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Body Composition, dietary intake and physical activity of young survivors of childhood cancer

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Aim

To describe the body composition, dietary intake and physical activity and of paediatric, adolescent and young adult childhood cancer survivors (CCS) and examine the factors that impact body composition after treatment.

Methods

This prospective cross-sectional study involved 74 subjects who were at least three years post treatment. Measurements included anthropometry, whole body potassium counting, air displacement plethysmography, and three day physical activity and diet diaries.

Results

The CCS had significantly reduced body cell mass index Z-scores compared to controls (p=0.0001), with 59% considered undernourished. The CCS had a significantly higher percent fat (p=0.002) than the controls, with 27% classified as obese. The intake of 60% of CCS met estimated energy requirements, but the CCS consumed high amount of energy from fat and low amount of energy from carbohydrates. A high percentage of CCS did not meet their dietary requirements for calcium (61%), magnesium (46%), folate (38%) and iodine (38%). The CCS group had a light active lifestyle with 64% spending more than two hours daily on screen time. Receiving a bone marrow transplant (r=-0.27; p=0.02) and physical activity level (r=0.49; p=0.0001) were significantly correlated with body cell mass index.

Conclusions

This study demonstrates that increased fat mass and decreased body cell mass is a concern for CCS and that CCS have poor health behaviours including light active lifestyles, excessive screentime, high fat intake, and poor intake of essential nutrients. This study has highlighted that CCS are at risk of both obesity and undernutrition and that increasing body cell mass as well as decreasing fat mass should be a focus of energy balance interventions in survivorship. There is a need for parents and children undergoing treatment for cancer to be educated about diet quality and importance of daily physical activity to ensure healthy habits are established and maintained into survivorship.

Keywords: childhood cancer survivors; body composition; dietary intake; physical activity

Abbreviations: AMDR, Acceptable Macronutrient Distribution Range ; BCM, body cell mass; BCMI, body cell mass index; BMT, bone marrow transplant; BMI, body mass index; CCS, childhood cancer survivors; EAR, estimated average requirement; EER, estimated energy requirements; %FM, percent fat mass; FM, fat mass;

FMI, fat mass index; FFM, fat free mass; FFMI, fat free mass index; METs, metabolic equivalents; MVPA, moderate to vigorous physical activity PAL, physical activity level; TBK, total body potassium

The five-year relative survival rate for all children diagnosed with cancer has improved over recent decades and is approximately 80% in developed countries [1-4]. The improvement in survival of cancer patients has placed an increased focus on the long term effects of treatment, with late effects of childhood cancer representing a continuing emotional and physical burden on children and families. It has recently been reported that 70% of survivors exhibit at least one chronic health condition five years post treatment [2] and it is recognized that adult survivors of childhood cancer are at increased risk of developing second cancers [5, 6], cardiovascular disease [7, 8], diabetes [9, 10], and obesity [11, 12]. The development of obesity in this population is particularly alarming because increased fat mass may exacerbate the other chronic health conditions experienced by childhood cancer survivors (CCS). Increased fat mass is not the only body composition alteration that is a concern in cancer patients and survivors, as recent studies in adult patients have shown that it may be the reduced lean mass that influences outcomes in cancer [13-16].

Body composition is modifiable by nutritional intake and physical activity; however the impact of cancer on dietary intake and physical activity in paediatric and adolescent survivors before reaching adulthood is still poorly understood. Recent studies provide some evidence that young survivors of childhood cancer have increased body mass index [17] and poor adherence to dietary and physical activity guidelines [18-21], but there is limited research examining both body composition and influencing factors in young childhood cancer survivors who have undergone treatment for a range of cancers on recent protocols. The aim of this study was to define the body composition, physical activity and dietary intake of paediatric, adolescent and young adult survivors of childhood cancer and to examine the effect of lifestyle and clinical factors on body composition in CCS.

