Purpose: Body mass index (BMI) is an inadequate measure of nutritional status in children and adolescents with cancer as it does not distinguish muscle from adipose tissue. However, arm anthropometry offers simple assessments of fat mass and lean body mass; especially valuable in low- and middle-income countries where the great majority of young people with cancer live and access to sophisticated expensive measures of body composition is markedly limited.

Methods: The nutritional status of 75 long-term survivors of acute lymphoblastic leukemia was assessed by arm anthropometry, in addition to BMI, in a cross-sectional cohort study. Normal ranges for triceps skin fold thickness (TSFT, a surrogate for fat mass) and mid-upper arm circumference (MUAC, a surrogate for lean body mass) were between the 15th and 85th percentiles for age and sex. Overweight/obesity was classified as a TSFT >85th percentile and sarcopenia as an MUAC <15th percentile. Height normalized indices for TSFT and MUAC were also calculated.

Results: Overweight/obesity was identified in 1/3 of subjects by a BMI >25 and by TSFT; and 20% of the subjects had a TSFT >95th percentile. Only two subjects were sarcopenic. None met the combined criteria for sarcopenic obesity. TSFT and MUAC/height indices did not add sensitivity to identification of sarcopenia or obesity.

Conclusions: TSFT is a useful measure of overweight/obesity in this population, but MUAC does not identify a notable proportion with sarcopenia. Further resolution may be provided by more sophisticated measures of body composition.

Keywords: anthropometry, acute lymphoblastic leukemia, survivors

Introduction

There is general agreement that the measurement of nutritional status is important in children and adolescents with cancer. Given its dominant prevalence there has been special attention devoted to acute lymphoblastic leukemia (ALL), the commonest form of cancer in this age group worldwide. Overweight and obesity, measured by body mass index (BMI), have been associated with poorer response to chemotherapy, higher risk for relapse, increased treatment-related toxicity, and worse survival in children with ALL than in those with normal nutritional status. In two recent meta-analyses, the association of overweight/obesity with poorer survival has been confirmed in children and adolescents with ALL and related to an increased risk of relapse. Furthermore, long-term survivors with an elevated BMI are at greater risk of adverse “late effects” from therapy. However, in a recent publication Orgel et al. reported that BMI correlated poorly, in individual patients, with body fat measured by dual-energy X-ray absorptiometry (DXA). This resulted in an underestimation by BMI of sarcopenic obesity that is being recognized increasingly in children and adolescents with ALL during and after treatment. It is not surprising that this limitation was revealed, for BMI, being calculated from height and weight, does not distinguish muscle from adipose tissue.

By contrast, arm anthropometry, as developed by Frisancho, offers simple surrogate estimates of lean body mass (mid-upper arm circumference, MUAC) and fat mass (triceps skin fold thickness, TSFT). The advantages of arm anthropometry over BMI in assessing the nutritional status of children with cancer, including ALL, are increasingly appreciated. This is especially important in low- and middle-income countries (LMICs), where the great majority of young people with cancer live and where sophisticated measures of body composition are seldom available. In our comprehensive study of body composition and bone health in long-term survivors of ALL in childhood and adolescence, there are various elements directed to the
assessments of nutritional status. In this study, we report the findings of BMI and arm anthropometry because of the relevance to the resource-limited circumstances in LMICs. These address the a priori hypotheses that BMI will correlate poorly with MUAC and TSFT and that sarcopenic obesity, defined by arm anthropometry, will be detectable in survivors of ALL in childhood and adolescence.

Patients and Methods

Details of the comprehensive study have been published. In summary, from a cohort of patients who had been diagnosed with ALL at least a decade previously, a study sample of 75 subjects was assembled. All had been treated according to protocols of the Dana-Farber Cancer Institute (DFCI) and Childhood ALL Consortium. The study sample was almost entirely Caucasian and consisted of 41 males and 34 females ranging in age from 1.5 to 17.6 (median 4.4) years at diagnosis and 13.5 to 38.5 (median 21.2) years at the time of study. Absolute values for BMI were 16.6 to 34.9 (median 23.6) for the whole sample. Only six subjects were undernourished (BMI <18.5), none severely. One-third of the subjects were overweight or obese (none morbidly); only six subjects (8%) were actually obese. The mean BMI values for males and females were 24.4±3.7 and 24.4±3.8, respectively, obviously no significant difference between the sexes. There was no significant difference between those who had (n=51; BMI 24.6±3.6) or had not (n=24; BMI 24.0±4.1) received cranial irradiation, and there was no correlation between BMI and cumulative steroid dose measured as mg. prednisone-equivalent/m² of body surface area (correlation coefficient −0.019, p=0.869). The BMI Z scores, for those under 20 years of age (the range for which these Z scores are applicable), are shown in Table 1.

