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Published in:
Clinical Nutrition

DOI:
10.1016/j.clnu.2022.10.021

Publication date:
2022

Clinical Nutrition 41 (2022) 2778–2785

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original Article

Changes in body size and body composition in survivors of childhood cancer: seven years follow-up of a prospective cohort study

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ARTICLE INFO

Article history:
Received 27 May 2022
Accepted 27 October 2022

Keywords:
Childhood cancer
Survivors
Nutritional status
Body composition
Obesity

SUMMARY

Background & aims: Cancer treatment is known to have impact on nutritional status, and both underweight and overweight have been reported in several studies in survivors. A limitation of most studies is that they relied on retrospective data or were limited to a subgroup of patients. The current study aims to describe changes in body size and body composition prospectively seven years after diagnosis in a heterogeneous sample of childhood cancer survivors and to evaluate associated factors.

Methods: The study population consisted of children diagnosed with hematological, solid and brain malignancies aged 0–18 years at diagnosis. Data of body size, body composition, and associated factors were collected at diagnosis, one year and seven years after diagnosis.

Results: In the total cohort mean BMI z-score increased during treatment. In children with hematological and brain malignancies BMI z-score continued to increase after end of treatment leading to quadrupling of the prevalence of obesity seven years after diagnosis. BMI at diagnosis ($\beta = -0.34$, $P = 0.007$) and maternal BMI ($\beta = 0.25$, $P = 0.046$) were associated with the increase in BMI z-score. Mean fat mass (FM) z-score, already high at diagnosis, increased during treatment in children with hematological and brain malignancies and evened out during follow-up. Changes in FM z-score were predicted by type of malignancy (hematologic malignancy versus solid tumor $\beta = 0.48$, $P = 0.008$; brain tumor versus solid tumor $\beta = 0.45$, $P = 0.012$). Mean fat free mass (FFM) z-scores started low at diagnosis, particularly in patients with brain tumors, increased during treatment in patients with solid and brain malignancies, though decreased in children with hematological malignancies. At 7 years follow-up a clear increase to normal was seen. Age at diagnosis ($\beta = 0.43$, $P = 0.004$) and initial FFM ($\beta = -0.49$, $P = 0.001$) were found to be significant predictors for changes in FFM z-scores.

Conclusions: The finding that the once obtained extra weight and FM during treatment persisted after termination of treatment in children with hematological and brain malignancies, stresses the importance to create awareness about the risk of developing overweight in children during cancer treatment.

1. Introduction

In recent decades, childhood cancer survival rates have significantly increased by means of improved diagnostics, multimodal treatment options and high standards of supportive care [1]. With improving treatment outcomes, the challenge is to minimize short- and long-term adverse treatment effects.

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https://doi.org/10.1016/j.clnu.2022.10.021
0261-5614/

Nutritional status has long been known to have prognostic implications in children diagnosed with cancer [2]. Both overweight and underweight patients suffer from more complications and are at higher risk of adverse treatment outcome [3–6]. Not only does nutritional status influence outcome of childhood cancer treatment, treatment in turn may cause changes in nutritional status. Obesity, for example, is a recognized complication in childhood cancer survivors, well-documented for acute lymphatic leukemia [7–11]. In recent years, efforts have been made to identify factors responsible for these changes. Cranial and craniospinal radiotherapy [12] and weight gain during the first year of treatment [13] have been found to correlate with long-term risk of overweight. However, also ALL patients treated without cranial radiation have been found to be at risk for overweight [11]. Although glucocorticoids cause overweight and obesity during treatment [14], conclusive evidence for a long-term effect is lacking [10,15,16]. Conversely, an increased risk of underweight was observed in female and male survivors of Hodgkin's disease, Wilms tumor, and male survivors of non-Hodgkin lymphoma, neuroblastoma, and soft tissue sarcoma [17]. Treatment with anthracyclins and alkylating agents were associated with being underweight [12,17]. For survivors of brain tumors the literature reports both higher risk for overweight and obesity [18] as well as underweight [19]. An important risk factor in this patient group is hypothalamic damage, either due to tumor, surgery or radiation [18,20]. These data, however, mainly derive from retrospective or cross-sectional studies and data from prospective longitudinal studies are scarce.