Methods

Participants

All children, adolescents and young adults attending the After Cancer Clinic of the Royal Children's Hospital, Brisbane, who were (1) diagnosed with cancer at an age younger than 21 years, (2) between the ages of 5 to 25 years at time of study, and (3) at least two years post treatment completion, were approached to be involved in the study. Patients were excluded if they had conditions know to influence dietary intake or energy expenditure. Clinical data were retrospectively collected from medical records, including data on type of cancer, age at diagnosis, duration of treatment, time since completion of treatment and type of treatment (radiation, chemotherapy, bone marrow transplant).The study protocol was approved by the University of Queensland Medical Research Committee and the Royal Children's Hospital Brisbane Ethics Committee. Written consent was obtained from all parents of children under 18 years, participants over 12 years and verbal assent was obtained for children under 12 years.

Measurements

Body Composition

All measurements in each subject were carried out in the Children's Nutrition Research Centre Body Composition Laboratory at the Royal Children's Hospital on the same day. Body weight was measured to the nearest 0.05 kg using calibrated digital scales (Tanita BWB-600, Wedderburn Scales, Australia) and height was measured to the nearest 0.1 cm using a wall-mounted stadiometer (Seca 222, Germany). Body mass index (BMI) was calculated as weight divided by height squared. Height, weight and BMI Z-scores were calculated using data published by the Centers for Disease Control and Prevention; all subjects over 20 years of age had Z-scores calculated relative to a 20 year old [22].

Measurements of body cell mass (BCM) by whole body potassium counting (TBK) represents the metabolically active component of fat free mass (FFM) and is independent of extracellular fluid changes that may occur as a result of disease state [23]. TBK counting was performed as described previously using a sodium iodide shadow shield whole-body counter (Accuscan, Canberra Industries, MA, USA) [24]. BCM was then calculated from TBK using the equation of Wang et al. [25]: BCM (kg) = (TBK (g) * 9.18)/39.1. BCM was adjusted for height (BCM index (BCMI)), with height being raised to the power of 2.5 for females and 3 for males [24]. The BCMI was expressed as a Z-score relative to laboratory reference data for subjects, all subjects and controls over 18 years of age were calculated compared to 18 year old reference data. A cut off of BCMI Z-score <–1.65 was used to determine those individuals who have a reduced BCM and considered undernourished.

Air displacement plethysmography was used to measure percent fat mass (%FM), fat mass (FM) and FFM using the Bod Pod® Body Composition System, adhering to the manufacturer's instructions (Life Measurement Inc, Concord, Ca, USA; software version 1.91) and described previously (30). Fat mass index (FMI) was calculated as

FM/height^2 and fat free mass index (FFMI) as FFM/height^2. Obesity was defined as %FM over the 95th centile from the reference curves [26], all subjects and controls over 18 years of age were assessed relative to 18 year old reference data. Body composition was compared to 1:1 age and gender matched controls from the Laboratory database. The control subjects were recruited as part of the Normative Study undertaken by the Children's Nutrition Research Centre. An exclusion criterion was any condition known to affect body composition. From the healthy reference subject pool, subjects were sex- and age-matched to the cancer patients involved in the study.

Dietary intake

Information about the participant's diet was collected using a three day food diary. Parents or participants were asked to record all they ate and drank on three consecutive days (2 weekdays and 1 weekend day). Participants were given written and verbal instructions to complete the diary and were asked to record the time, type, brand, portion size of all food and drink. At the end of the recording period, the diary was checked for completeness and any clarification of entries was sought from parents of the child participating. These data were analysed using FoodWorks® 7 Pro. From these dietary data, the mean daily energy intakes were calculated and expressed as a percentage of their estimated energy requirement (EER). The age-appropriate Schofield equation was used to predict basal metabolic rate [27] and the physical activity level (PAL) from physical activity diaries (described below) was used to calculate estimated energy requirements. The intake for energy from fat, carbohydrates and protein was assessed against the Acceptable Macronutrient Distribution Range (AMDR) and the mean daily nutrient intake was calculated and expressed as a percent of their age-appropriate estimated average requirement (EAR) [28].

