Pediatric Radiology (2023) 53:854–861
https://doi.org/10.1007/s00247-022-05583-5

ORIGINAL ARTICLE

The impact of sarcopenia and sarcopenic obesity on survival in children with Ewing sarcoma and osteosarcoma

Onur Buğdaycı[1] · **Nurşah Eker**[2]

Received: 10 October 2022 / Revised: 10 December 2022 / Accepted: 23 December 2022 / Published online: 5 January 2023

Abstract

Background Sarcopenia is an indicator of negative outcomes in many diseases in adults. Reports indicate this might also be true in children.

Objective To evaluate the effect of sarcopenia and sarcopenic obesity on event-free survival (EFS) and overall survival (OS) in children with Ewing sarcoma and osteosarcoma.

Materials and methods We retrospectively measured total muscle areas of the pectoralis, paraspinal (T12 level) and psoas (L4 level) muscles and total abdominal muscle area (L3 level) on computed tomography images in 60 children diagnosed with either Ewing sarcoma ($n=34$) or osteosarcoma ($n=26$). Skeletal muscle indices (SMI) were calculated by normalizing muscle area to patient height. Vertebral morphologic parameters of T12 and L4 vertebrae were measured and correlated to patient height to use as a substitute in cases of missing height data (SMI_{T12} and SMI_{L4}). We calculated sarcopenic obesity index by dividing SMI by body mass index. We subdivided children into two groups according to the median value of each parameter and assessed the differences in survival between the groups.

Results No skeletal muscle index or sarcopenic obesity index parameter significantly affected event-free or overall survival in the total group analysis. In the non-metastatic group, higher values of SMI–paraspinal and SMI_{T12}–psoas were correlated with longer event-free survival and no patient died in this group. Boys and children in the metastatic group with higher SMI_{T12}–paraspinal values had significantly longer event-free survival and both event-free and overall survival, respectively.

Conclusion Although some parameters were correlated with event-free and overall survival, neither sarcopenia nor sarcopenic obesity were reliably associated with survival in children with Ewing sarcoma or osteosarcoma.

Keywords Adolescent · Children · Computed tomography · Ewing sarcoma · Mortality · Obesity · Osteosarcoma · Sarcopenia

Introduction

Broadly speaking, sarcopenia is the loss of muscle mass and function. The European Working Group on Sarcopenia in Older People defined it as a progressive and generalized skeletal muscle disorder associated with an increased likelihood of adverse outcomes including falls, fractures, physical disability and mortality [1]. While primary sarcopenia is a result of muscle loss from aging, secondary sarcopenia may result from disease (e.g., cancer, neurodegenerative disease, endocrine processes), immobility, medications or reduced calorie intake [2].

In adults, sarcopenia is associated with adverse outcomes, especially in those with cancer [1]. In recent years, increasing attention has been given to sarcopenia research in children. Sarcopenia and adverse outcomes have been documented in children [3]. Impaired muscle quality and function are seen not only in those who succumb to cancer, but also in survivors. It is thought to be one of the reasons for the early onset of chronic conditions in cancer survivors [4].

Body weight and body mass index (BMI) are often used to assess nutritional status. However, they are not necessarily markers of muscle mass [5]. In adults, sarcopenic obesity,

✉ Onur Buğdaycı
onur.bugdayci@marmara.edu.tr

[1] Department of Radiology, Marmara University School of Medicine, Fevzi Çakmak Mah. Muhsin Yazıcıoğlu Cad., No: 10 Üst Kaynarca, Pendik, Istanbul, Turkey

[2] Department of Pediatric Hematology and Oncology, Marmara University, School of Medicine, Istanbul, Turkey

which is the combination of sarcopenia with obesity, has been documented to be an independent marker for adverse outcomes in many cancer patients [6]. In limited studies in children, sarcopenic obesity prevalence has been reported to be 8–10% and has also been associated with negative outcomes [5, 7].

This study investigated the impact of sarcopenia and sarcopenic obesity on event-free survival and overall survival in children with Ewing sarcoma and osteosarcoma.