The PeCanNut (Pediatric Cancer and Nutrition) study, is a prospective cohort study in which nutritional status of children newly diagnosed with cancer was followed over time. Data of the PeCanNut I study showed that BMI, as well as percentage of fat mass significantly increased during the first 12 months after diagnosis, leading to doubling of the prevalence of obesity 12 months after treatment was started [21]. A later longitudinal study confirmed these alarming increases in body and fat mass during treatment [22]. The current article presents the results of the second part of the PeCanNut study, in which the follow-up period in this cohort was extended to seven years after primary diagnosis. With these data, we address the following research questions: 1. How do body size and body composition change after treatment in childhood cancer survivors? 2. Which factors (age, gender, parental body mass index, socioeconomic status, type of malignancy, nutritional status at diagnosis, energy intake, tube feeding, corticosteroid treatment and physical activity) are related to these changes?

2. Methods

2.1. Participants

All patients who participated in the first part of the PeCanNut study were eligible for participation in the second part. These patients were newly diagnosed with cancer between September 2007 and December 2009 and the follow-up time was 12 months (until December 2010). The amendment for the PeCanNut II study was approved by the Medical Ethics Committee of the University Medical Center Groningen, a new informed consent was asked and data were obtained seven years after the start of therapy. To diminish the burden of participation, data collection was planned during regular follow-up visits to the outpatient clinic of the Department of Pediatric Oncology and Hematology of the Beatrix Children's Hospital (situated in Groningen, the Netherlands).

3. Measures

3.1. Anthropometry

All anthropometric measures were performed identically as in PeCanNut I [21]. Weight was recorded to the nearest 0.1 kg and height was recorded to the nearest 0.1 cm. MUAC and Triceps skinfold thickness (TSF) were recorded to the nearest 0.1 cm and 0.1 mm respectively. All data were expressed as z-scores calculated from the Dutch population and the same reference values were used as in PeCanNut I [23,24]. FFM, FM and %FM were derived from bioelectrical impedance analyses (BIA) using a 50 kHz frequency BIA (BIA 101, Akern, Italy). FFM, FM, and %FM were also expressed as z-scores using Dutch reference values [25]. Underweight was defined as BMI or FFM z-score ≤ -2; overweight was defined as BMI or FM z-score ≥ 2.

3.2. Patient characteristics

The following patient characteristics were included in the study: age, gender, type of malignancy, nutritional status at diagnosis, parental BMI, socio-economic status (SES) parents, corticosteroid treatment, energy intake, tube feeding, and physical activity. SES was based on the highest education of the father and divided into three groups: low (elementary or lower vocational education), middle (general intermediate vocational or general secondary education), and high (higher vocational, college or university). For corticosteroid treatment it was noted whether children had received corticosteroids (yes or no) as part of their anti-cancer therapy or not.

3.3. Energy intake and tube feeding

Energy intake during survivorship was based on a 3-day dietary diary. Total kcal intake was calculated and expressed as percentage energy intake of individual requirements (based on Schofield's formula [26]). Tube feeding was expressed as receiving tube feeding (yes or no) at any time during treatment or not.

3.4. Physical activity

3.4.1. Activity diary

Participants kept activity diary records for seven consecutive days. Days were divided into 96 time slots of 15 min each. Participants and their parents were instructed to indicate their level of physical activity during each time slot by means of a numeric rating scale, ranging from 1 (resting) to 9 (very high to maximal intensity work or sports activities). Physical activity level (PAL) for each day was calculated by adding up 15-min slots for each 1–9 category, dividing the sum by 96 and multiplying by the respective physical activity ratio (PAR) [27].

3.4.2. Accelerometer

Physical activity level was objectively measured by means of the accelerometer (Actical, Philips Respironics, Bend, OR, USA), a device translating accelerations in any plane of movement into activity counts. Participants wore the accelerometer, from getting up in the morning to going to bed in the evening, on the right hip for the same seven consecutive days as they kept the activity diary. Based on counts per minute, 1-min time slots were categorized as sedentary (0–100 counts per minute), light (101–1500 counts per minute), moderate (1501–6500 counts per minute) or vigorous (>6500 counts per minute) physical activity [28].

