

Relation between nutritional status and dependency on mechanical ventilation in critical oncologic patients

Relação do estado nutricional e dependência de ventilação mecânica em pacientes críticos oncológicos

Relación entre estado nutricional y dependencia de ventilación mecánica en pacientes críticos oncológicos

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ABSTRACT | Bad nutrition is related with the loss of muscle mass, which, in turn, may be responsible for the poor prognosis of patients in the intensive care unit (ICU). The relationship between nutritional status and cancer has been widely studied. However, the relationship between nutritional status and time spent under invasive mechanical ventilation (IMV) in cancer patients is not yet fully understood. The aim of this study was to investigate the relationship between the nutritional status in cancer patients in the ICU and their time of permanence under IMV. Fifty seven patients admitted to Hospital Erasto Gaertner's ICU on invasive ventilatory support for at least 48 hours were included in this study. Patient data were collected regarding gender, age, body mass index (BMI), topographic location of the cancer, clinical stage of the disease, anatomopathological examination, treatment administered, reason for ICU admission, and APACHE II score. The nutritional diagnosis were malnutrition (22.81%), normal weight (50.88%), overweight (14.04%), and obese (12.28%). The APACHE II score average was 26.4 points and the expected rate of mortality was 60%. The average time on mechanical ventilation

was 11.2 days. The correlation between body mass index and time on IMV was $r=0.076$ and $p=0.575$. We concluded that most cancer patients' nutritional classification was normal weight, and their time of permanence under IMV was high. Still, when analyzed in isolation, the nutritional status is not related to the time of permanence under IMV.

Keywords | body mass index; neoplasms; respiration, artificial; intensive care units.

RESUMO | O estado de má nutrição está ligado com a perda de massa muscular que, por sua vez, pode ser responsável pelo mal prognóstico de pacientes internados em unidade de terapia intensiva (UTI). A relação entre câncer e estado nutricional tem sido amplamente estudada. No entanto, a relação entre estado nutricional e tempo de permanência em ventilação mecânica invasiva (VMI) em pacientes oncológicos ainda não está totalmente esclarecida. O objetivo do estudo foi verificar a relação do estado nutricional dos pacientes oncológicos em UTI com o tempo de permanência em VMI. Participaram do estudo 57 pacientes que estiveram internados na UTI do Hospital Erasto Gaertner e necessitaram de suporte ventilatório

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Presentation: May 2012 - Accepted for publication: Jun. 2013 - Financing source: none - Conflict of interests: nothing to declare - Approval at the Ethics Committee n. PP1853.

invasivo por no mínimo 48 horas. Foram coletados dados referentes ao gênero, à idade, ao índice de massa corporal (IMC), à localização topográfica do câncer, ao estágio clínico (EC) da doença, ao exame anatomopatológico (AP), ao tratamento realizado, ao motivo de internamento na UTI e ao APACHE II. O diagnóstico de desnutrição encontrado foi de 22,81%, 50,88% eram eutróficos, 14,04% tinham sobrepeso e 12,28% eram obesos. O escore de APACHE II obteve média de 26,4 pontos e taxa prevista de mortalidade de 60%. A média geral de tempo sob VMI foi de 11,2 dias. A correlação entre índice de massa corporal e tempo de permanência sob VMI foi de $r=0,076$ e $p=0,575$. Concluímos que a maior parte dos pacientes possui classificação nutricional de eutrofia e tempo de permanência sob VMI elevado. Ainda, o estado nutricional avaliado isoladamente não está relacionado com o tempo de permanência em VMI.

Descritores | índice de massa corporal; neoplasias; respiração artificial; unidades de terapia intensiva.