Physical activity and screen time

Physical activity was measured via a three-day self-reported diary, using a simplified version of activity dairies as described previously and collected on the same days as the dietary intake diaries [29]. Subjects were given verbal and written instructions with an example of how to complete the diary. At the end of the recording period, the diary was checked with a researcher for completeness and any clarification of recorded activities was sought from parents of the child participating. Each day was divided into 96 × 15 minute intervals and the subjects were asked to record their activities on each day. On completion, these activities were categorised into nine levels according to their average energy costs, representing multiples of their respective metabolic equivalents (METs) [30]. Total daily METs values were calculated and averaged over the three days to give a PAL value for each subject. Time spent in daily moderate to vigorous intense activity and screen time daily was averaged across the three days. Results were compared to the recommendations that 'Children and young people should accumulate at least 60 minutes of moderate to vigorous intensity physical activity every day' and 'limit their screen time to no more than two hours per day'[31].

Statistical Analysis

Descriptive statistics were used to characterise the CCS. For the dietary and physical activity data, the control subjects did not have dietary intake or physical activity data recorded, so the proportion of the CCS sample who did not meet the physical activity guidelines, AMDR and EAR was assessed. The body composition of the CCS and controls were compared using independent t-tests and chi-squared for categorical data. Correlational analysis examined the clinical, dietary and physical activity variables associated with body composition, adjusting for age and sex. When multiple variables were found to be significantly associated to the outcome variables ($p<0.05$), a multivariable linear regression model was created, retaining only those predictors that were statistically significant.

Results

Seventy-four children, adolescents and young adults between 6.5 and 24.7 years were recruited to the study between 2012 and 2014. The participants were treated for cancer during the period of 1995 to 2011, with the mean age at diagnosis of 4.3 ± 3.8 years and mean time since treatment of 9.4 ± 3.3 years. There were 53 subjects diagnosed with a haematological malignancy and 21 subjects with a solid tumour. Subject characteristics are presented in Table 1.

Anthropometry and body composition results for the CCS and controls are reported in Table 2. There was no significant difference in the mean weight Z-score ($p=0.63$) and mean BMI Z-score ($p=0.30$) between the CCS and the healthy controls, however the CCS had significantly lower mean height Z-scores than the controls ($p=0.03$). According to BMI, 8% were underweight, 67% were normal weight, 23% were overweight and 2% were obese. Ninety-two percent of the matched controls were normal weight and 8% were overweight. There was a significant difference between the BCM of the CCS and the age and sex matched controls, with the CCS having a significantly lower BCMI (p=0.02) and BCMI Z-score (p=0.0001). The CCS had a significantly higher %FM (p=0.002) and FMI (p=0.003) than the controls. There was no significant difference in the FFMI (p= 0.09) between the CCS and the controls.

When CCS were separated based on BCMI Z-score into well-nourished and under nourished groups, 59% of CCS were considered under nourished. The only significant difference in clinical, physical activity and dietary variables between the well-nourished and under nourished groups was for PAL, with malnourished subjects having a significantly lower PAL (1.39 ± 0.19) than well-nourished subjects (1.57 ± 0.32) (p=0.01). When subjects were separated based on %FM into obese and non-obese groups, 27% were considered obese, and the obese subjects had significantly lower PAL than the non-obese groups (1.37 ± 0.16 vs 1.51 ± 0.30; p=0.03). There were no other significant differences in clinical, physical activity and dietary intake variable between the obese and non-obese groups.

The relationship between body composition and clinical variables (type of cancer, age at diagnosis, time since treatment completion, bone marrow transplant (BMT) or any radiation), physical activity (PAL and total energy expenditure) and energy intake (energy intake, energy intake as percent of estimated requirements, protein, fat and carbohydrate intake) was analysed. When adjusted for gender and age, receiving a BMT (r=-0.27; p=0.02) and PAL (r=0.49; p=0.0001) were significantly correlated with BCMI. When significant variables were combined in regression model; gender, BMT and PAL remained significantly associated with BCMI (Table 3). Receiving a BMT (r=-0.27; p=0.02) and PAL (r=0.61; p=0.0001) were also significantly correlated with FFMI. When age, gender, BMT and PAL were combined in regression model, all variables remained significantly associated with FFMI (Table 3). No variables were significantly associated with FMI.