3.5. Statistical analyses

Descriptive statistics were used to describe the course of the nutritional status at diagnosis (T0), and at respectively 12 months (T1) and seven years follow-up (T2). In order to compare the changes in body size and body composition during therapy with the period of follow-up, z-scores of BMI, FM, and FFM at T0 were subtracted from z-scores at T1 ($=\Delta z_{T1\text{-}T0}$) and z-scores at T1 were subtracted from z-scores at T2 ($=\Delta z_{T2\text{-}T1}$). Then, Pearson's correlation coefficients were computed for $\Delta z_{T1\text{-}T0}$ and $\Delta z_{T2\text{-}T1}$ of BMI, FM and FFM. Subsequently, participants were divided into two groups for each parameter: children who experienced gain of BMI, FM and FFM (BMI[+], FM[+] and FFM[+]) and children who experienced loss of BMI, FM and FFM (BMI[−], FM[−] and FFM[−]) during treatment, respectively. Independent *t*-tests were used to compare children with gain [+] or loss [−] of z-score during treatment for changes in z-score of BMI, FM, and FFM during follow-up ($=\Delta z_{T2\text{-}T1}$).

Based on significant outcomes of univariate analyses, variables were entered in multiple linear regression model to identify the explanatory variables for changes in BMI, FM and FFM from diagnosis to follow-up. Stepwise, variables with the highest (non-significant) p-values were deleted to determine the best model. IBM SPSS Statistics Version 26 was used for all statistical analyses.

4. Results

4.1. Cohort characteristics

Of the 115 patients who completed part 1 of the PeCanNut study, 66 agreed to participate in part 2. Patients were diagnosed with hematological (43.9%), solid (36.4%) and brain (19.7%) malignancies and mean time since diagnosis was 7.1 years. Patient characteristics are summarized in Table 1. Median percentage energy intake was 82.7% (43.3–144.6) of individual requirements. Median time spent in moderate-to-vigorous activity (MVPA) based on accelerometer was 27 [16–37] minutes and physical activity level (PAL) based on the diary was 1.23 (1.14–1.32). Unfortunately, not all patients completed the data for energy intake or physical activity.

4.2. Change of body size and body composition over time

Mean z-scores for anthropometric measurements at diagnosis, one and seven years after diagnosis are presented in Fig. 1. Considering weight-for-age (WFA), an increase in z-scores during the first year after diagnosis was most clearly observed in patients with solid and brain tumors (Fig. 1a). This increase continued during follow-up in patients with hematological and brain malignancies. The decrease in height-for-age (HFA) during treatment seen in all diagnosis groups leveled off, but did not recover during follow-up (Fig. 1b). Patients with hematological malignancies had the lowest HFA z-score. Mean HFA z-score for all patients at follow-up was −0.08 (Table 2), not significantly lower than normal. Whereas patients in all diagnosis groups showed an increase in BMI during treatment, z-scores flattened during follow-up in patients with solid malignancies, though BMI still increased in patients with hematological and brain malignancies (Fig. 1c). The patterns of mid-upper arm circumference (MUAC) were very similar to the patterns of BMI (Fig. 1d). Triceps skinfold (TSF), FM and %FM, already high at diagnosis, increased in patients with hematological and brain malignancies during treatment and evened out during follow-up, although the absolute FM in patients with hematological malignancies still gradually increased. Mean FFM z-score started low at diagnosis, particularly in patients with brain tumors, increased during the first year after diagnosis in patients with solid and brain malignancies and during follow-up a clear increase to normal was seen in patients with brain tumors. FFM patterns of patients with hematological malignancies showed opposite patterns: decrease of mean FFM z-score during treatment and a recovery during follow-up.

At follow-up, mean z-scores of WFA, BMI, FFM and FM were all significantly higher than at diagnosis whereas HFA was significantly lower (Table 2). The percentage of underweight children decreased from 18.2% at diagnosis to 10.6%. However, the percentage of overweight children quadrupled from 6.1% at T0 to 27.3% at follow-up (Table 3).