RESUMEN | El estado de mal nutrición está ligado con la pérdida de masa muscular que, por su vez, puede ser responsable por el mal pronóstico de pacientes internados en la unidad de terapia intensiva (UTI). La relación entre cáncer y estado nutricional ha sido ampliamente estudiada. Sin embargo, la relación entre estado nutricional y tiempo

de permanencia en ventilación mecánica invasiva (VMI) en pacientes oncológicos todavía no está totalmente esclarecida. El objetivo del estudio fue verificar la relación del estado nutricional de los pacientes oncológicos en la UTI con el tiempo de permanencia en VMI. Participaron del estudio, 57 pacientes que estuvieron internados en la UTI del Hospital Erasto Gaertner y que necesitaron de soporte ventilatorio invasivo por un mínimo de 48 horas. Fueron recolectados los datos referentes al género, edad, índice de masa corporal (IMC), localización topográfica del cáncer, estadio clínico (EC) de la enfermedad, examen anatomopatológico (AP), tratamiento realizado, motivo de internación en la UTI y APACHE II. El diagnóstico de mal nutrición encontrado fue de 22,81%; 50,88% eran eutróficos, 14,04% tenían sobrepeso y 12,28% eran obesos. El score de APACHE II obtuvo una media de 26,4 puntos y la tasa prevista de mortalidad de un 60%. La media general del tiempo de permanencia bajo VMI fue de $r=0,076$ y $p=0,575$. Concluimos que la mayor parte de los pacientes tuvo clasificación nutricional de eutrofia y tiempo de permanencia bajo VMI elevada. Además, el estado nutricional evaluado aisladamente no está relacionado con el tiempo de permanencia en VMI.

Palabras clave | índice de masa corporal; neoplasias; respiración artificial; unidades de terapia intensiva.

INTRODUCTION

Cancer causes a depletion of nutritional reserves, which results in weight loss¹. The loss of body mass indicates that malnutrition and cachexia are associated with decreased response to specific treatment and quality of life, favoring higher risk of infection and increased morbidity and mortality².

When patients are under intensive care, malnutrition is considered to be an alarming and independent risk factor for survival, because an inadequate nutritional input causes changes in body composition, leading to a decrease in muscle mass³, affecting the diaphragm and the intercostals.

The respiratory system is among the most affected³ owing to the effects of nutritional depletion of its muscle proteins³⁻⁵. Malnutrition at muscle levels cause mineral, electrolyte, and energy disorders, which are responsible for decreased contractility of the muscles⁶ and negatively affect the structure, elasticity, function, muscle mass, strength, endurance, and the pulmonary immune defense mechanisms, as well as breath control^{7,8}.

According to Mota et al.⁹, the compromising of the respiratory system, secondary to malnutrition, induces the reduction of body cell mass, which can lead to muscle fatigue and, consequently, to acute respiratory failure. However, according to Laaban¹⁰, a reduced ability to maintain adequate levels of ventilation has important clinical implications in respiratory failure leading to lower muscle endurance, in efforts and difficulty for weaning from mechanical ventilation.

The treatment for acute respiratory failure relies on many resources, including invasive mechanical ventilation (IMV)¹¹. The use of IMV aggravates malnutrition and prolongs hospitalization, which, in turn, favors the development of protein-calorie malnutrition in those patients¹², resulting in the loss of lean body mass¹³, thus closing a vicious cycle.

The relationship between malnutrition and the loss of muscle mass and poor prognosis is well described in literature. However, the relationship between the nutritional status and the time of permanence under IMV is not yet fully understood. Therefore, the aim of this study is to investigate the relationship of the nutritional status of cancer patients in intensive care and their time of permanence under IMV.

METHODOLOGY

This retrospective, descriptive study was approved by the Research Ethics Committee of Hospital Erastus Gaertner (HEG), under protocol number 1853.

Sixty-one records of patients who were hospitalized in the intensive care unit (ICU) of the HEG, from January 2007 to June 2010 were included in the study. Those patients requiring IMV for at least 48 hours and who had nutritional diagnosis made by the hospital's nutrition service, based on their body mass index (BMI)¹⁴, obtained by dividing body weight (in kg) by height squared (in m), were included. These anthropometric values were measured with the patient standing on a properly calibrated biometric scale, within a period not exceeding 2 months of their ICU stay, because we understand that the possible variations of these values in a period of 60 days do not significantly affect the final result. In adults, the proposed cutoff points for BMI by the World Health Organization are as follows: 18.5, 25, and 30 kg/m² for the diagnosis of malnutrition, overweight, and obesity, respectively¹⁴.

Four patients were excluded from the study, due to three of them not presenting a closed neoplastic diagnosis, and one other for not presenting sufficient data in their medical records. Therefore, the final sample consisted of 57 patients.