Materials and methods

Patients

We obtained approval from the local ethics committee for this study. Pediatric patients diagnosed at or referred to our tertiary center with either Ewing sarcoma or osteosarcoma between August 2012 and October 2020 constituted our study population. Children and adolescents were included in the study if computed tomography (CT) scans of the thorax or abdomen were obtained within 1 month of the initiation of chemotherapy. All children were required to have at least 12 months of follow-up after the start of treatment. Children who died within this period were also included in the study.

Data and measurements

Using patient records, we retrieved patient age, sex, height, weight (measured at the initiation of chemotherapy), presence of metastases, date of last visit and, if present, the date of relapse or death. We calculated each child's BMI from available data.

Computed tomography scanning was performed on either a SOMATOM Flash or Emotion 16 scanner (Siemens Healthineers, Erlangen, Germany). Scan parameters varied among children according to their age and size. All CT measurements were performed manually on the local picture archiving and communication system (PACS) software (Infinitt PACS; Infinitt Healthcare, Seoul, South Korea) by a single radiologist with 18 years of experience (O.B.). All muscle area measurements were performed on the axial plane with density thresholding between –29 Hounsfield units (HU) and + 150 HU. We measured the following muscle areas: total pectoral muscle area, total paraspinal muscle area at the mid-vertebral level of the T12 vertebra, total abdominal muscle area at the mid-vertebral level of the L3 vertebra, and total psoas muscle area at the mid-vertebral level of the L4 vertebra (Fig. 1). Pectoral muscle measurements were performed at the level of the manubriosternal junction. Both the pectoralis major and pectoralis minor muscles were included. For the pectoralis, paraspinal and psoas muscles, we measured left and right sides and recorded their sum.

To normalize muscle area for each child, we calculated muscle indices for every muscle group using the following formula:

$$\text{Skeletal muscle index (SMI)} = \text{muscle area (cm}^2\text{)}/(\text{height in meters})^2.$$

From this formula, we calculated the SMI–pectoral, SMI–paraspinal, SMI–abdominal and SMI–psoas.