4.3. Comparison of children with gain or loss of BMI, FM, or FFM

Mean BMI and FM z-score change during treatment ($\Delta BMI_{T1\text{-}T0}$ and $\Delta FM_{T1\text{-}T0}$) was significantly negatively correlated with mean BMI and FM z-score change during follow-up ($\Delta BMI_{T2\text{-}T1}$ and $\Delta FM_{T2\text{-}T1}$) (Pearson's $r = -0.495$; $P < 0.000$ and Pearson's $r = -0.503$; $P = 0.002$ respectively), so decrease in BMI or FM during treatment was associated with increase during follow-up.

A significant difference was observed in BMI z-score change after treatment ($\Delta BMI_{T2\text{-}T1}$) in children with weight loss during treatment (BMI[−] group) compared with children with weight gain during treatment (BMI[+] group) namely $\Delta BMI_{T2\text{-}T1} = 0.97$, SD = 0.91 in the BMI[−] group versus $\Delta BMI_{T2\text{-}T1} = -0.05$, SD = 1.40 in the BMI[+] group; $t(62) = 2.91$, $P = 0.005$ (Fig. 2). The group with weight loss during treatment showed increase of mean BMI z-score during follow-up, whereas the mean BMI z-score of the group with weight gain during treatment stabilized after treatment.

A significant difference was observed in FM change after treatment ($\Delta FM_{T2\text{-}T1}$) in children with FM loss during treatment (FM[−] group) ($\Delta FM_{T2\text{-}T1} = 0.32$, SD = 0.80) compared with children with

Table 1

Patient characteristics (n = 66)		
Age at diagnosis median (range)	8.2	(0.1–17.7)
Age at T2 median (range)	15.5	(5.6–25.9)
Time since Dx mean (range)	7.1	(4.8–9.1)
	n	%
Gender: female	39	(59.1)
Diagnosis:		
Hematological	29	(43.9)
Leukemia	23	(34.8)
ALL	21	(31.8)
AML/JML	2	(3.0)
Lymphoma	6	(9.1)
Solid tumors	24	(36.4)
Neuroblastoma	4	(6.1)
Wilms tumors	5	(7.6)
Bone tumors	5	(7.6)
Solid other	10	(15.2)
Brain tumors	13	(19.7)
Medulloblastoom	3	(4.5)
Astrocytoma/glioma	6	(9.1)
Other	4	(6.1)
SES		
Low	7	(10.6)
Middle	31	(47.0)
High	19	(28.8)
Unknown	9	(13.6)
Received corticosteroids	39	(59.1)
Received tube feeding	27	(41.5)
%Energy intake median (range) (n = 38)	82.7	(43.3–144.6)
Activity, Actical device, minutes (n = 37)	median	IQR
Wearing time	798	(727–826)
Sedentary	596	(486–633)
Light	182	(154–219)
Moderate-to-vigorous (MVPA)	27	(16–37)
PAL diary (n = 30)	1.23	(1.14–1.32)

