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Original Article

Prevalence of malnutrition in adult patients previously treated with allogeneic hematopoietic stem-cell transplantation

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SUMMARY

Introduction: Malnutrition is common after allogeneic hematopoietic stem cell transplantation (allo-HSCT), and is a well-known prognostic factor for survival. The nutritional status of patients in a long term after allo-HSCT is less well documented. The main objective of this study was to evaluate the prevalence of malnutrition in adult patients who underwent allo-HSCT more than one year ago. Secondary objectives were to assess body composition, muscle strength, and factors associated with malnutrition.

Patients & methods: All allo-HSCT patients admitted into the University Hospital of Clermont-Ferrand between 1st January 1985 and 31st December 2012 were screened. Clinical and biological nutritional assessments included anthropometric measurements, serum nutritional proteins, body composition assessed by bioelectrical impedance, and upper-limb muscle strength (MS) measured by dynamometry. Hematological and nutritional data during and after hospital stay for allo-HSCT were retrospectively collected.

Results: Eighty four allo-HSCT patients (52% men; mean age 54.4 ± 12.5 years) were enrolled. Average follow-up after allo-HSCT was 56.4 ± 47.5 months. Prevalence of malnutrition at the end of follow-up was 20%. Compared to well-nourished patients (WN group), undernourished patients (UN group) at the end of follow-up were significantly more likely to be undernourished (50% vs. 21%, $p = 0.04$) at hospital admission, and to have a Nutritional Risk Index of <97.5 (47% vs. 20%, $p = 0.004$). Compared to a reference population, mid-arm muscle circumference and MS were significantly more likely to be decreased in the UN group than in the WN group (35.3% vs. 8.9%, $p = 0.017$; 24% vs. 3%, $p = 0.005$, respectively); fat-free mass index and appendicular skeletal muscle mass index were decreased in 30.5% and 36.6% of all patients, respectively, with no difference between UN and WN groups. Chronic graft-versus-host disease was more frequent, although not significantly in the UN group (76% vs. 52%, $p = 0.071$). In multivariate analyses, the presence of malnutrition at hospital admission for allo-HSCT trended towards an increased risk of longer-term malnutrition (OR = 3.60 [0.95; 13.67], $p = 0.06$).

Conclusion: Malnutrition is a frequent consequence of allo-HSCT, and may occur several months or years after allo-HSCT, particularly if malnutrition existed before allo-HSCT. Our findings support the need for specialized nutritional care for both before and after allo-HSCT. Furthermore, assessment of muscle mass may be a pertinent parameter of malnutrition in this instance.

1. Introduction

Malnutrition is a frequent and well known issue in cancer disease, notably in digestive cancer but also in hematology cases [1]. Thus, a recent multicenter epidemiological study conducted in France on 1903 patients treated for cancer found that 34% of patients with lymphoma or acute leukemia were malnourished [2].

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Before allogeneic hematopoietic stem cell transplantation (allo-HSCT), most patients have a good nutritional status, and only 10–15% are undernourished [3–6]. *Allo-HSCT and associated treatments, such as immunosuppressive* drugs, antibiotics and steroids have frequent side effects, which are mainly metabolic and digestive. In addition, treatments such as total body irradiation and intensive chemotherapy, but also anorexia, mucositis, nausea, vomiting, graft versus host disease (GvHD) and infectious complications can induce a significant reduction in oral food intake but also intestinal malabsorption [7]. Thus, almost all patients lose weight within the 4–6 weeks after allo-HSCT. This results in an average of 4–7% loss of body weight, and even more than 10% for 25% of patients, with or without a nutritional support [6,8]. At present, malnutrition is well recognized as an independent prognostic factor for survival in children and adults with hematologic malignancies treated with allo-HSCT [3,9–11]. Moreover, malnutrition decreases quality of life, increases length of stay in hospital, and the engraftment period [4,12,13].

Few studies have investigated the long term nutritional status of patients after allo-HSCT, and most of them no more than the first year [5,8,11,14,15]. The main goal of this study was to evaluate the prevalence of persistent malnutrition in adult patients who had undergone allo-HSCT. Secondary objectives were to assess body composition, muscle strength, and possible factors associated with long term malnutrition after allo-HSCT.

2. Patients and methods

2.1. Patients

We conducted a transversal monocentric cohort study. Patients were included if they were aged more than18 years, had undergone an allo-HSCT with myeloablative (MA) or non-MA conditioning for more than 6 months within the unit of adult cell therapy and clinical hematology at the University Hospital of Clermont-Ferrand, and if they had healthcare insurance cover and had given their signed informed consent.

