)
% Adequacy of prescribed infused volume	89.1
% Adequacy of prescribed infused calories	92
% Adequacy of prescribed infused proteins	91.9

ENT: Enteral Nutrition Therapy

Table 3: Characteristics of enteral nutrition therapy in critical oncologic patient at risk nutritional.

	Total	Adults	Elderly	*p value*
Total calorie deficit (kcal/day)	-296 (± 339.0)	-358.9 (± 305.4)	-91.6 (± 190)	p<0.003*
Total protein deficit (g/day)	-28 (IQ -58:-2.95)***	-33.1 (± 14.2)	-18 (± 7.96)	p<0.002**

Cachexia Syndrome according to Fearon et al. [12]; Malnutrition according to OPAS, 2002 [15] to patients ≥60 years. *Difference between the caloric deficit in the adult compared to the elderly malnourished with Cachexia Syndrome. **Difference between the protein deficits in the adult compared to the elderly malnourished with Cachexia Syndrome. Significance level p <0.05. ***Result expressed as median.

Table 4: Enteral nutrition therapy in critical oncologic patient at nutritional risk: adults vs. elderly malnourished with cachexia syndrome.

0.003) and protein (p < 0.002) deficits (Table 4). The values dispersion of energy and protein balance with their outliers, according subgroups analyzed are shown in Figure 1.

In total, the main barriers to control the energetic-protein deficit were extubation 38%, hemodynamic instability 29%, tracheostomy, diarrhea and vomiting, both 6.5% (Figure 2). By subdividing the sample, the extubation (p=0.03) was the main barrier to malnourished elderly patients with cachexia syndrome, while hemodynamic instability (p=0.02) and hours to nutritional goal (p=0.02) were for adults patients. There were no significant differences between the variables such as: ICU time (p=0.054), MV time (p=0.14) and ENT time (p=0.06) in these subgroups which allowed the comparison between them (Table 5).

Discussion

Critical patients, on MV, on EN, with NUTRIC score ≥ 6, malnourished and with age ≥ 60 years, are usually associated with an adverse clinical outcome. In the present study, it was verified 47% of the sample had some degree of malnutrition. In addition to this, it was also found 70% of patients had syndrome cachexia, 26% pre cachexia, 64% cachexia and 10% refractory cachexia.

Besides the low calorie-protein intake, associated with anorexia, items present in cancer patients with cachexia syndrome, these patients are also known to secrete catabolic agents, that stimulate muscle proteolysis (Proteolysis Inducing Factor - PIF), as well as mobilization of lipids (Lipid Mobilizing Factor - LMF). The LMF is responsible for increasing lipolysis, hence, leads to severe loss of fat. PIF, on the other hand, is able to induce protein catabolism directly into skeletal muscle, and can be found elevated levels in the serum and urine of patients with cancer [16].

Several studies showed that PIF may activate ubiquitin proteasome system, which is known to perform an important role in muscle catabolism in a variety of debilitating conditions [17-19]. Even considering all these catabolic agents, in our study, it was observed that elderly patients, malnourished and with cachexia syndrome had a lower and significant energy-protein deficit when compared to adult patients.

In this case, it is worth considering the body weight of the subgroups, the elderly, malnourished and with cachexia syndrome usually has low weight in the ICU, which relates to the lower caloric and protein needs when compared to adult. The nutritional goal can be quickly reached in the early days in the ICU, and it can also present a good tolerance of the gastrointestinal tract due to the reduced diet diary volume, positively impacting the control of the deficits.