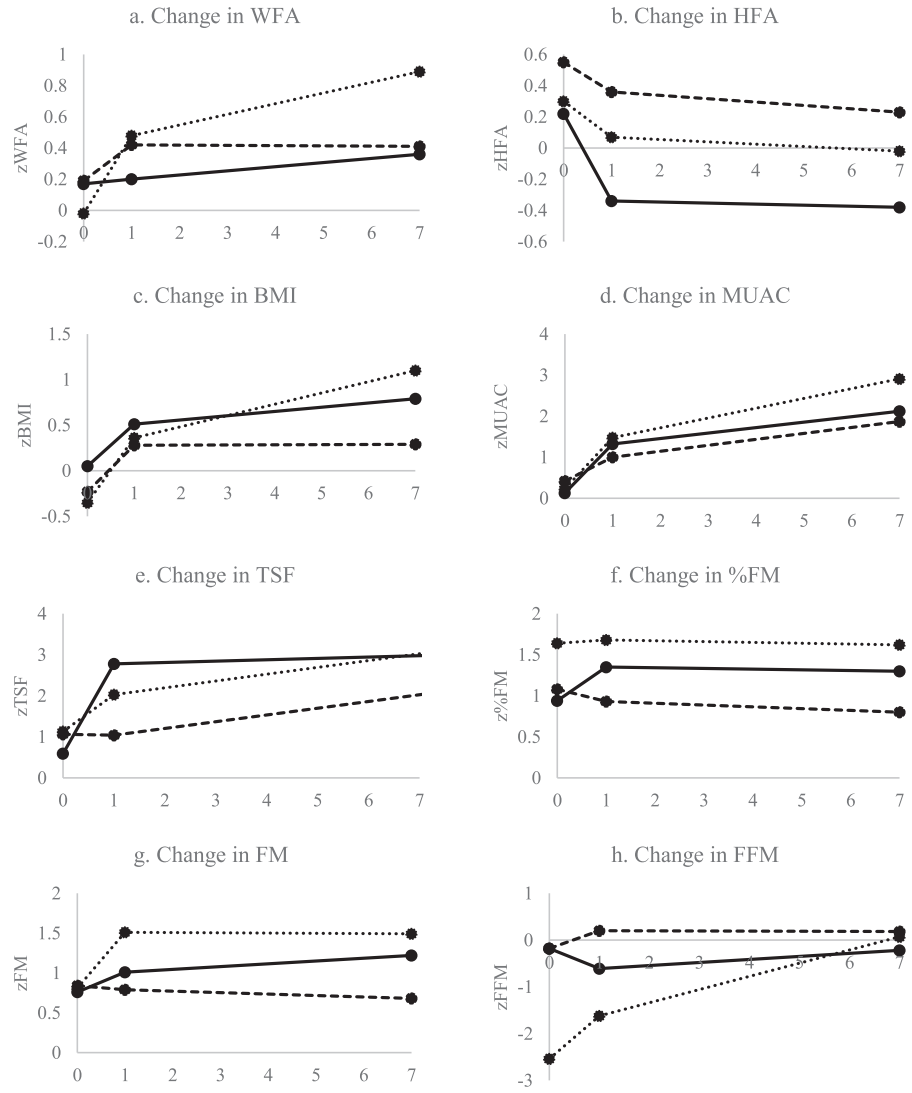

Fig. 1. Change in parameters of body size and body composition from diagnosis (time = 0) till extended follow-up (time = 7) expressed in z-score. Data are presented of patients with hematological, solid, and brain malignancies. —— hematological; - - - solid; ····· brain.

FM gain (FM[+] group) ($\Delta FM_{T2\text{-}T1} = -0.27$, SD = 0.87); t [33] = 2.08, $P = 0.046$ (Fig. 2).

The change in FFM after treatment ($\Delta FFM_{T2\text{-}T1}$) did not differ significantly between the FFM[−] group ($\Delta FFM_{T2\text{-}T1}$ = 1.30, SD = 1.91) and the FFM[+] group ($\Delta FFM_{T2\text{-}T1} = 0.42$, SD = 1.72); t [36] = 1.47, P = 0.151 (Fig. 2). These patterns of loss during treatment and gain during follow-up were seen across all three diagnosis groups, however the subgroups were too small for testing.

Table 2
Nutritional status at diagnosis and follow-up expressed in z-scores.

	At diagnosis (T0)	Follow-up (T2)	t-value	P value
WFA	0.14	0.48	−2.312	0.024
HFA	0.34	−0.08	3.167	0.002
BMI	−0.13	0.67	−5.318	0.000
FFM	−0.53	−0.03	−2.938	0.006
FM	0.80	1.10	−1.742	0.090

4.4. Factors related to changes in BMI, FM, and FFM from diagnosis to follow-up

Initial BMI was negatively associated ($\beta = -0.34$, $P = 0.007$) and maternal BMI was positively associated ($\beta = 0.25$, $P = 0.046$) to the increase in mean BMI z-score from diagnosis to follow-up ($\Delta BMI_{T2\text{-}T0}$) (see Table 4 model 2).

Regarding the increase in mean FM z-score ($\Delta FM_{T2\text{-}T0}$), in the univariate analyses both type of malignancy and corticosteroid treatment were associated with increase in FM. However, given the strong correlation of corticosteroid treatment with diagnosis group (hematologic malignancy and brain tumor versus solid tumor), the variables displaced each other in the multiple regression analyses.

Table 3
Percentage under- and overweight patients at different measurement times.