Sixty-one subjects completed the three day food diaries and results are shown in Table 4. For the average intake over the 3 days, 18% of the survivors were consuming more than 110% of their EER, while 22% of the survivors were consuming less than 75% of their EER. The percentage of children not meeting their dietary requirements for calcium was 61%; with a high percentage of the survivors also not meeting needs for magnesium (46%), folate (38%) and iodine (38%). Sixty-seven percent of subjects had a usual intake that exceeded the upper limit for sodium. The mean macronutrient distribution of total energy intake consisted of 46% carbohydrates, 34% fat and 20% protein. When assessed against the AMDR, 38% of population had a usual intake of carbohydrate as a proportion of total energy below the lower limit, while 48% of the subjects had energy intake from fat above the upper limit. Eighty percent of survivors met protein AMDR, with 11% below and 10% above limits.

Fifty-seven subjects completed a physical activity diary. The subjects had a mean PAL of 1.45 ± 0.19, with males (PAL = 1.50 ± 0.20) having a significantly higher PAL level than females (PAL = 1.39 ± 0.14) (p=0.04). The average PAL of 1.45 for this population was characteristic of a population with a sedentary or light activity lifestyle. From the respondents, 74% participated in at least 1hr of moderate to vigorous physical activity (MVPA) per day and participated in an average of 117 minutes of MVPA per day. The survivors in this study participated in more daily MVPA than reported for 5-18 year olds in the Australian Health Survey (117 minutes/day versus 91 minutes/day), with only 60% of Australian children meeting recommendations in the Australian Health Survey [32]. Sixty-four percent of the survivors did not meet the recommendation of “no more than two hours of screen-based entertainment” every day, with the average amount of time spent in sedentary screen–based activities being 159 mins per day over the assessment period. Survivors in this study spent a longer average amount of time in sedentary screen–based activities than the Australian population (136 minutes/day) [32].

Discussion

Childhood cancer occurs during the critical period of growth and development so both the cancer treatment and behaviours developed during this time may affect long term nutritional health. This study aimed to examine the physical activity, dietary intake and body composition of children, adolescents and young adults who had completed cancer treatment and the impact of clinical and lifestyle factors on body composition in CCS.

The weight and BMI Z-scores of the CCS were not significantly different to their peers, and despite being significantly shorter than the controls, the height Z-score was within expected range. According to BMI, 25% of the CCS were overweight or obese compared to 8% of the controls. The prevalence of overweight and obesity according to BMI in the CCS was the same as the reported prevalence of overweight and obesity in Australian children of around 25% [33], but was lower than previous studies have reported in young CCS [34-36]. As previous studies have shown, BMI is not an accurate assessment of nutritional status in children and survivors with cancer [37-39], so it is essential to report on FM and FFM components when evaluating the impact of cancer on nutritional health. Our study showed that the CCS had significantly higher %FM and FMI compared to controls, which is in agreement with previous studies who examined FM in CCS by dual energy x-ray absorptiometry [40-42]. The survivors in this study also had significantly reduced BCMI, which we have shown previously with a cohort of 53 of the current 74 subjects [43]. More research is needed to examine the clinical implications of decreased BCM and increased FM on clinical outcomes for CCS.

Although obesity is a recognised late effect of childhood cancer, the important finding of this study is that under nutrition, as indicated by reduced BCM, is actually more prevalent than obesity in this group of CCS, with 59% of survivors considered under nourished compared to 27% who were obese. The clinical implications of these findings are that CCS clinics be aware that both malnutrition and obesity may be a late effect for CCS and should screen for both. It is also highlights an important consideration for diet and exercise intervention programs for CCS, which is that the intervention needs to not only target obesity, but also on improving the metabolically active lean tissues.

In this study the only clinical variable that was associated with body composition, was that having received a BMT was related to low BCMI and FFMI. The conditioning regimens, mucositis and gut graft-versus-host disease can result in poor functional integrity of the gastrointestinal tract during BMT, which affects nutritional status in the short term [44, 45]. Our study demonstrates that having had a BMT continues to influence nutritional status in the long term and that consequently nutritional support should be an important consideration before, during and after BMT.

