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Original article

The use of computed tomography images as a prognostic marker in critically ill cancer patients

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SUMMARY

Background & aims: In the intensive care unit (ICU) setting, body composition is typically estimated through anthropometry, which does not specifically quantify skeletal muscle (SM). Recent findings have shown that computed tomography (CT) is a useful tool to identify low SM in critically ill patients, which in turn is associated with poor clinical outcomes. So, the present study aims at comparing low SM assessed by CT to BMI anthropometric data and its association with outcomes in critically ill patients.
Methods: Observational study was used, which included >18 year-old patients, with over 72 h of ICU length of stay, who had an abdominal CT at ICU admission. Demographic, body mass index (BMI), hospital outcomes and abdominal CT data (SM and adipose tissue at the 3rd lumbar vertebrae) were collected for analysis. ROC curve optimal stratification analysis for hospital mortality was applied to classify people into low SM (sarcopenic) versus normal SM (non-sarcopenic). A Cox regression was applied to find independent associations between sarcopenia and 30-day survival.
Results: The study involved 99 patients, 56% male, mean-age of 61.6 years old, BMI 24.19 ± 4.49 kg/m^2; hospital mortality was 26%. According to BMI, 19.4% of the patients were underweight. However, a poor correlation was observed between BMI and SM index by CT: $R^2 = 0.39$, $P < 0.001$. The cutoff point for determining sarcopenia by CT was 41.2 cm^2/m^2 (sensitivity 70%, specificity 69.5%, AUC 70.3) for both sexes. The sarcopenia diagnosis by CT as nutritional evaluation parameters was correlated with malnutrition BMI diagnosis in only 35.5%. When compared to non-sarcopenic patients, those with sarcopenia presented worse 30-day survival adjusted by age and SAPS 3 (HR = 2.74, 95%CI = 1.02–7.35, P = 0.04), higher hospital mortality (41.9% vs 14.6%, P = 0.006) and ICU non-infectious complications (76.7% vs 52.1%, P = 0.016).
Conclusion: Sarcopenia assessed by abdominal CT demonstrated low correlation with BMI and was a risk factor for lower 30-day survival, higher hospital mortality and higher complications in critically ill patients.

1. Introduction

The use of anthropometric methods for evaluating nutritional status in critically ill patients has important limitations such as limited precision in evaluating body composition in those patients. Changes in body composition, particularly skeletal muscle (SM) loss in those patients are substantial due to exacerbated hypermetabolism and catabolism [1,2]. As a simple tool, body mass index (BMI)

Abbreviations: SM, skeletal muscle; CT, computed tomography; ICU, intensive care unit; BMI, body mass index.

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has been widely used as a preliminary screening of patients at risk. Although BMI is useful for populational studies, it fails to appropriately stratify patients risk and status at the individual level, as it does not differentiate patients body composition [3–5]. As such, its use in patients with cancer has been questioned [6].

SM loss is a serious complication inherent to critical disease [7]. Puthucheary et al. [8] report nearly 20% reduction in SM during the first 10 days of a stay in the intensive care unit (ICU). Studies have shown a close relation between SM loss with longer mechanical ventilation, longer length of stay in the ICU and higher mortality [9,10]. Moreover, ICU survivors may present functional changes that impact their quality of life over the years following hospital discharge [11,12].

The SM assessment of a cross-sectional area of the lumbar spine (L3) through computed tomography (CT) allows the identification of low body SM, also called sarcopenia, in specific cohorts of oncological and critically ill patients. This method enables direct visualization of cross-sectioned areas of various SM and adipose tissue, which reflect the whole-body composition [13]. CT images used for the initial purpose of diagnosing and monitoring cancer progression are available in clinical records and can be used conveniently for the evaluation of body composition and its changes over time [6,14].

Based on these assumptions, the aim of this study was to compare muscle mass assessed by CT to BMI diagnosis and its relationship with 30-day survival rate in a specific cohort of critically ill oncological patients.

2. Methods

Following approval by the Research Ethics Committee (REC), a retrospective cohort study was conducted in the ICU of an oncology tertiary hospital (Hospital do Cancer de Barretos, SP, Brazil). The medical records of patients admitted to the ICU from July 2010 to July 2014 were selected. Patients of both sexes, older than 18 years old, who stayed in the ICU for more than 72 h for clinical or surgical reasons, and who underwent abdominal CT scan within 72 h or more after ICU admission, were included in the study. Patients whose CT scans presented inadequate quality to enable muscle mass evaluation were excluded.