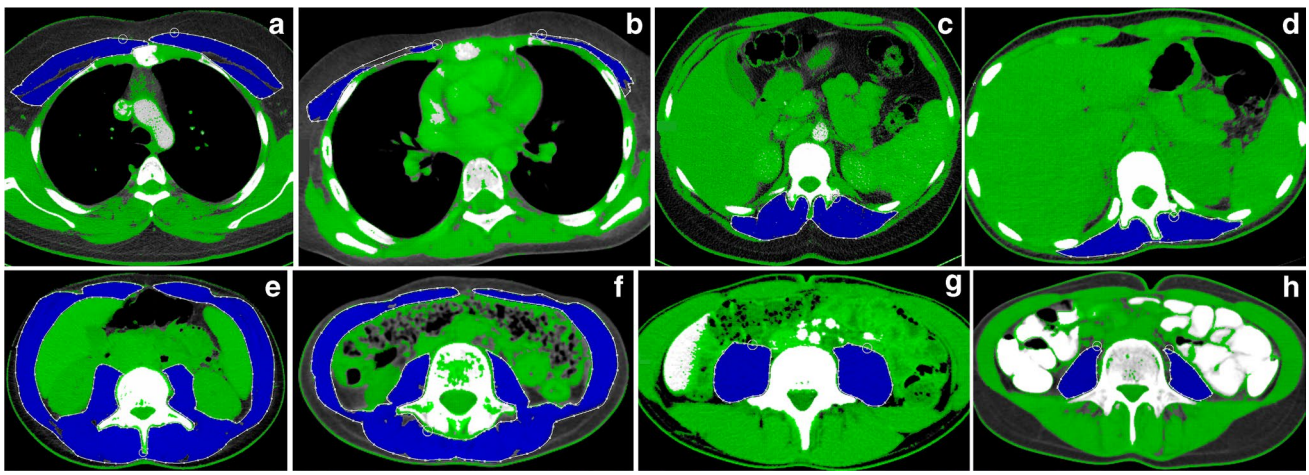

Fig. 1 Muscle area measurements (*blue*) on axial computed tomography images. **a–h** Pectoral (**a,** 17-year-old boy with Ewing sarcoma; **b,** 16-year-old girl with osteosarcoma), paraspinal (**c,** 17-year-old boy with Ewing sarcoma; **d,** 17-year-old girl with osteosarcoma), abdominal (**e,** 15-year-old boy with osteosarcoma; **f,** 16-year-old girl with osteosarcoma) and psoas (**g,** 17-year-old boy with Ewing sarcoma; **h,** 16-year-old girl with osteosarcoma). Images (**a**), (**c**) and (**g**) are intravenously contrast enhanced; images (**b**), (**d**), (**e**), (**f**) and (**h**) are not. *Green* areas represent densities between –29 Hounsfield units (HU) and + 150 HU that were not measured. Images (**a**), (**c**), (**e**) and (**g**) are in children with high skeletal muscle index (SMI), whereas images (**b**), (**d**), (**f**) and (**h**) are in children with low SMI. Notice the fatty areas within the blue regions in some children that were discarded because of density thresholding

To measure sarcopenic obesity, we divided the BMI by the SMI for each muscle group, which is also the weight divided by muscle area.

Sarcopenic obesity index (SOI) = BMI/SMI = weight (kg)/muscle area (cm^2).

We report the results for different muscle groups as SOI–pectoral, SOI–paraspinal, SOI–abdominal and SOI–psoas.

Because some children had missing height data, we measured/calculated vertebral parameters in every child to find a suitable normalization value. We recorded the following parameters for the T12 and L4 vertebrae: anteroposterior (AP) and mediolateral (ML) dimensions measured at the upper end plate, and the vertebral height (H) measured at the posterior border. From these measurements, we calculated the vertebral area by multiplying AP and ML. We calculated the vertebral volume by multiplying this area by height.

Statistical analysis

We performed statistical analyses using the SPSS software version 23 (IBM Corp., Armonk, NY). Demographic and clinical characteristics of the children are presented using descriptive analyses as percentages (%), frequencies (*n*), medians and minimum–maximum values. We assessed the normal distribution of continuous variables using visual methods (histograms and probability charts) and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk tests). If no normal distribution occurred, we used the Mann–Whitney *U* test for comparison between two groups. We assessed the correlation between vertebral measurements and height using Spearman correlation analysis and analyzed the differences between contrast-enhanced and non-contrast-enhanced CT scans using the Mann–Whitney *U* test.

To assess the effect of our parameters on overall and event-free survival, we identified the median value for each parameter considering the entirety of the study population. Then we divided patients into two groups for each parameter, those being above or below the median value. In addition, we stratified children according to tumor type (Ewing sarcoma/osteosarcoma) and according to the presence of metastases at the time of diagnosis. All analyses were repeated by sub-grouping children according to sex. We used the Kaplan–Meier analysis and the log–rank test to assess survival. Statistical significance was set at two-tailed $P < 0.05$.

Results

Sixty children and adolescents between the ages of 16 months and 18 years (median age: 13 years) were included in the study. The demographics of the patient population, as well as the diagnoses, metastatic status at diagnosis, follow-up information and information from available CT scans are given in Table 1. All children had CT scans of the thorax, while 34 also had CT scans of the abdomen, performed at the time of thoracic CT imaging. Abdominal imaging was performed for staging purposes or to evaluate bony involvement of the primary tumor. CT was performed in cases where sedated magnetic resonance imaging (MRI) was not available or when access to MRI would delay treatment.

In one child, movement artifacts prevented measurement of the pectoral muscles; in another child, technical artifacts prevented measurement of the total psoas muscle area. In six (10%) children, BMI and SMI could not be calculated because of missing height data.

All vertebral parameters significantly correlated with patient height. The highest correlation was observed with T12 vertebral volume (r = 0.86). This was followed by T12 vertebral height (r = 0.85), L4 vertebral volume (r = 0.83), L4 vertebral AP diameter (r = 0.81) and L4 vertebral height

Table 1 Demographics of the study population, diagnosis, follow-up information and type of CT scans available