Exclusion criteria were an inability to understand the study's protocol (language barrier, cognitive disorders …), refusal to participate in the study, relapse at time of inclusion, another current disease unrelated to allo-HSCT that could interfere with nutritional status (e.g., another cancer, chronic organ failure, digestive supra-mesocolic surgery …), or a past or current psychiatric disease.

2.2. Study design

The list of all allo-HSCT patients that had attended our unit between 1st January 1985 and 31st December 2012 has been obtained from the European PROMISE database. Patients were contacted by phone and asked to participate in the study. Inclusion and exclusion criteria were verified. Patients who met the criteria and agreed to participate in the study (Fig. 1) were invited to undergo clinical and biological nutritional assessments, and to complete a functional capacity evaluation using the Performans Status (PS) of the World Health Organization (WHO). The examination enabled us to clarify the patient's usual weight before the disease, any intercurrent events after the allo-HSCT, any current drug treatments, and the existence or not of dietary management (with or without a prescription of enteral and/or parenteral nutrition) after hospital discharge.

Retrospective clinical and biological data were collected concerning allo-HSCT: initial hematological disease, type of conditioning, number of days between the day of transplantation and the day of the study consultation (i.e. duration of follow-up), body weight, serum albumin, serum transthyretin, C-reactive protein (CRP) at admittance and discharge from hospital, nutrition support received during and after hospitalization, and the occurrence of any complications (such as acute GvHD and/or hepatic veno-occlusive disease).

2.3. Nutritional assessment

Body height was measured to the nearest 0.5 cm and body weight was measured to the nearest 0.1 kg on an electronic scale. Mid-arm circumference was measured on the non-dominant arm, with a tape measure, at mid-distance between the acromion and the olecranon. At the same level, the triceps skinfold (TSF) was measured using a Harpenden Skinfold Caliper (HSK-BI, British Indicators). TSF was considered decreased when its value was below the 5th percentile for a reference population [16]. Mid-arm muscle circumference (MAMC) allowed estimation of fat-free mass (FFM), which was calculated using the formula: MAMC (cm) = Mid-arm circumference (cm) − [3.14 × *TSF* (mm)]. MAMC was considered decreased when its value was below the 5th percentile for a reference population [16].

The Nutritional Risk Index (NRI) at admission into hospital for allo-HSCT was calculated using the formula: NRI = 1.519 × albumin (g/L) + 41.7 × [measured weight (kg)/usual weight (kg)] [17].

Body composition was assessed using multi-frequency bioelectrical impedance analysis (BIA) (QuadScan 4000, Bodystat). Measurements were conducted using electrodes placed on the hands and feet, with the patient in a supine position, for 10 min. Parameters checked were the phase angle (PA), reactance, and resistance to 50 Hz.

Fat-free mass (FFM) and appendicular skeletal muscle mass (ASMM) were calculated according to the following equations:

FFM (kg) = −4.104 × [0.518 × height^2 (m^2)/resistance (ohm)] + [0.231 × weight (kg)] + (0.130 × reactance (ohm)) + [4.229 × gender] (with male = 1 and female = 0) [18];

ASMM (kg) = −4.211 × (0.267 × (height (m)/resistance (ohm))) + (0.095 × weight (kg)) + (−0.012 × age (years)) + (0.058 × reactance (ohm)) + (1.909 × gender) (male = 1 and female = 0) [19].

Fat mass (FM) was calculated as the difference between total body weight and FFM.

FFM index (FFMI) and ASMM index (ASMMI) were calculated according to the following equations: FFMI (kg/m^2) = FFM (kg)/height^2 (m^2); ASMMI (kg/m^2) = ASMM (kg)/height^2 (m^2).

FFM, FFMI, ASMM, and ASMMI were considered decreased if their values were below the 5th percentile compared to the standard values from a reference population matched for age and gender [18,20].

Muscle strength (MS) in the upper limb was evaluated using a hydraulic dynamometer (Hydraulic Hand Dynamometer, Saehan Corporation) in a standing patient, forearm bent at 90° and away from the body. Three measurements were made on each side, and the highest of the six values was chosen. The values were considered decreased when they were lower than the standard values from a reference population matched for age and gender [21].

Daily calorie and protein ingesta were calculated from a home food survey conducted during the 3-day period before the hospital visit.

Serum albumin, serum transthyretin, and CRP were measured. An inflammatory syndrome was characterized if CRP was >15 mg/dL.

Malnutrition was defined using the criteria and thresholds recognized by the French Speaking Society of Clinical Nutrition and Metabolism (SFNEP) and the French Health Authority (HAS) [22,23]. Thus, in adults aged <70 years, malnutrition was defined by a weight loss (WL) compared to a usual weight either >5% in 1 month or >10% in 6 months, or a body-mass index (BMI = [weight

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