The main barriers for the pause of ENT identified in our study were extubation and hemodynamic instability. According to the

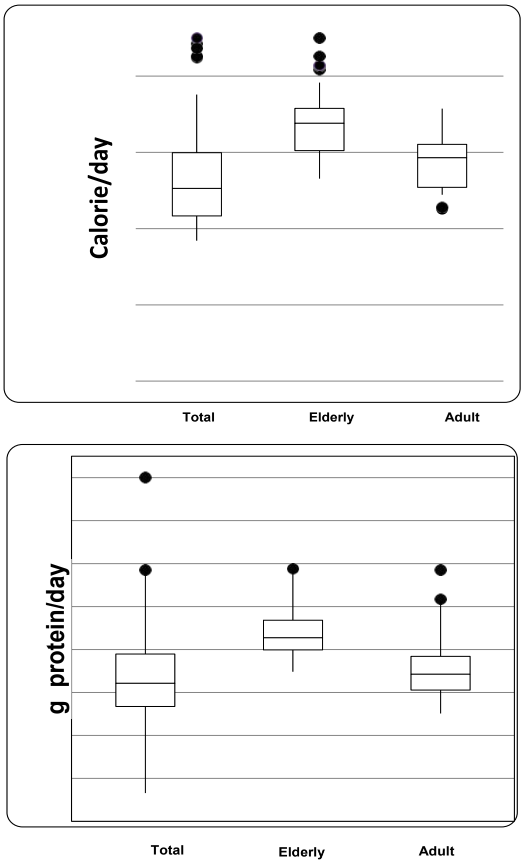
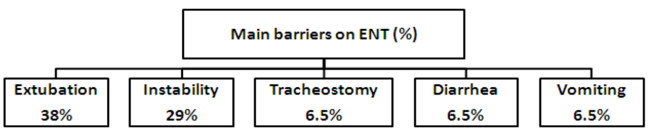


Figure 1: Dispersion of calorie and protein balance values in enteral nutrition therapy, according to study groups.



ENT: Enteral Nutrition Therapy.

Figure 2: Main barriers in control of energy-protein deficit in critical oncologic patient at nutritional risk.

Variables	Adult	Elderly	*p* value
ICU time (days)	7.5 (± 2.5)	9.6 (± 2.7)	0.054
MV time (days)	7.36 (± 2.4)	9.1 (± 2.4)	0.14
ENT time (days)	6.29 (± 2.3)	8.17 (± 2.4)	0.06
Main barriers in control of energy-protein deficit (hours)			
Extubation	15.75 (± 4.6)	27.75 (± 10.6)	0.03*
Hemodynamic instability	18 (± 8.9)	0	0.02*
Hours to nutritional goal	63.02 (± 29)	51.9 (± 25.5)	0.02*

Cachexia Syndrome according to Fearon et al. [12]; Malnutrition according to OPAS, 2002 [15] to patients ≥60 years. ICU: Intensive Care Unit, MV: Mechanical Ventilation, ENT: Enteral Nutrition Therapy. *Difference between the pause reasons in hours in the adult compared to the elderly malnourished with Cachexia Syndrome. Significance level p <0.05.

Table 5: Main barriers in control of energy-protein deficit in critical oncologic patient at nutritional risk: adult vs. elderly malnourished with cachexia syndrome.

American guideline [6], the ENT is contraindicated in those patients with a worsening in the hemodynamic profile and they are dependent on high doses of vasoactives drugs. This group of patient is susceptible to adverse effects of ENT, such as abdominal distention, vomiting and bowel ischemia. The pause of extubation procedure is also one of the main barriers to control the calorie and protein deficit, Honda et al. [20], reported in their study that hemodynamic instability and extubation were the most recorded reasons in medical records.

The battle against the caloric and protein deficits in patients underwent exclusive ENT in an ICU is daily, however, this can be overcome through the creation and implementation of protocols in partnership with the multidisciplinary team. In a multicenter, randomized and controlled with 5497 patients, Heyland et al. [21] found that the implementation of specific protocols in Nutrition Therapy contributed to the early onset of ENT (p=0.0003).

Another important finding in our research was the early ENT. McClave et al. [6] reported that this conduct has impacted positively on mortality and ICU length of stay, favoring to the stricter control of underfeeding. In order to assess the impact of ENT infusion in small quantities in 389 critically ill patients, Berger et al. [22] found that underfeeding favored the reduced supply of protein (p < 0.0001), increased mechanical ventilation days (p=0.004), ICU time (p=0.0036) and hospital stay (p=0.028).