Parameter	Range (median) or *n* (%)
Age	1.5–18 y (13 y)
Sex	
Male	31 (51.6%) (mean 13.7 y; median 15 y)
Female	29 (48.4%) (mean 11.7 y; median 12 y)
Diagnosis	
Ewing sarcoma	34 (56.6%)
Osteosarcoma	26 (43.4%)
Location of primary tumor	
Lower extremity	35 (58.3%)
Pelvis	9 (15%)
Soft tissue	7 (11.7%)
Upper extremity	3 (5%)
Ribs	3 (5%)
Skull	2 (3.3%)
Vertebra (cervical)	1 (1.7%)
Metastatic at diagnosis	12 (20%)
Location of metastases	
Lung	7 (58.3%)
Lung + other sites	4 (33.3%)
Bone	1 (8.3%)
Follow-up period (months)	6–108 (41 months)
Deaths during follow-up	14 (23.3%) (range 6–32 months)
Relapses during follow-up	12 (20%) (range 6–63 months)
CT	
Thorax	60: 24 (–C); 36 (+C)
Abdomen	34: 27 (–C); 7 (+C)

+*C* contrast-enhanced, -*C* non-contrast-enhanced, *y* years

(r = 0.81). Because of missing height data in six children, we chose the T12 and L4 vertebral heights for their simplicity and potential clinical use for calculating muscle indices in addition to the indices calculated from patient height. We calculated these indices for every child and reported them using the prefixes SMI_{T12} or SMI_{L4}. These vertebrae were not affected by any disease process in any child.

There was no statistically significant difference between the muscle areas of the contrast-enhanced and non-contrast-enhanced groups ($P = 0.24–0.96$). Therefore, all further analysis was performed without regard to the use of intravenous contrast agent.

The median values and interquartile ranges of muscle areas and SMI values are presented in Table 2. Examples of children with low and high SMI values are presented in Fig. 1.

Overall survival

In the overall study group, we found no statistical significance between any skeletal muscle index or sarcopenic obesity index. There was also no statistical correlation between any SMI or sarcopenic obesity index when grouping children into pathological subgroups.

Among children without metastases at the time of diagnosis, no deaths were recorded in those with higher SMI–paraspinal values ($n = 20$) and higher SMI_{T12}–psoas values ($n = 14$), whereas 22.7% (5/22) and 30% (3/10) of children with lower values died in the respective categories. (Survival analysis could not be performed because no events occurred in children with higher indices). In children with metastatic disease at the time of diagnosis, higher values of SMI_{T12}–paraspinal correlated significantly with longer overall survival (54 months vs. 17.7 months, $P = 0.04$).

When all groupings were further sub-grouped by sex, boys with SMI_{T12}–paraspinal values above the median value had significantly longer overall survival compared to those with values below (96.7 months vs. 51.6 months, $P = 0.01$).

Table 2 The median and interquartile ranges (IQR) of the respective muscle areas and skeletal muscle indices (SMI)

Variable	Median	IQR
Muscle area (cm^2)		
Paraspinal	19.4	15.9–26.4
Pectoralis	18.7	12.9–26.5
Abdominal	81.4	65.1–101.3
Psoas	13.8	10.7–19.1
SMI (cm^2/m^2)		
Paraspinal	8.6	7.4–9.7
Pectoralis	8.3	6.1–11.4
Abdominal	34.4	29.3–39.1
Psoas	5.7	4.9–7.2

Other parameters did not significantly correlate with overall survival.

Event-free survival

In the overall study group, no parameter was significantly correlated with event-free survival. There was also no statistical correlation between any SMI or sarcopenic obesity index when grouping children into pathological subgroups.

In children without metastases at diagnosis, higher SMI–paraspinal and SMI_{T12}–psoas values were significantly correlated with longer event-free survival (102.8 months vs. 59.8 months, $P = 0.01$; and 96.1 months vs. 48 months, $P = 0.03$) (Fig. 2). In children with metastatic disease, higher SMI_{T12}–paraspinal values were significantly correlated with longer event-free survival (54 months vs. 17.7 months, $P = 0.04$).

Sub-grouping patients by sex did not yield any significant correlation in terms of event-free survival, neither did other parameters correlate significantly with event-free survival. Results for SMI parameters are presented in Table 3.

