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Original article

Changes in nutritional status in childhood cancer patients: A prospective cohort study☆

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SUMMARY

Background & aims: Under- and overnutrition are linked to adverse outcomes during and after childhood cancer treatment. Therefore, understanding the timing of weight loss and weight gain and their contributory factors is essential for improving outcomes. We aimed to determine in which period of treatment changes in nutritional status occurred and which factors contributed to these changes.
Methods: A prospective cohort study of 133 newly diagnosed cancer patients with hematological, solid, and brain malignancies was performed. Anthropometric data and related factors were assessed at 0, 3, 6 and 12 months after diagnosis.
Results: Despite initial weight loss at the beginning of treatment in patients with hematological and solid malignancies, body mass index (BMI) and fat mass (FM) increased within 3 months with 0.13 SDS ($P < 0.001$) and 0.05 SDS ($P = 0.021$) respectively. Increase continued during the following months and resulted in a doubling of the number of overnourished patients. Fat free mass (FFM), which was already low at diagnosis, remained low. During the entire study period about 17% of the patients were undernourished on the basis of low FFM. Tube feeding and diminished activity level were related to increases in BMI and %FM respectively. No relationship was found between energy intake or corticosteroids and increase in BMI or %FM.
Conclusions: BMI and FM increased during and after the period of intensive treatment, while FFM remained low. Improvement of nutritional status might be accomplished by increasing physical activity from the early phase of treatment.

1. Introduction

Poor nutritional status is linked to adverse outcomes both during treatment of childhood cancer and during survivorship. During cancer treatment under- and overnutrition result in more complications, higher relapse rates, and lower survival rates.[1,2] During survivorship, overnutrition is one of the risk factors for diabetes mellitus type II, hypertension, and cardiovascular diseases.[3] This is especially a problem in cancer survivors, who run the additional risk of developing cardiovascular disease due to treatment with potential cardiotoxic chemotherapy or radiotherapy.[4] Undernutrition in the general population is also associated with morbidity and increased all-cause mortality.[5] Although previous studies have presented data of under- and overnutrition

List of abbreviations: ADP, air-displacement plethysmography; ALL, acute lymphoblastic leukemia; BIA, bioelectrical impedance analyses; BMI, body mass index; FFM, fat free mass; FM, fat mass; %FM, percentage fat mass; HFA, height-for-age; ITR, Intensity of Treatment Rating scale; MSAS, Memorial Symptom Assessment Scale; MUAC, mid-upper arm circumference; PPS, Play Performance Scale; SDS, standard deviation score; TSF, triceps skinfold thickness; WFA, weight-for-age.

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in childhood cancer patients, little is known about the timing of the onset of under- and overnutrition and their respective causes. It is therefore necessary to study the timing and the causes of changes in nutritional status in order to develop adequate intervention strategies.

Nutritional status can be represented by both body size and body composition. Body size is measured using weight, height, and body mass index (BMI), and represents the general impression of the child's growth. Body composition is expressed in fat mass (FM) and fat free mass (FFM), which represent the nutritional stores of the body.[6,7] Body composition can be measured both by complex methods, such as air-displacement plethysmography (ADP) or simple methods such as bioelectrical impedance analyses (BIA). Patients can be undernourished because of low BMI and/or low FFM, or overnourished because of high BMI and/or high FM. Both criteria are not necessarily present at the same time. For example, low FFM can be present in patients with normal BMI. In this study both body size and body composition are considered to be relevant.

Presumably, changes in nutritional status are caused by the malignancy or its treatment and continue into survivorship. Therefore, it is important to gain insight in the course of weight loss or weight gain and changes in body composition during treatment, but also to determine the factors related to these changes. Up till now, most studies assessing nutritional status relied on cross-sectional data.[7] The few prospectively conducted longitudinal studies that did report on changes in nutritional status predominantly concerned patients with acute lymphoblastic leukemia (ALL) and described time intervals of 6 months or more, making a detailed analysis of the timing of changes difficult.[8,9] Longitudinal studies in patients with solid and brain malignancies are scarce.[7] Therefore, we conducted a prospective cohort study among newly diagnosed cancer patients with heterogeneous malignancies and registered body size, body composition, and related factors during 12 months after diagnosis. Our research questions were:

1. In which period of treatment do changes in body size and body composition arise?
2. Which factors contribute to those changes in body size and body composition?