Sixty-one percent of the CCS had energy intake between 75% and 110% of predicted energy requirements, with around 1 in 5 consuming above and 1 in 5 consuming below the predicted requirements. The energy intake of this cohort of paediatric cancer survivors appears comparable to that of the general Australian population which is consistent with previous research in CCS [20]. The macronutrient distribution of total energy intake consisted of 46% carbohydrates, 34% fat and 20% protein, which demonstrated that the survivors consumed more energy from fat and protein and less from carbohydrates than Australian population [46]. Our study showed that 48% of the CCS population consumed energy from fat above the upper end of the recommended range compared to 15% of Australian population (4-18 year olds) and that 38% of CCS had a usual intake of carbohydrate as a proportion of total energy below the lower limit of the AMDR, compared to the 19% of Australian 4-18 year olds [46]. The results of this study demonstrate that CCS have overall energy intake that meets energy requirements, but that the CCS consumed high amount of calories from fat and low amount of calories from carbohydrates. Although no dietary variables were related to body composition in this study, consuming higher fat than AMDR may be a contributing factor to the increased fat mass seen in our subjects.

We observed a high intake of sodium (77% exceeded upper limit) in CCS, which is consistent with the Australian Health Survey in which 91% of males and 74% of females aged 2-18 years exceeded the upper limit [46]. Our study found that a high percentage of the CCS were not meeting needs for intake of calcium (61%), magnesium (46%), iodine (38%) and folate (38%), which were consistent with findings in previous CCS cohorts [20, 47]. The inadequate intakes of calcium and magnesium were consistent with the Australian Health Survey where 50% of 4-18 year olds were not consuming recommended intakes of calcium and 34% of 4-19 year olds were not consuming recommended intakes of magnesium [46]. However, the low intakes of iodine and folate of the CCS were not observed in the Australian Health Survey [46]. Calcium, magnesium, folate and iodine are essential for healthy brain, muscle and bone growth and functioning. Reduced intake of these nutrients during the rapid growth periods of childhood and adolescents can lead to poor muscle and bone development and exacerbate the chronic health conditions commonly experienced in CCS.

The majority of survivors in this study met the recommendations for daily physical activity and were more active than children in the community [32] and previous studies into CCS [48]. However, they spent a longer daily amount of time in sedentary screen–based activities than the Australian population and were less likely to meet the screen based entertainment recommendations, which was consistent with previous research into CCS [48]. Although the CCS in this study did not have activity patterns different to Australian children, due to their increased FM and decreased BCMI, it is vital that the CCS population has active lifestyles with minimal screen time to improve body composition and reduce risk of associated late effects.

The survivors had a sedentary/light active lifestyle classified by PAL of 1.45, which was below the PAL of 1.75 for adolescents and adults that is considered to be compatible with a healthy lifestyle [49]. In this study, PAL was significantly reduced in the CCS group who were classified as under nourished and the CCS group classified as obese. When the relationship between physical activity and body composition was examined, PAL was significantly related to BCMI and FFMI. These findings indicate that increasing the physical activity level of CCS is an important component for interventions which aim to improve body composition in CCS.

This study demonstrates that young CCS are at risk of both undernutrition and obesity, with BMT and current PAL important contributing factors to reduced BCM in this group. The CCS in this study had poor dietary and physical activity habits, with low carbohydrate and high fat contribution to energy intake, poor intake of essential nutrients, light active lifestyle and excessive screen time. Limitations of the study are the small subject numbers and that the control group did not have physical activity and dietary results so CCS results could only be compared to population values; future studies should explore these findings in a larger case-control study. There is a need for parents and children undergoing treatment for cancer to be educated about diet quality and importance of daily physical activity to ensure healthy habits are developed, which may lead to improving body composition and reducing risk of developing nutrition related late effects. Future research should focus on investigating intervention programs that target both increasing BCM and decreasing FM for CCS through physical activity and good dietary habits.