Discussion

This study evaluated the correlation of sarcopenia and sarcopenic obesity with event-free and overall survival in pediatric patients with Ewing sarcoma and osteosarcoma. Overall, no marker for sarcopenic obesity correlated with event-free or overall survival. Although sarcopenia did not

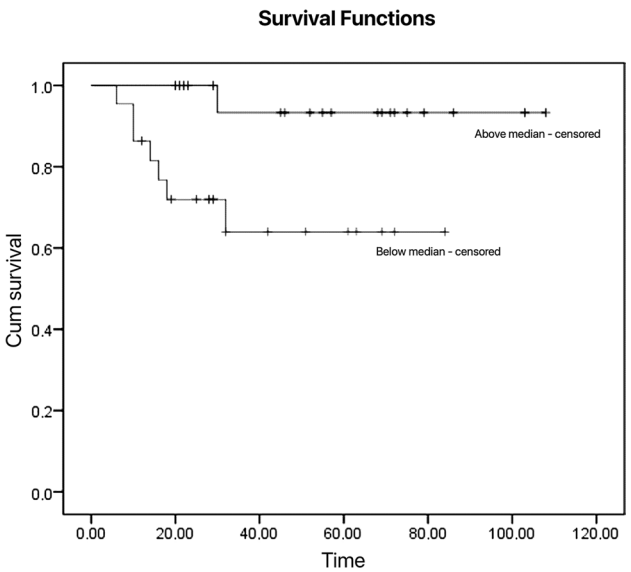

Fig. 2 Event-free survival curves for the skeletal muscle index (SMI) derived from paraspinal muscles at the T12 level (SMI–paraspinal) in non-metastatic children. Survival was significantly longer in children with values above the median than in those with values below the median. Time is presented as months

Table 3 The correlation of sarcopenia with overall and event-free survival. Numbers represent *P*-values

Variable	Pectoralis		Paraspinal		Abdominal			Psoas		
	SMI	SMI_{T12}	SMI	SMI_{T12}	SMI	SMI_{T12}	SMI_{L4}	SMI	SMI_{T12}	SMI_{L4}
Overall survival	0.67	0.90	0.81	0.13	0.60	0.48	0.38	0.62	0.12	0.09
Sex (M/F)	0.52/0.46	0.91/0.50	0.49/0.50	0.01/0.74	0.34/0.89	0.81/0.66	0.30/0.93	0.07/0.74	0.14/0.56	0.05/0.90
Metastatic status (+/–)	0.39/0.60	0.97/0.35	0.06/NA[a]	0.04/0.38	0.53/0.14	0.66/0.07	0.32/0.75	0.22/0.13	0.51/NA	0.63/0.98
(M+/M–) (F+/F–)	(0.06/NA) (0.90/0.49)	(0.61/NA) (0.90/0.33)	(NA/NA) (0.18/NA)	(0.06/NA) (0.40/0.34)	(NA/NA) (0.58/NA)	(0.15/NA) (0.38/NA)	(0.80/NA) (0.40/NA)	(NA/NA) (0.35/NA)	(0.15/NA) (0.20/NA)	(0.80/NA) (0.40/NA)
Tumor type (ES/OS)	0.84/0.74	0.83/0.86	0.88/0.94	0.36/0.25	0.85/0.30	0.45/0.80	0.42/0.93	0.85/0.56	0.12/0.48	0.05/0.67
(ES M/F) (OS M/F)	(0.65/0.85) (0.54/NA)	(0.89/0.42) (0.80/NA)	(0.78/0.50) (NA/NA)	(0.06/0.54) (0.28/NA)	(0.37/NA) (NA/0.30)	(NA/0.52) (NA/NA)	(NA/0.60) (0.24/0.66)	(0.09/NA) (NA/0.30)	(NA/0.64) (NA/NA)	(NA/0.78) (0.72/0.99)
Event-free survival	0.68	0.86	0.73	0.51	0.90	0.41	0.26	0.87	0.10	0.06
Sex (M/F)	0.66/0.80	0.27/0.44	0.55/0.86	0.10/0.63	0.77/0.89	0.79/0.38	0.42/0.48	0.29/0.74	0.08/0.38	0.06/0.67
Metastatic status (+/–)	0.39/0.61	0.97/0.74	0.06/0.01	0.04/0.80	0.53/0.56	0.66/0.09	0.32/0.71	0.22/0.42	0.51/0.03	0.63/0.39
(M+/M–) (F+/F–)	(0.06/0.23) (0.90/0.97)	(0.61/0.44) (0.90/0.27)	(NA/NA) (0.08/0.30)	(0.06/0.43) (0.40/0.24)	(NA/0.5) (0.58/NA)	(0.15/0.49) (0.38/0.06)	(0.80/0.49) (0.40/0.87)	(NA/0.14) (0.35/NA)	(0.15/0.06) (0.20/0.16)	(0.22/0.06) (NA/0.54)
Tumor type (ES/OS)	(0.90/0.57)	0.49/0.28	(0.84/0.52)	0.69/0.76	0.85/0.76	0.37/0.89	0.18/0.99	0.83/0.61	0.10/0.53	0.08/0.72
(ES M/F) (OS M/F)	(0.65/0.85) (0.34/0.94)	(0.89/0.34) (0.19/0.48)	(0.78/0.50) (0.73/0.60)	(0.06/0.33) (0.94/0.35)	(0.37/NA) (NA/0.30)	(NA/NA) (NA/NA)	(0.08/0.99) (0.19/0.66)	(0.09/NA) (NA/0.30)	(NA/0.64) (0.45/NA)	(NA/0.78) (0.73/0.99)