The following data were recorded from the medical records: gender; age; BMI; topographic location of the cancer; clinical stage (CS) of the disease; anatomopathological examination (AP); treatment administered; reason for ICU admission and scores from APACHE II (Acute Physiology And Chronic Health Evaluation II), which is a measure of the severity index of ICU patients, usually used in the first 24 hours of admission to assess patients' risk of death and prognosis¹⁵; estimated mortality risk; use of sedatives; time under mechanical ventilation; and outcome of the ICU stay.

Criteria for weaning from IMV, used in all patients, followed the guidelines of the III Brazilian Consensus Conference on Mechanical Ventilation¹⁶, and consisted of conscious, hemodynamically stable patients without use of vasoactive drugs, patients who were able to remain in spontaneous ventilation (pressure support ventilation of 8–7 cmH₂O and continuous positive airway pressure of 5 cmH₂O) with a normal heartbeat, normal blood pressure (normotensive), normal respiration (eupneic), with peripheral oxygen saturation greater than 90% to a fraction of inspired oxygen of 0.4, acid-base balance and with an oxygen pressure and fraction of inspired oxygen relation greater than 200.

Statistical analysis was performed by calculation of frequencies, averages, and standard deviations.

In cases where the standard deviation included individuals in different classifications of averages, median was used. Associations were assessed by calculation of the correlation and significance coefficients, using the Statistical Package for Social Science (SPSS) version 20.0 software for Windows®.

RESULTS

The sample consisted of 57 patients, 61.40% males and 38.60% females. The mean age was 57.2 (± 15.84) years.

The median BMI was 21, with mode equal to 20. Based on this evaluation, the nutritional diagnosis outlined by the sample shows that 22.81% were malnourished, 50.88% were eutrophic, 14.04% were overweight, and 12.28% were obese.

The topographic distribution and frequency of primary neoplasms of the sample are shown in Table 1.

CS IV was the most frequent, with 22.81% of the cases, followed by CS III (19.30%) and lastly, CS II (10.53%). However, 47.37% of patients had no CS described in their records.

Regarding histological type, carcinoma was the most frequent (41.38%), followed by adenocarcinoma (22.41%), lymphoma in 8.62% and leukemia in 3.45%

Table 1. Topographic distribution and frequency of primary neoplasms of the sample

Topography	Frequency	%
Bladder	1	1.8
Cardiac	1	1.8
Cervical	1	1.8
Osseous	1	1.8
Thyroid	1	1.8
Pancreas	2	3.5
Prostate	2	3.5
Stomach	3	5.3
Lymphatic system	3	5.3
Breast	3	5.3
Kidney	3	5.3
Brain	3	5.3
Lung	5	8.8
Rectum	5	8.8
Oropharynx	6	10.6
Blood system	7	12.3
Esophagus	10	17.5
Total	57	100

of cases. Adenoma, glioblastoma, myeloma, and pineocytoma represented less than 2% each. Still, 17.24% of the records analyzed had no records of the patients' histological type.

Out of the 57 patients, 71.92% underwent surgical treatment. Of these, 43.90% had also undergone chemo or radiotherapy.

The reasons for ICU admission were immediate postoperative, in 47.37% of cases, followed by clinical complications such as respiratory failure and low level of consciousness, which amounted to 35.09%, and cardiorespiratory arrest, 17.54%.

The APACHE II score had an average of 26.4 (± 8.51) points and expected rate of mortality had an average of 60% (± 0.24). And the overall average time under mechanical ventilation was 11.2 (± 8.84) days.

Patients remained, on average, 172 hours in use of sedation with continuous infusion of midazolam, and 183 hours in use of combined fentanyl for analgesia. Regarding the use of neuromuscular-blocking drugs, used in 54.4% of patients, it has been saved for specific situations of endotracheal intubation, at the calculation of the ideal positive end-expiratory pressure, and alveolar recruitment, in cases of acute respiratory distress syndrome.

The values found in the verification of correlations, obtained by Pearson's parametric test, between the variables studied, are described in Table 2.

Regarding the outcome of intensive support, 31.58% of patients were discharged from the ICU and 68.42% passed away.