Percentile distributions for MUAC and TSFT are displayed in Table 2. While the values for MUAC are fairly normally distributed, those for TSFT are skewed to higher values. There was a strong positive correlation between BMI and MUAC (correlation coefficient 0.797, p<0.0001) and a moderate positive correlation between BMI and TSFT (correlation coefficient 0.348, p=0.002), but a weak correlation between MUAC and TSFT (correlation coefficient 0.147, p=0.212).

Overweight/obesity, defined by TSFT, was exhibited by 26 subjects (12 males and 14 females), and 15 (5 males and 10 females) were >95th percentile. Of these obese patients defined by TSFT, 8/15 (53%) had received cranial irradiation compared to 68% (51/75) of the entire study population and 70% (43/60) of those who were not obese. Sarcopenia, defined by MUAC, was identified in only two subjects (one male and one female). No subject fulfilled the original definition of sarcopenic obesity. Even relaxing the criteria to

### Table 1. Body Mass Index Z Scores at Diagnosis and in Long-Term Survivors

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
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<tbody>
<tr>
<td>Median</td>
<td>0.11</td>
<td>0.12</td>
<td>0.75</td>
</tr>
<tr>
<td>Minimum</td>
<td>−2.72</td>
<td>−2.65</td>
<td>−1.37</td>
</tr>
<tr>
<td>Maximum</td>
<td>4.73</td>
<td>4.73</td>
<td>2.91</td>
</tr>
<tr>
<td>Mean</td>
<td>0.06</td>
<td>0.20</td>
<td>0.83</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>1.36</td>
<td>1.30</td>
<td>0.98</td>
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A, the entire cohort at diagnosis; B, the cohort at diagnosis who were <20 years of age at follow-up; and C, the cohort at follow-up who were <20 years of age.

### Table 2. Arm Anthropometry Percentile Distributions

<table>
<thead>
<tr>
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<th>5–10</th>
<th>10–25</th>
<th>25–50</th>
<th>50–75</th>
<th>75–90</th>
<th>90–95</th>
<th>&gt;95</th>
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</thead>
<tbody>
<tr>
<td>MUAC</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>13</td>
<td>29</td>
<td>17</td>
<td>5</td>
</tr>
<tr>
<td>TSFT</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>10</td>
<td>15</td>
<td>19</td>
<td>11</td>
</tr>
</tbody>
</table>

MUAC, mid-upper arm circumference; TSFT, triceps skin fold thickness.

Statistical analyses

The differences between males and females in BMI, and between cranially irradiated and nonirradiated subjects in BMI, were assessed by two-tailed t-tests. A p value of <0.05 was interpreted as statistically significant. The correlations between BMI and cumulative steroid dose, BMI and TSFT-based index, BMI and MUAC-based index, and TSFT-based index with MUAC-based index were measured by Spearman’s rho for nonparametric data, while the correlations of BMI with TSFT, BMI with MUAC, and TSFT with MUAC were measured by Pearson’s correlation coefficient.

The study was approved by Hamilton Integrated Research Ethics Board (Project No. 10-508-S) that represents Hamilton Health Sciences, McMaster University, and St. Joseph’s Healthcare Hamilton.
MUAC <25th percentile (n=5 subjects) and TSFT >75th percentile (n=44 subjects) resulted in the capture of only one subject, a 21-year-old male with a BMI of 21.3.

The values for the MUAC and TSFT-based indices are given in Table 3. The values are markedly left skewed. Only one subject had an MUAC index <−2SD (7.67), a 22-year-old female with a BMI of 16.6. Only two subjects had TSFT indices >2SD (15.75 and 19.09), 24- and 29-year-old females with BMIs of 29.7 and 34.9, respectively. No subject met the criteria for sarcopenic obesity based on indices derived from arm anthropometry and height. There was a strongly positive correlation between BMI and the MUAC index (correlation coefficient 0.732, p < 0.0001) and a moderate positive correlation between BMI and the TSFT index (correlation coefficient 0.325, p = 0.002).

Discussion

Measurement of body composition by techniques such as total body water (H or 18O dilution), estimation of 40K, and neutron activation are not applicable in clinical practice. However BIA is useful and has the advantage of instrumental portability, although it is less reliable than DXA in the setting of maldistribution of body water. In earlier studies we demonstrated that children and adolescents with ALL who were treated on DFCI protocols manifested excessive weight gain, as measured by BMI,26 and disproportionate increase in fat mass, as revealed by DXA,27 during the 2-year treatment program. The current study explored whether these trajectories were sustained or modified in long-term survivors using MUAC and TSFT as surrogate measures of lean body mass and fat mass, respectively. In particular the focus was on overweight/obesity for, as concluded in a recent meta-analysis, “Additional evidence is needed to determine whether obesity is persistent in long-term ALL survivors.”28

As determined by BMI, the prevalence of overweight/obesity was one in three long-term survivors of ALL, but only 8% were obese, proportions lower than in young adults (ages 20–39) in the Canadian general population.29 However, by TSFT, a surrogate for fat mass, 20% of the survivors were obese. This difference from BMI was reported also in a large heterogeneous sample of long-term cancer survivors in the St. Jude Lifetime Cohort Study (SJLCS) with obesity rates of 20% by BMI, 62% by three site skinfolds, and 85% by DXA-determined whole body fat mass.30