[a] NA values denote calculations where survival analysis could not be performed either due to low patient count or because no events occurred for the specific analysis

ES Ewing sarcoma, *F* female, *M* male, *NA* not available, *OS* osteosarcoma, *SMI* skeletal muscle index, SMI_{L4} normalization using the L4 vertebra, SMI_{T12} normalization using the T12 vertebra

(+) and (-) for metastatic status denote the presence or absence of metastases, respectively

affect survival in the overall analysis, in some subgroups, larger muscle mass was correlated with longer survival.

Recently, Romano et al. [8] studied the effects of sarcopenia in children with bone and soft-tissue sarcomas. Their analysis included 21 children, most with Ewing sarcoma and some with rhabdomyosarcoma or desmoplastic tumor, none with osteosarcoma. They used previously reported reference values by Lurz et al. [9] to classify patients according to the total psoas muscle area measured at the L4–5 intervertebral level, without normalizing measurements. Romano et al. [8] reported that 57.1% of children were sarcopenic at the time of diagnosis but that sarcopenia was not associated with overall survival. However, a decrease in total psoas muscle area by more than 25% in the 12 months following diagnosis was significantly associated with poor overall survival in their study [8].

Our study differed in several ways. We did not use previously reported reference values. We used thresholding for our muscle area measurements, and for analysis, we normalized these values to patient height (SMI) or to vertebral height (SMI_{T12} or SMI_{L4}). Regarding total psoas muscle area, we measured this parameter at a slightly higher level; we chose to measure at the mid L4 level, which is more frequently used in adults, compared to the slightly lower level of the L4–5 intervertebral disc chosen by Romano et al. [8]. Last, our study consisted of only cases with Ewing sarcoma and osteosarcoma. Nonetheless, our endpoints were similar in that sarcopenia did not affect overall survival in either study.

Most reported reference values for muscle area only take age and sex into consideration, without any normalization using patient height or weight. On the other hand, a study by Metzger et al. [10] and a more recent study by Somasundaram et al. [11] also reported muscle indices for total psoas muscle area and total abdominal muscle area, respectively. The study by Somasundaram is especially valuable because it was performed in 2,168 patients. However, neither study used thresholding to isolate muscle tissue from intra/intermuscular fat, as is recommended for sarcopenia measurements in adults [12]. In that regard, it should also be noted that no previous study we reviewed performed thresholding. The use of specific density limits, however, requires attention to the use of intravenous contrast agent because it affects muscle density [13]. One critical issue is that reference values may be different in different populations [14]. Therefore, reference values for each population are needed for accurate diagnosis.

Like in adults, many studies have found sarcopenia to be a marker for worse survival or disease outcome in children [7, 15–17]. In our study, children in the non-metastatic group with higher SMI–paraspinal and SMI_{T12}–psoas values had longer event-free survival and no deaths. Boys with higher SMI_{T12}–paraspinal values had longer overall survival. In the metastatic group, children with higher SMI_{T12}–paraspinal values had longer overall and event-free survival compared to those with lower values.