	At diagnosis (T0)	Follow-up (T2)
Well-nourished (−2 < z-score BMI/FFM < 2)	75.8%	62.1%
Underweight (BMI or FFM z-score ≤ −2)	18.2%	10.6%
Overweight (BMI or FM z-score ≥ 2)	6.1%	27.3%

Since the model with diagnosis groups had the highest R^2 (namely 0.191 for diagnosis groups and 0.124 for corticosteroids), treatment with corticosteroids was left out in the final analysis. So the best predicting factor for FM was type of malignancy (hematologic malignancy versus solid tumor $\beta = 0.48$, $P = 0.008$; brain tumor versus solid tumor $\beta = 0.45$, $P = 0.012$).

Age at diagnosis was positively associated ($\beta = 0.43$, $P = 0.004$) and initial FFM z-score was negatively associated ($\beta = -0.49$, $P = 0.001$) with the increase in mean FFM z-score ($\Delta FFM_{T2\text{-}T0}$) in multiple regression analysis (see Table 5 model 2). The other factors (gender, SES, energy intake, tube feeding, or physical activity) were not related to changes in body size or body composition.

5. Discussion

This longitudinal study of a prospective cohort of children diagnosed with cancer demonstrates that the increase of BMI during treatment, leveled off during follow-up in children with solid malignancies. However, BMI of children diagnosed with hematological and brain malignancies kept rising after termination of treatment. Children who lost BMI during treatment demonstrated gain in BMI after treatment. This could be interpreted as a catch-up growth of nutritional status. Contrarily, BMI of children with increase of BMI during therapy stabilized during follow-up. Comparable patterns were seen for FM. So the once obtained extra weight during treatment and the acquired excess of fat mass, did not diminish once the treatment was ended. These data emphasize that overweight and high fat mass of childhood cancer survivors started during therapy and remained throughout survivorship, leading to quadrupling of the prevalence of overweight from 6.1 to 27.3%. This percentage is considerably higher than 15.5% and 18.6% overweight in respectively Dutch children and adolescents [29]. The enduring weight gain and high FM in survivors of childhood cancer was demonstrated in other studies as well [7,9,13,30–33]. However, unlike the current study, these studies relied on retrospective or cross-sectional data. FFM normalized after termination of therapy. Other studies reported conflicting results regarding FFM in survivors. Some reported lower FFM in survivors of ALL [34,35] and solid malignancies [9] whereas others found normal FFM in survivors of heterogeneous malignancies [32,33]. Though Murphy et al. found similar FFM compared to controls, body cell mass of survivors was lower than in healthy controls [32,33].

Mean height-for-age z-score decreased during treatment and no catch-up growth was observed after treatment. Several studies reported catch up growth immediately after cessation of treatment in survivors of ALL, however they reported height deficits as well [7,36,37].

Mean baseline BMI z-score was negatively associated and maternal BMI was positively associated with the gain in BMI. So children with low BMI at diagnosis and children with mothers with high BMI increased more in BMI. The association of maternal BMI with gain in BMI suggests the influence of genetic factors or the impact of certain life style behaviors within a family. Both factors are known to play a pivotal role in the development of overweight [38,39]. The predictive impact of maternal BMI on weight gain has been demonstrated before in survivors of ALL [40]. Baseline BMI has been mentioned in previous studies as predictor for BMI during survivorship, however contrarily to the current finding, as a positive predictor [13,41]. It seems obvious that a high BMI at diagnosis is positively associated with a high BMI at follow-up and that after weight gain those children are more at risk of becoming obese than children starting with a low initial BMI. However, the current study demonstrates that the children with lower initial BMI gained the most in weight. This association was already demonstrated in the PeCanNut I study: initial low BMI was one of the predictors for