Heyland et al. [23] in a prospective, multicenter study with a sample of 3390 patients hospitalized in an ICU and on MV, assessed the prevalence of iatrogenic hypo-feeding in patients at nutritional risk according to NUTRIC. In this study it was verified ENT was averaged started in 38.8 (± 39.6) hours after ICU admission, the prescribed infused relation was 61.2% calories and 57.6% proteins and 74% of patients did not receive at least 80% of their nutritional needs. In this study, the majority of critically ill patients, including high nutritional risk patients, fail to receive adequate nutritional intake. There is low uptake of strategies designed to optimize nutrition delivery in these patients [23].

Ribeiro et al. [24], evaluated the quality of nutrition therapy in 93 adult patients hospitalized in an ICU, underwent ENT for at least 72 hours. In this study, the researchers investigated different aspects related to the quality of ENT, from the initial dietary prescription to the recovery of oral feeding. Early ENT in 86% of patients, reached nutritional goal within 36 hours, percentage of adequacy of prescribed received volume 81.6%, beyond the calories and protein administered above 80% of adequacy were the main findings referred in that investigation. It was also found that the main reason for ENT pause was the extubation process, with a prevalence of 29.9% in total hours of pause and in patients > 60 years had a lower recovery rate of oral feeding (p=0.014) compared to patients < 60 years. Early enteral nutritional therapy and the adequacy for both energy and protein of the nutritional volume infused were in accordance with the established guidelines. Possible inadequacies of energy and protein balance appeared to be associated with an acute inflammatory response, which was characterized by elevated C-reactive protein levels. The main cause of interruption of the enteral nutritional therapy was the time spent in extubation [24].

Machado et al. [25] studied prospectively the relationship between the quality of ENT and clinical prognosis in septic patients in an ICU. 53 patients were included, with a minimum time of ENT 72 hours and more than 7 days in an ICU. Factors related to quality of ENT were assessed percentage of adequacy of calories received; percentage prescribed infused volume, factors associated with the ENT interruption and the gastrointestinal tract tolerance. The ENT was early in 77% of patients, 96% reached the nutritional goal in < 72 hours, 78% the prescribed volume has been infused, there was a 13.4% diarrhea frequency, while it was observed a prevalence of 58.5% constipation. It was also seen a high mortality in patients receiving < 80% calorie requirements (p=0.001) compared with the group that received > 80%. Thus the authors concluded that septic patients who received > 80% caloric needs have received a favorable clinical prognosis.

Waitzberg and Correia [26] recently published the main strategies that resulted in quality improvement of nutrition therapy in Brazil. The authors pointed out that a rigorous monitoring by nutrition therapy team is paramount, in addition to the creation/execution of continuous education projects to all members of the multidisciplinary team and the periodical selection and application of quality indicator in nutrition therapy [27]. Based on the definition of these actions, the authors concluded that the implementation of these strategies had directly impacted on the improvement of nutrition care quality in Brazilian hospitals.

In our investigation the management of ENT was in accordance with the national [28] and international guidelines of ENT [6]. Patients at nutritional risk had the ENT initiated within the first 24-48 hours of ICU admission, > 80% of the volume, calories and prescribed proteins were administered, in addition to the reduced pause frequency of ENT due intolerance of the gastrointestinal tract as diarrhea and vomiting. However, it is noteworthy that our efforts will also be directed to reduction in hours of the ENT pause in patients with extubation programming, in order to improve the calorie-protein supply daily. This set of actions will be possible through regular training and continuing education projects defined in conjunction with the multidisciplinary team.

We emphasize that our study has some limitations due to fact that it was developed in a single ICU, at a hospital reference in oncology, which resulted in a small sample out of the study. For better results, more studies are needed to quantify the calorie-protein deficit in critical cancer patients.

Conclusion

The main barriers in control of energy-protein deficit in critical oncologic patient at nutritional risk on MV were extubation and hemodynamic instability. After subgroup analysis, it was observed an important and significant calorie-protein deficit in adult patients when compared to elderly malnourished with cachexia syndrome.

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