Table 2. Verification of the correlation between variables

Crossed variables	r value	p-value
BMI \times APACHE II	-0.049	0.715
BMI \times mortality rate	0.027	0.841
BMI \times time of permanence under IMV	0.076	0.575
Time of permanence under IMV \times mortality rate	0.196	0.144

APACHE II: Acute Physiology And Chronic Health Evaluation II; BMI: body mass index; IMV: invasive mechanical ventilation

Table 3. Patients' characteristics

Characteristic	Malnourished	Eutrophic	Overweight	Obese
No. of patients (Men/Women)	13 (8/5)	29 (20/9)	8 (5/3)	7 (2/5)
Age in years (\pm SD)	60.23 (± 14.17)	54.93 (± 15.63)	50.25 (± 15.73)	69.29 (± 15.22)
BMI in kg/m ² (SD)	16.73 (± 0.97)	21.15 (± 1.59)	27.11 (± 1.61)	33.28 (± 3.82)
Time of ventilation (days)	10.92 (± 9.66)	11.55 (± 8.42)	10.13 (± 8.43)	11.57 (± 11.30)
APACHE II	27.54 (± 8.06)	26.59 (± 8.53)	18.75 (± 7.72)	32.29 (± 4.03)
Expected mortality rate	0.66 (± 0.24)	0.63 (± 0.25)	0.42 (± 0.22)	0.83 (± 0.06)

APACHE II: Acute Physiology And Chronic Health Evaluation II; BMI: body mass index

The outcome of patients in the malnourished group was three ICU discharges and ten deaths. The evolution of the eutrophic patients resulted in 10 ICU discharges and 19 deaths. The outcome of the overweight patients group was two ICU discharges and six deaths. Among the obese patients, three were discharged from the ICU and four died. The nutritional characteristics of these groups are shown in Table 3.

DISCUSSION

In this study, there was a predominance of males with a mean age of 57.2 (± 15.84) years, which is similar to other studies^{17,18}. The most frequent primary neoplasm was in the esophagus, followed by the blood system and oropharynx, in most cases, in patients in the immediate postoperative period of elective and emergency surgery. This result may be due to the protocol of upper abdominal and thoracic compartment surgery used in the institution, where patients are admitted to the ICU immediately after surgery because of the higher incidence of morbidity and mortality from respiratory causes^{19,20}.

The mean APACHE II score was 26.40 points with expected average mortality rate of 60%. We can observe from this result that the higher APACHE II has a direct correlation with increased mortality. According to a study²¹ conducted over 13 months in the general ICU of Hospital São Paulo, where 520 patients were selected and the APACHE II prognostic index was applied, patients with scores above 25 showed a significant progress to death.

Changes in the water balance are commonly associated with critical patients, causing significant changes in body mass. Thus, the use of anthropometric data in the period following admission to the ICU may lead to misinterpretation of nutritional status. The BMI data used in this study were evaluations performed over a period

of up to 60 days before ICU admission, whereas distortions or changes in this index in the 2-month evolution do not significantly compromise the final result.

Some studies suggest^{12,25-27} that the inclusion of BMI in mortality predictive scores should be considered.

A study²⁵ conducted in six general ICUs evaluated the association between BMI and mortality in 1,698 ICU patients, divided into four groups based on BMI: <18.5; 18.5–24.9; 25–29.9, and >30 kg/m². Approximately half of the patients presented a normal BMI, 10% were underweight, and 40% overweight, and a significantly higher mortality was observed in patients with BMI <18.5 and BMI >30 kg/m², as a protective factor against mortality. According to Fontoura et al.¹², studies analyzed showed BMI as a good evaluation method, and therefore it was concluded that low BMI is a mortality predicting factor, and high BMI seems to be associated with favorable outcomes, independent of the conventional predictors. However, Goulenok et al.²⁶ showed an increase in mortality in morbidly obese patients (BMI >40 kg/m²) and Cislagui et al.²⁷ stated in their study that a BMI >27 kg/m² is predictive of increased mortality associated with a prolonged ICU stay, increased disease severity and higher mortality rate, and no difference in the duration of mechanical ventilation was observed. Based on this, studies that evaluated the influence of BMI, involving critically ill patients, have shown mixed results. Still, most of these studies highlight the limitations of the method, since critical patients have changes in their weight due to changes in intracellular and extracellular compartments¹².