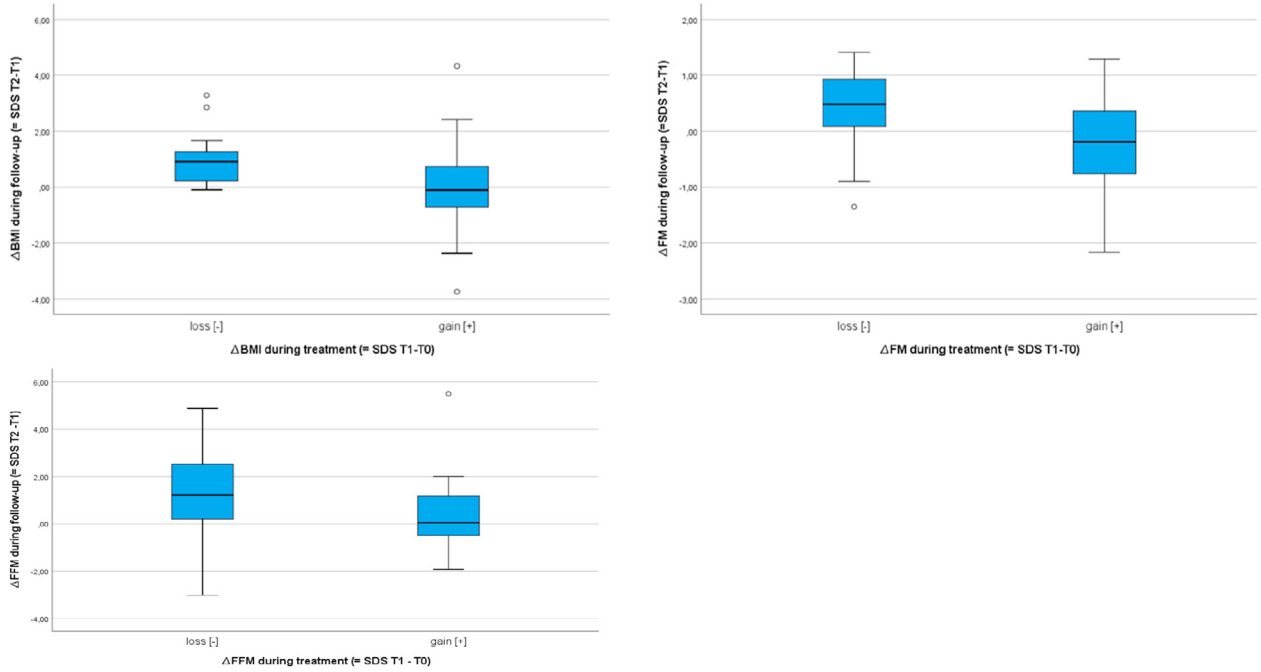

Fig. 2. Boxplots of change in z-score during follow-up of patients with loss [−] or gain [+] during treatment.

Table 4
Results of stepwise regression analyses: variables associated with ΔzBMI $_{T2-T0}$.

Variable	Unstandardized B	95% CI	Standardized coefficient β	*P*-value
Model 1				
Constant	−2.64	−4.91; −0.38		0.023
BMI at diagnosis	−0.16	−0.35; 0.02	−0.21	0.086
Maternal BMI	0.07	0.01; 0.13	0.29	0.018
Paternal BMI	0.06	−0.02; 0.13	0.17	0.157
Hematologic vs solid	−0.24	−0.73; 0.26	−0.12	0.348
Brain vs solid	0.77	0.15; 1.39	0.31	0.017
Model 2				
Constant	−1.22	−3.09; 0.65		0.196
BMI at diagnosis	−0.31	−0.53; −0.09	−0.34	0.007
Maternal BMI	0.08	0.00; 0.15	0.25	0.046

Model 1: adjusted R^2 was 0.272.
Model 2: adjusted R^2 was 0.173.

weight gain during the first three months of treatment [21]. Initially, this weight gain was denoted as catch-up growth. However, in PeCanNut I we also found indications for overfeeding, particularly in the beginning of treatment [21,42]. Regrettably, it is sometimes difficult to draw a line between desirable catch-up growth and undesirable weight gain. We now demonstrated that children with a normal or even low initial BMI gained more in weight than children with an initial high BMI. These children are at risk of becoming obese as well. So it is essential to monitor weight gain in all children diagnosed with cancer and not only in children with a high BMI at diagnosis. Finally, survival bias might have influenced the increase of BMI in survivors. Since mortality is known to be higher in malnourished patients [6], children with normal or high BMI may be over-represented in the group survivors.