Data were obtained from the medical records and included: anthropometric data at the time of admission (usual body weight, current weight and height to calculate the body mass index) [3,15], reason for hospitalization (clinical or surgical), prognostic index by simplified acute physiology score (SAPS 3) [16,17], infectious complications (defined by the use of antibiotics, other than prophylactic or diagnostic ones, described in the medical records), non-infectious complications (ileum, fistula, or additional surgical approach) [18], length of ICU stay, in-hospital mortality abdominal CT scan for muscle analysis. Institutional protocols based on the recommendations of the centers disease control (CDC) were applied for the introduction of antibiotics and infections diagnosis [19].

As established in literature, the third lumbar vertebra (L3) was selected for muscle analysis [13,20] since SM and adipose tissue at the L3 are highly correlated with the whole-body measurements [13,21]. This field contains visceral and subcutaneous adipose tissue, psoas, and posterior paravertebral muscles, as well as abdominal wall muscles, Fig. 1. These images were analyzed by using Slice-O-Matic V5.0 (Tomovision, Montreal, Canada) which allowed the specification and demarcation of specific tissue by using the Hounsfield Unit limits of −29 to +150 for skeletal muscles (psoas, erector spinae, quadratus lumborum, transversus abdominis, obliquus externus, obliquus internus, and rectus abdominis), −150 to −50 for visceral adipose tissue, and −190 to −30 for subcutaneous and intramuscular adipose tissue. The

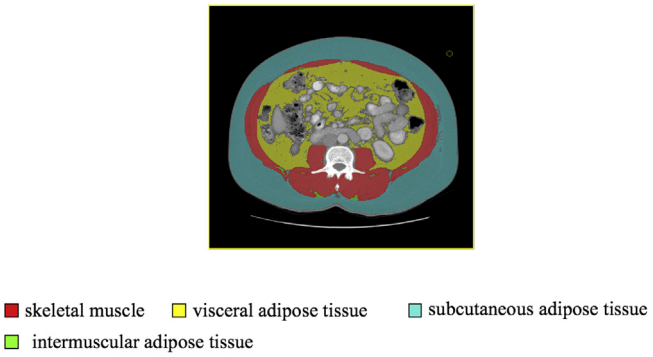

Fig. 1. Third lumbar vertebrae of a critically ill cancer patient.

cross-sectional areas (cm^2) were calculated for each tissue by the sum of pixels multiplied by the surface area. SM index was calculated by dividing SM in cm^2 by the patient's height in m^2 (cm^2/m^2) [22]. In addition, through L3 cross-sectional area, a quantification of muscle mass area, adipose tissue area (visceral, subcutaneous and intramuscular), and muscle attenuation were obtained. This method presents high sensitivity and specificity for the detection of muscle changes.

2.1. Statistical analysis

Sample size was based on the objective of comparing BMI vs low SM (sarcopenia) and in predicting 30-day survival in critically ill patients. Therefore, considering a 40% correlation between the variables per preview studies [6,23], a type I error of 5%, and a sample power of 95%, 75 patients would have to be included. However, in order to associate sarcopenia with 30-day survival according to previous literature [24,25] and by using the minimal clinically significant difference between groups, a 40% survival was considered in the sarcopenic group versus 80% in the non-sarcopenic group. A type I error of 5% and a sample power of 95% in a ratio of 1 sarcopenic to 2 non-sarcopenic patients was considered. Therefore, for a total of 90 patients nearly 30 were expected to be sarcopenic and 60 non-sarcopenic. Thus, the study aimed at including from 90 to 100 patients in the sample.

Mean, median, standard deviation and quartiles were calculated for the quantitative variables and absolute frequencies or percentages for the qualitative variables as appropriate. Student's t-test and Mann Whitney test were used for the quantitative variables according to the distribution of the variable. Either Chi-square or Fisher's tests were applied for the categorical variables as appropriate. Normality was determined by the Shapiro Wilk test.

Spearman's correlation was used to establish the relation between the BMI and SM. Data were analyzed by using SPSS 20.0 Version (IBM Corp., Armonk, NY) and a p-value lower or equal to 0.05 was considered statistically significant in the two-tailed test.

A ROC (receiver operating characteristic) curve analysis was used in the identification of the sarcopenic and non-sarcopenic groups by using the Youden index method (sensitivity + specificity − 1). By using the optimal stratification approach, the value presenting the greater sensitivity and specificity to discriminate mortality was used as the cutoff point for identifying the SM groups (low vs normal). The cutoff points were then separated by male and female, prioritizing the greater sensitivity for mortality. After defining groups, demographic data, CT measured values and outcomes were compared.

Subsequently, to confirm the relation between the groups with mortality, a Cox progressive and conditional regression model were performed by applying stepwise selection with backward

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