2. Methods

2.1. Participants

All children newly diagnosed with cancer, who were consecutively admitted to the Pediatric Oncology Department of the University Medical Center Groningen (UMCG) between September 2007 and December 2009 were asked to participate in a prospective cohort study called the Pecannut (Pediatric Cancer and Nutrition) study. The follow-up period was 12 months and ended in December 2010. Eligible patients were between 0 and 17.99 years of age, had no prior diagnosis of cancer, had sufficient command of the Dutch language, and received treatment with curative intent. In total, 150 patients were eligible for inclusion. Fifteen patients refused participation because they found the study too burdensome ($n = 13$), or because a lack of motivation ($n = 2$) (response rate 90%). After inclusion, 2 patients died before assessments, resulting in a total of 133 patients who participated in the study. Patients were divided in three groups: hematological, solid, and brain malignancies. Ethical approval was obtained from the Medical Ethics Committee of the UMCG, and parents and children aged $\geq$12 years gave their written consent.

2.2. Procedure

Nutritional status was assessed within one week after diagnosis and at 3, 6, and 12 months after diagnosis by two trained observers. In addition, weight, height, and mid-upper arm circumference (MUAC) were measured at 3, 6, and 9 weeks. Measurements of the patient characteristics were taken at diagnosis; the other related factors were assessed simultaneously with the measurements at diagnosis, 3 months, 6 months, and 12 months. The follow-up measurements were taken mostly during visits to the outpatient department and between courses of chemotherapy to make study participation more acceptable to patients.

2.3. Measures

2.3.1. Nutritional status

Weight was measured using a calibrated digital scale and recorded to the nearest 0.1 kg (for infants to the nearest 0.01 kg). During measurements children only wore underwear. Height was measured using a calibrated digital stadiometer or an infantometer for infants, and recorded to the nearest 0.1 cm. MUAC was measured halfway between the tip of the acromion and olecranon process using a non-stretchable measuring tape SECA 212 to the nearest 0.1 cm triceps skinfold thicknesses (TSF) was measured as a proxy for FM. TSF was measured using a Harpenden skinfold caliper in the same region and recorded to the nearest 0.1 mm. Both measures were performed in duplicate on the left arm. Data were expressed as standard deviation scores (SDS) calculated from Dutch reference standards.[10,11] These Dutch reference standards were based on data of the fourth nationwide growth study performed among 14,500 healthy children[10] and a study population of 2333 healthy children.[11] Furthermore, FFM was determined by bioelectrical impedance analyses (BIA) using a 50 kHz frequency BIA (BIA 101, Akern, Italy). BIA was performed on the left side of the body with the patients in supine position, arms and legs apart, in the absence of fever, intravenous hyper-hydration, and edema. To calculate FFM, the equation of Goran was used.[12] Subsequently, FM and %FM were calculated. FFM, FM, and %FM were also expressed as SDS using Dutch reference values.[13] Undernutrition was defined as BMI<-2SDS or FFM<-2SDS, overnutrition as BMI>2SDS or FM $>$ 2SDS, and relevant weight loss or weight gain was defined as $>$5% change between 2 sequential measurement times.

2.3.2. Related factors

2.3.2.1. Patient characteristics. The patient characteristics included in this study were age, gender, diagnosis, initial nutritional status and body composition, and parental BMI.

2.3.2.2. Energy intake. Energy intake was assessed using a 3-day dietary diary and total kcal was calculated using food calculation software (Eetmeter 2002, The Netherlands Nutrition Centre, The Netherlands). Percentage intake of individual energy requirement (using Schofield's formula[14]) was calculated. In addition, it was registered whether the child received oral or tube feeding.

2.3.2.3. Treatment intensity and treatment phase. Treatment intensity was rated with the Intensity of Treatment Rating scale (ITR-3).[15] Since only a few patients were rated either in the least intensive or most intensive categories, the ITR-scale was reduced to two categories: least/moderate intensive and very/most intensive. Furthermore, at each measurement time it was recorded whether a patient was still in active treatment or whether therapy was terminated.

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