However, no single parameter demonstrated sufficient robustness to be regarded as an independent indicator of survival. Because every child underwent chest CT and most children had no metastases, the SMI–paraspinal values could be considered as the most useful index in our study. However, we observed no significant correlation between this parameter and event-free or overall survival in the total group or other subgroup analyses. Although fewer children underwent abdominal imaging, the same was true for the SMI_{T12}–psoas index. This lack of correlation may have several explanations. First, the low number of children in the subgroups might have resulted in statistical discrepancies. Additionally, the skeletal muscle index might not be useful in children. Skeletal muscle might scale differently to height in children than in adults. It is, for example, known that body weight is proportional to height cubed and not height squared during puberty [16]. In the work by Metzger et al. [10], the psoas muscle index was not a linear function but was lower around the age of 8 years than in other age groups and was more pronounced in boys.

Puberty might be another confounding factor. Although fat mass and fat-free mass during early childhood are comparable in girls and boys, girls gain more fat mass during puberty, whereas boys acquire more muscle mass [14–16]. These reasons might have contributed to the SMI_{T12}–paraspinal values being correlated with overall survival in boys but not in girls, given that boys were older than girls in our study. The fact that the SMI_{T12}–paraspinal index was useful in metastatic children might be attributed to the lower number of metastatic children ($n = 12$) in this group and hence could be considered a statistical bias.

Many studies that reported negative outcomes in children with sarcopenia were performed on very few patients, some as few as 13 [18–21]. Therefore, more studies are necessary to verify the results [3]. Supporting our findings and those of Romano et al. [8], a recent study with 164 children found no association between total psoas muscle area and event-free and overall survival in pediatric patients with cancer, although there was a weak correlation with days spent in a neutropenic state [22].

The pectoralis muscle area is not widely studied for assessing sarcopenia. In adults, it has been shown to correlate with the psoas muscle area [23]. Low pectoralis muscle area has been associated with worse survival in people with breast cancer and negative outcomes in those with coronavirus disease 2019 (COVID-19) pneumonia [24, 25]. Given that people with Ewing sarcoma and osteosarcoma routinely undergo CT imaging of the thorax, we assessed the pectoralis muscle in our study. However, we did not find any association between the pectoralis muscle area and survival.

Weight-based metrics like BMI or body surface area do not provide information about body composition. Individuals with identical height and weight might exhibit different

percentages of fat, muscle and bone [6]. BMI z-scores in children can misclassify as much as 25% of children with excess fat mass because they have low muscle mass but healthy weight-for-height [16]. In adults with cancer, muscle mass is not strongly correlated with BMI or body surface area, and these patients do not lose or gain fat and muscle tissue in equal proportions. Sarcopenic obesity defines a subgroup of patients who have high amounts of fat while at the same time having a low amount of muscle tissue. In adults, it is reported to be seen in between 9.3% and 17.9% of patients studied and is correlated with many negative outcomes [6]. In limited studies, sarcopenic obesity has been reported to have a prevalence of 8–10% in children [7]. Obesity not only contributes to low muscle mass but also impairs function. Accumulated fat causes a systemic inflammatory response, which can add to the already present inflammatory state in cancer patients [16]. Sarcopenic obesity has been documented in pediatric cancer patients and survivors, with a negative impact on quality of life [5]. Detection of loss of muscle and increased inter-/intramuscular fat (myosteatosis) in these children is only possible if thresholding is applied to CT-based measurements as opposed to only measuring muscle area. This is one of the reasons why CT is considered to be superior to dual-energy X-ray absorptiometry in assessing sarcopenic obesity [15].

Despite all of this, the sarcopenic obesity index used in our study, which is a ratio of weight to muscle area, did not correlate with event-free or overall survival. This might be the result of our more direct approach using a singular index for quantification. We did not evaluate myosteatosis but used thresholding to exclude fat from muscle tissue. There are no standard parameters or reference values to diagnose sarcopenic obesity. Therefore, the sarcopenic obesity index might vary at different stages of growth in children.