These high proportions of obesity in long-term survivors of cancer in childhood may be a peculiarly American phenomenon. Based on self-reported height and weight in the Childhood Cancer Survivor Study (CCSS), 17% of ALL survivors were obese, as measured by BMI, at a median age of 24 years.31 This proportion rose to 31.7% by age 32.32

However, in studies in the United States with BMI measured objectively, higher proportions were observed. In 2001 Oeffinger et al.,4 reported obesity rates in long-term survivors of ALL of 31.3% at age 22.3 years and 42.8% at 32.4 years, compared to 30.3% in 20–39-year-olds in the United States general population.33 In the more recent SJLCS30 42.5% of survivors of leukemia were obese at a median age of 32.4 years compared to 31.6% in age-, sex-, and race-matched controls provided by the NHANES database.34 Somewhat different results were reported by investigators in the CCSS. In a study of 75 survivors of ALL at a median age of 30.2 years Ness et al., found no difference in BMI to age- and sex-matched controls.35 This group reported results later in a larger cohort in the SJLCS,36 but again did not report on the BMI-determined proportion of subjects who were obese.

By contrast with the U.S. experience, much lower rates of obesity have been reported from other countries in survivors of ALL in childhood. In Denmark there was no difference in BMI between survivors and controls with corresponding obesity rates of zero, although 26% of survivors had excess body fat measured by DXA.37 Likewise, in the Netherlands the rate of overweight/obesity (24.7%) was no different than in the general population and only 8% of 75 subjects were obese,38 results identical to the Canadian experience. In Australia there was no difference in BMI compared to healthy controls, and no subjects were obese, although 26% were so categorized by air displacement plethysmography.39 Interestingly, in India, a lower middle income country where obesity rates in the general population are 13% for women and 9% for men,40 2.7% of child/adolescent survivors of ALL have been found to be obese by BMI, with a corresponding rate in adult survivors of zero.31

The lack of correlations between obesity in long-term survivors of ALL, whether measured by BMI or TSFT, and earlier exposure to cranial irradiation or cumulative doses of corticosteroids may reflect the limited sample size of our study population. As summarized in a recent review,42 there are numerous reports of a higher prevalence of obesity in survivors who had been cranially irradiated, supported by a robust body of evidence on mechanisms. However, not all studies report an association between obesity, as defined by BMI, and cranial irradiation in survivors of ALL in childhood,37 even 1031 to 20 years44 after treatment. Association with cumulative steroid dose is less consistent. Moreover, in DFCI treatment protocols these doses were especially marked, particularly for those with high risk disease in the era when our subjects were treated and may exceed a limit on dose responsiveness with respect to obesity.

Contrary to an a priori hypothesis, there was a strong correlation of BMI with MUAC and a moderate correlation of BMI with TSFT, perhaps reflecting the fact that BMI does not distinguish muscle from adipose tissue.11 As expected, there was a weak correlation between MUAC and TSFT that was not statistically significant. Again contrary to a hypothesis, a population of survivors with sarcopenic obesity were not identified; although 20% of the subjects were obese by TSFT only 3% were sarcopenic according to MUAC. Arm anthropometry may not be sensitive enough to detect sarcopenic obesity in long-term survivors of ALL in childhood, and sensitivity was not improved by the calculation of

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</tr>
</thead>
<tbody>
<tr>
<td>MUAC</td>
<td>0</td>
<td>25</td>
<td>24</td>
<td>11</td>
<td>7</td>
<td>5</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>TSFT</td>
<td>22</td>
<td>34</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>7</td>
<td>1</td>
<td>3</td>
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Table 3. Arm Anthropometry/Height Indices
MUAC and TSFT indices based on height. It is likely that the use of DXA will result in enhanced sensitivity as demonstrated by Orgel et al. in children with ALL on active treatment.9 Sarcoenic obesity risks a double burden of morbidity, physical limitations resulting from low skeletal muscle mass and metabolic syndrome from excess body fat. Nevertheless, the strong correlations of BMI with MUAC are important. MUAC has long been used to identify undernutrition in children.45 This includes children with cancer, notably in LMICs as exemplified in Turkey,46 Brazil,47 and in our own studies in Central America15 and has been shown recently to exhibit a good correlation with obesity defined by BMI and % body fat measured by BIA, in 9- to 17-year-old children from 12 countries.48 Moreover, MUAC is important in older subjects as shown by its usefulness as a measure of all-cause mortality in Canadian men and women aged 20–69.39 There is good reason to continue to explore arm anthropometry in long-term survivors of cancer in childhood and adolescence, with an emphasis in LMICs.39 Indeed, a strong case can be made for its routine use in the assessment of nutritional status more broadly.

Author Disclosure Statement

No competing financial interests exist.

References


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