By evaluating aspects of each nutritional assessment method for critical patients, we observed that there was no consensus among authors about the best assessment method, so that it is not advisable to elect a single evaluation technique, especially when the focus is on the ICU patient¹².

The higher prevalence of a nutritional diagnosis was of eutrophic patients, followed by malnutrition, overweight, and obesity, and the average BMI was of 22.47 kg/m². A different result was found by Andr ejak et al.²², who observed a mean BMI of 26±4 kg/m² in a study in which they evaluated secondary complications to the admission and factors associated with mortality in patients with advanced lung cancer admitted to two ICUs of university hospitals.

The lack of correlation between BMI and APACHE II, as well as the mortality rate found, was also reported in another study²³, which evaluated the effect of BMI on the secondary complications of admission to a general ICU. We evaluated 2,148 patients divided into five groups according to their BMI: underweight (BMI <20 kg/m²), normal (20–24.9 kg/m²), overweight

(25–29.9 kg/m²), obesity (30–39.9 kg/m²), and severe obesity (≥40 kg/m²). The authors concluded that an increase in BMI is not associated with increased morbidity and mortality in ICU patients, and that BMI should not be considered a mortality-predictive factor.

However, in another multicenter analysis study by Garrouste-orgeas et al.²⁴, which evaluated the impact of BMI on the evolution of 63,646 critical cancer patients classified as underweight (BMI <20 kg/m²), normal or control (20–24.9 kg/m²), overweight (25–30 kg/m²), obese (30–40 kg/m²), and severely obese (>40 kg/m²), there was increased mortality in patients with low BMI associated with a worse functional status at the time of discharge.

The average time of permanence under mechanical ventilation found in this study (Table 3) can be considered a prolonged time of permanence, as it falls in the range from 8 hours to 7–14 days¹⁷. However, no correlation was observed between BMI and time spent under IMV. It is believed that this is due to the time spent under IMV being related to other factors, such as age, performance status, clinical stage of disease, respiratory muscle strength, and organ failure²⁸⁻³⁰, and not related to the nutritional status determined by the BMI, which is a subjective measure, not quantifying muscle compromising, which influences the time of permanence under IMV.

The study showed that there is a high mortality rate (Table 3) which, however, was not influenced by the time of permanence under IMV. The value was similar to the study by Depuydt et al.³¹, who observed a mortality rate of 65% in both groups of patients with hematological malignancies who had acute respiratory failure (ARF) and received non-invasive ventilation (NIV), and in the group receiving IMV. In some studies^{32,33}, the need for IMV has been considered as one of the factors associated with death in patients with cancer. It is believed that this lack of correlation is due to the fact that this study involved only patients who required IMV for more than 48 hours, that is, the severity of the patient's general status was higher and more homogeneous when compared WITH a sample containing associated non-intubated patients.

Another important issue is the time between ICU admission and the date of the intubation. According to Groeger et al.³⁴, cancer patients who developed ARF requiring IMV for more than 24 hours after admission have an expected mortality rate two times higher than patients who were mechanically ventilated within 24 hours of admission.

In this study, no difference was observed in relation to the BMI groups and the patients' outcome. This is explained by the fact that all the groups were exposed, to the same degree, to the presence of infection, the

development of multiple organ failure, need for IMV and severity of the disease, which are prognostic factors of mortality in patients with cancer^{29,30,35}.

Due to the sample size, it was not possible to separate cancer types and clinical stages to verify the relation between the time of permanence under IMV and these two variables. Because this was a retrospective study, laboratory tests were not collected for creatinine dosage and a pulmonary function test was not applied to quantify the consumption of muscle mass and for prior outlining of the lung profile.

Thus, we believe that prospective studies are essential to elucidate the results obtained here or expand them, including variables such as lung function, serum creatinine levels and add experiences in other oncology ICUs, increasing the sample size and statistical power of the research.

CONCLUSION

The nutritional status, as determined by the BMI, of cancer patients in the ICU, when evaluated in isolation, is not related to the time of permanence under IMV.

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