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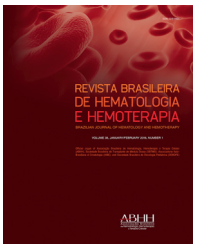

Original article

Pre-sarcopenia and bone mineral density in adults submitted to hematopoietic stem cell transplantation

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ABSTRACT

Background: The aim of this study was to evaluate the prevalence of pre-sarcopenia and bone mineral density after hematopoietic stem cell transplantation.
Methods: The study group consisted of over 18-year-old patients who had been submitted to allogeneic transplantation at least one year previously. Patients and healthy controls were matched by sex, ethnic background, age, and body mass index. Body composition and bone mineral density were measured by dual-energy X-ray absorptiometry. A 24-h food recall and food frequency survey were performed. The biochemical evaluation included calcium, parathormone and vitamin D. Eighty-seven patients (52 men; age: 37.2 ± 12.7 years; body mass index: 25 ± 4.5 kg/m^2) were compared to 68 controls [31 men; age 35.4 ± 15.5 years ($p = 0.467$); body mass index 25.05 ± 3.7 kg/m^2 ($p = 0.927$)].
Results: There was no significant difference in the dietary intake between patients and controls. The mean levels of vitamin D were 23.5 ± 10.3 ng/mL; 48 patients (68.6%) had insufficient and six (8.6%) deficient levels. A higher prevalence of reduced bone mineral density was observed in 24 patients (25%) compared to 12 controls (19.1% – $p < 0.001$). Pre-sarcopenia was diagnosed in 14 (14.4%) patients and none of the controls ($p = 0.05$). There was a higher prevalence of pre-sarcopenia (66%) in patients with grades III and IV compared to those with grades 0-II graft-versus-host disease (10.9%) ($p = 0.004$).
Conclusion: patients submitted to transplantation had a higher prevalence of pre-sarcopenia and greater changes in bone mineral density compared to controls; the severity of graft-versus-host disease had an impact on the prevalence of pre-sarcopenia.

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Introduction

Hematopoietic stem cell transplantation (HSCT) is a therapeutic modality used to treat malignant or benign diseases. Scientific advances have allowed an increasing number of transplants and longer disease-free survival. Consequently, there is an increment in post-transplant comorbidities secondary to the disease, conditioning regimen or complications, such as graft-versus-host disease (GVHD). Changes in bone mineral density (BMD) may occur due to the use of glucocorticoids, reduced physical activity, low exposure to sunlight, reduction in lean body mass, and vitamin D deficiency. These changes are observed as early as the first months after HSCT or as late as ten years after the procedure.[1–4] Recently, sarcopenia has been described after several types of transplants such as liver, kidney and lung, and may influence the outcome.[5–8]

The term sarcopenia characterizes loss of function related to loss of skeletal muscle mass. It is denominated pre-sarcopenia when only loss of muscle mass is detected. The etiology is multifactorial, but usually occurs due to neurodegenerative, endocrine or chronic diseases, malnutrition or lack of exercise, which leads to muscle atrophy.[9] After HSCT, the association of pre-sarcopenia and sarcopenia with the pre-existing disease may worsen the patient's baseline condition, increasing the risk of fractures, especially when associated with reductions in BMD. The early diagnosis of sarcopenia may allow preventive and/or curative treatment in these patients. This research evaluated the prevalence of pre-sarcopenia and changes in BMD in a group of HSCT patients.

Methods

This observational, transversal study enrolled over 18-year-old patients, regardless of ethnic background or sex, who underwent allogeneic HSCT at the Bone Marrow Transplant Unit of the Hospital de Clinicas da Universidade Federal do Paraná (STMO-HC-UFPR). The sample was selected by convenience; patients were invited to participate during their routine visit. To avoid the consequences of acute bone marrow transplantation complications, patients who had been transplanted less than one year previously were excluded, as were patients with a diagnosis of Fanconi anemia. A control group (CG) was formed of healthy subjects matched with the study group (SG) by sex, age, ethnic background, and body mass index (BMI). Patients and controls performed dual-energy X-ray absorptiometry (DXA) in a whole-body scanner (Lunar Prodigy; GE Medical Systems, Madison, WI, USA) used in conjunction with enCORE 2002 software (GE Medical Systems) to assess the body composition. The software provides data about lean body mass (bone mass plus fat-free mass), bone-free lean mass (lean mass minus fat-free mass), fat mass, and bone mineral density (BMD). Blood samples were collected for biochemical analysis, and a review of hospital records was carried out to search for data regarding the HSCT.

The BMD of total body, lumbar spine (LS), and femur (neck and total) were evaluated with the results being categorized as normal or abnormal following the International Society For Clinical Densitometry (ISCD).[10] The percentage of lean mass (%LM) and appendicular lean mass (ALM) were calculated.

Diagnosis of pre-sarcopenia

The diagnosis of pre-sarcopenia was performed considering three criteria available in the literature. Patients were categorized according to BMI as normal (BMI < 25 kg/m^2) or obese (BMI > 25 kg/m^2). After evaluating the ALM and for those with a normal BMI, the criterion of Baumgartner et al.[11] was used, which defines the reduction of appendicular skeletal muscle mass as two standard deviations (SDs) below the mean of young healthy controls, matched with the same ethnic group of the New Mexico population. Values <5.45 for women and <7.26 for men were considered positive. For individuals with BMI ≥25 kg/m^2, the diagnosis of pre-sarcopenia was calculated based on the criterion of Delmonico et al.[12] Initially, a linear regression model was adjusted for ALM (kg) including height (m) and total fat mass (kg) as explanatory variables. The residuals of the regression were used to identify individuals with a lean mass lower than the value predicted for a given fat mass (given by an equation derived from the model). A positive residual indicates a relatively muscular individual, whereas a negative residual indicates an individual with sarcopenia. The equations derived from the model were the following: for males – ALM (kg) = −30.54 + 30.88 × height (m) + 0.0823 × total fat mass (kg); and for females – ALM (kg) = −12.45 + 15.79 × height (m) + 0.1081 × total fat mass (kg). The 20th percentile of the distribution of residuals was used as the cut-off point for the diagnosis of sarcopenia according to the ALM adjusted for fat mass as previously defined. In this patient sample, the cut-off point corresponded to residuals of −2.021 for men and −1.082 for women.

Finally, the ALM/BMI criterion of The Foundation for the National Institute of Health (FNIH) was used, and the values of <0.789 for men and <0.512 for women were considered pre-sarcopenia.[13]

Food intake was assessed using an interview conducted by a registered dietician with a 24-h recall questionnaire based on type and quantities of food consumed the day before the interview, a tool appropriate to assess the consumption of a nutrient with a specific dietary recommendation.[14,15] Calcium, vitamin D, protein, and total calorie intake were calculated by AVANUTRI®, a nutritional assessment program, following the reference of the "recommended dietary allowance" (RDA) according to sex and age. The intake was considered adequate when it reached or exceeded the RDA. The RDA of calcium for ages 19–50 years is 1000 mg and for >50 years, it is 1200 mg; 15 μg of vitamin D is recommended for individuals between 19 and 70 years.[16]

Biochemical analysis

Serum levels of parathormone (PTH) [chemiluminescence – normal value (NV) = 15–68.3 pg/mL] calcium (Arzenago III – NV = 8.9–10 mg/dL) and vitamin D (chemiluminescence – Liaison® – 25OHD) were analyzed. The 25OHD results were classified according to the latest guidelines for vitamin D levels of the Endocrine Society: deficiency below 20 ng/mL,

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