Regarding alterations in body composition, type of malignancy was associated with increase of FM: the increase in FM was significantly higher in patients with hematological and brain malignancies compared to children with solid malignancies. For children with hematological malignancies, corticosteroid therapy might have influenced the increase in FM, however the evidence in the literature for this association is not unambiguous [10,15,16]. The increasing and high FM in children with brain malignancies could have been initiated by hormonal disorders i.e. hypothalamic-pituitary dysfunction [43] or lower levels of physical activity [44]. Seven years after diagnosis, physical activity levels for the whole cohort were very low and lower compared to what was earlier reported in Dutch cohorts. For instance, in a study of 76 children with juvenile idiopathic arthritis and 131 healthy controls [45] physical activity levels (PAL) were 1.6 and 1.8 respectively compared to 1.23 in the current study. What stands out most in our cohort is the short mean daily time spent in MVPA (median 27 min), well below the recommendation of 60 min a day (on average) according to the World Health Organization Guidelines [46]. Other data in childhood cancer survivors reported higher mean daily time spent in MVPA than in our cohort (between 38 and 76 min) [47,48]. Although no associations were found between the levels of physical activity and the changes in body size, a recent meta-analysis reported an OR of 0.70 for sufficient physical activity versus insufficient physical activity, meaning that in children sufficient physical activity reduced the risk of obesity by 30% [49].

Table 5
Results of stepwise regression analyses: variables associated with ΔzFFM $_{T2-T0}$.

Variable	Unstandardized B	95% CI	Standardized coefficient β	*P*-value
Model 1				
Constant	−1.21	−3.23; 0.82		0.233
Age at diagnosis	0.18	0.42; 0.32	0.38	0.013
Hematologic vs solid	−0.43	−1.66; 0.79	−0.12	0.478
Brain vs solid	1.48	−0.27; 3.23	0.29	0.096
FFM at diagnosis	−0.31	−0.66; 0.04	−0.29	0.080
Model 2				
Constant	−1.60	−3.15; −0.05		0.044
Age at diagnosis	0.20	0.01; 0.34	0.43	0.004
FFM at diagnosis	−0.53	−0.83; −0.22	−0.49	0.001

Model 1: adjusted R^2 was 0.310.
Model 2: adjusted R^2 was 0.296.

Baseline FFM and age predicted increase in FFM: children with the lowest initial FFM and the older children, showed the most repair in FFM. This observation of recovery of FFM, particularly in those children with low initial FFM, is a very encouraging result. Very few studies reported on predictors for alterations of FFM in survivors. One study reported differences in recovery of FFM based on type of malignancy: they found, after end of treatment, recovery of FFM in survivors of hematological malignancies though decrease of muscle mass in survivors of solid malignancies [9].

A limitation of the current study is the relatively small sample size, particularly for the separate diagnosis groups, and the incompleteness of data on energy intake and physical activity. The strength of the study is the prospectively and simultaneously collection of so many relevant parameters of both body size and body composition from diagnosis into survivorship. Given the lack of prospective studies on this subject, we believe the results of the PeCanNut study are useful for developing strategies to prevent obesity in survivors of childhood cancer.

In conclusion, our findings showed continuing increase of BMI after end of treatment in survivors of brain and hematological malignancies. In the latter group, also FM still gradually increased after the end of treatment. This resulted in a quadruplicating of the percentages of overweight. The once obtained extra weight and FM during treatment, remained throughout survivorship. Important predictors for weight and fat gain were low initial BMI, high maternal BMI, and hematological or brain malignancy. These findings imply the relevance to prevent excessive gain in weight and fat mass from the start of treatment and beyond both for children with low and high BMI and particularly for children diagnosed with hematological and brain malignancies. Close monitoring of nutritional status and the creation of awareness among health professionals, children, and parents about the risk of developing overweight in children during cancer treatment are needed.

Funding statement

None of the authors received funding for this study.

Author contributions

AB participated in study design, collected data, conducted data analysis and interpretation, and wrote the original draft. ES collected data, participated in interpretation of the data. TWK participated in data analysis and writing of the manuscript. OTHML participated in study design, data analysis, and interpretation of the data. AMB performed statistical analysis and provided scientific input for the final version. JGMB performed statistical analysis, participated in interpretation of the data. WJET participated in study design, supervised its execution, and had responsibility for the final content. All authors critically revised the manuscript and approved the final version.

Conflicts of interest

The authors have declared no conflict of interest.

Acknowledgements

The authors wish to thank all children and their parents for participating in PeCanNut II and Marjet Post for her contribution in data collection.

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