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Table 1 Subject characteristics

	Mean ± SD (n=74)
Female, n (%)	35 (47)
Age, y	15.0 ± 4.5
Cancer diagnosis, n (%)	
Leukemias, myeloproliferative diseases, and myelodysplastic diseases	45 (61)
Lymphomas and reticuloendothelial neoplasms	8 (11)
CNS and miscellaneous intracranial and intraspinal neoplasms	4 (5)
Neuroblastoma and other peripheral nervous cell	6 (8)
tumors	2 (3)
Retinoblastoma	2 (3)
Hepatic Tumours	3 (4)
Soft tissue and other extraosseous sarcomas	2 (3)
Germ cell tumours, trophoblastic tumours, and	
neoplasms of gonads	1 (1)
Renal Tumors	1 (1)
Other malignant epithelial neoplasms and malignant Melanomas	
Age at diagnosis, y	4.3 ± 3.8
Time since treatment, y	9.4 ± 3.3
Bone Marrow Transplant, n (%)	23 (31%)
Radiation, n (%)	17 (23%)

[1]International Classification for Childhood Cancer (ICCC) definitions based on site and morphology coded according to ICD-O-3 [50]

Table 2 Comparison between body composition of survivors and controls

	Survivors (*n*=74)	Control (*n*=74)
Age	14.9 ± 4.4	14.9 ± 4.5
Height Z score	0.06 ± 1.10[c]	0.46 ± 0.99
Weight Z score	0.14 ± 1.09	0.21 ± 0.80
BMI Z score	0.14 ± 0.98	-0.01 ± 0.74
BCMI	5.42 ± 0.91[c]	5.75 ± 0.68
BCMI Z score[3]	-1.90 ± 1.17[a]	-0.38 ± 0.99
Percent fat, %[4]	24.0 ± 9.8[b]	20.1 ± 6.8
FMI[4]	5.1 ± 2.7[b]	4.0 ± 1.6
FFMI[4]	15.4 ± 2.6	15.8 ± 2.6

[1]All values are mean ± SD. BMI, body mass index; BCMI, body cell mass index; FMI, fat mass index; FFMI, fat free mass index. [2]Cancer and 1:1 matched controls were compared by paired t-test

[3]CCS group and control group, *n*=65

[4] CCS group and control group, *n*=72

[a]Significant difference between cancer group and controls $P < 0.0001$

[b]Significant difference between cancer group and controls $P < 0.01$

[c]Significant difference between cancer group and controls $P < 0.05$

Table 3 Multiple regression analysis

Dependent variable	Independent Variables	B	SE	β	P
BCMI[1]	Gender (0=male, 1=female)	-0.72	0.19	-0.40	0.0001
	Age	-0.001	0.02	-0.007	0.95
	BMT	-0.61	0.20	-0.32	0.004
	PAL	2.01	0.50	0.43	0.0001
FFMI[2]	Gender (0=male, 1=female)	-1.80	0.48	-0.35	0.0001
	Age	0.38	0.06	0.59	0.0001
	BMT	-1.19	0.50	-0.21	0.02
	PAL	5.79	1.23	0.42	0.0001

[1]Adjusted R2 = 0.44; F=11.97; p=0.0001

[2]Adjusted R2 = 0.61; F=21.98; p=0.0001

Table 4 Mean daily dietary intake of subjects

	Mean ± SD (n = 61)	Percentage of subjects meeting estimated average requirements
Energy Intake (kcal)	2024 ± 596	60
Protein (g)	99 ± 42	79
% calories	20 ± 5	
Carbohydrates (g)	222 ± 73	62
% calories	46 ± 8	
Fat (g)	78 ± 28	52
% calories	34 ± 6	
Sodium (g)	2830 ± 1023	23
Thiamin (mg)	1.8 ± 0.9	87
Riboflavin (mg)	2.3 ± 0.9	98
Vitamin C (mg)	113 ± 157	90
Folate (µg)	406 ± 241	62
Vitamin A (µg)	782 ± 356	77
Magnesium (mg)	276 ± 99	54
Calcium (mg)	776 ± 309	39
Phosphorus (mg)	1500 ± 521	89
Iron (mg)	12 ± 5	84
Zinc (mg)	30 ± 135	90
Iodine (µg)	104 ± 45	62

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