Although vertebral parameters have been demonstrated to be useful to determine stature in adults [26], various authors have used different levels or methods to estimate stature. In children, cervical vertebrae have been used to assess growth and development [27–29]. However, we were unable to find a study that evaluated the prediction of stature from vertebral parameters at different levels in the pediatric age group. We evaluated the T12 and L4 vertebral parameters and their association with stature because they were also the levels at which muscle measurements were performed. The L4 level was chosen over the L3 because this level was studied more in the literature for adults [26]. At both levels, vertebral volume was (albeit only slightly) more strongly correlated with patient height. Volume calculations are cumbersome in clinical practice, therefore, we preferred to use vertebral heights at both levels. The T12 level is especially useful because it is usually also visible on abdominal CT scans and can be used to normalize muscle measurements for thoracic and abdominal body regions. It also appears to be better correlated with patient height. Nonetheless, the number of children in our study precludes any wider generalization. If such data were available, it would be possible to report SMI without the need for information about patient height. Additionally, retrospective evaluations from archived images would be possible in children for whom height measurements were not recorded at the time of the CT scans (or are unavailable).

Our study has several limitations. First, available data (such as height or weight) relied on patient records that were obtained by different individuals on different equipment, which might have introduced variations in measurement. Our sample size was limited, which prevented some subgroup analyses. This limitation also restricted our outcomes regarding vertebral parameters, which need to be verified on larger sample sizes. Because of the limited sample size, we did not group children into similar age groups, which might have affected the results. Some CT scans were performed using intravenous contrast agents, which, despite having no overall statistical significance, might have resulted in an error in some subgroup analyses. Finally, measurements were only performed by a single observer and intra- and inter-observer reliability were not assessed.

Conclusion

Although some parameters in our study were correlated with event-free or overall survival, we could not reliably conclude that sarcopenia or sarcopenic obesity was associated with survival in children with Ewing sarcoma or osteosarcoma. The change in body composition from birth to adulthood and the lack of sound diagnostic criteria challenge research in this field. Normalization of measurements to anatomical landmarks such as the vertebrae should be further studied to allow for opportunistic or retrospective assessment of body composition.

Acknowledgments The authors would like to thank Dr. Zeynep Altas, MD, for her contributions to the statistical analysis of study data.

Data Availability All data generated or analyzed during this study are included in this published article.

Declarations

Conflicts of interest None

References

1. Cruz-Jentoft AJ, Bahat G, Bauer J et al (2019) Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 48:16–31
2. Cederholm T, Barazzoni R, Austin P et al (2017) ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr 36:49–64

3. Metzger GA, Carsel A, Sebastião YV et al (2021) Does sarcopenia affect outcomes in pediatric surgical patients? A scoping review. J Pediatr Surg 56:2099–2106
4. Goodenough CG, Partin RE, Ness KK (2021) Skeletal muscle and childhood cancer: where are we now and where we go from here. Aging Cancer 2:13–35
5. Triarico S, Rinninella E, Mele MC et al (2022) Prognostic impact of sarcopenia in children with cancer: a focus on the psoas muscle area (PMA) imaging in the clinical practice. Eur J Clin Nutr 76:783–788
6. Baracos VE, Arribas L (2018) Sarcopenic obesity: hidden muscle wasting and its impact for survival and complications of cancer therapy. Ann Oncol 29:ii1–ii9
7. Gilligan LA, Towbin AJ, Dillman JR et al (2020) Quantification of skeletal muscle mass: sarcopenia as a marker of overall health in children and adults. Pediatr Radiol 50:455–464
8. Romano A, Triarico S, Rinninella E et al (2022) Clinical impact of nutritional status and sarcopenia in pediatric patients with bone and soft tissue sarcomas: a pilot retrospective study (SarcoPed). Nutrients 14:383
9. Lurz E, Patel H, Lebovic G et al (2020) Paediatric reference values for total psoas muscle area. J Cachexia Sarcopenia Muscle 11:405–414
10. Metzger GA, Sebastião YV, Carsel AC et al (2021) Establishing reference values for lean muscle mass in the pediatric patient. J Pediatr Gastroenterol Nutr 72:316–323
11. Somasundaram E, Castiglione JA, Brady SL, Trout AT (2022) Defining normal ranges of skeletal muscle area and skeletal muscle index in children on CT using an automated deep learning pipeline: implications for sarcopenia diagnosis. AJR Am J Roentgenol 219:326–336
12. Lenchik L, Boutin RD (2018) Sarcopenia: beyond muscle atrophy and into the new frontiers of opportunistic imaging, precision medicine, and machine learning. Semin Musculoskelet Radiol 22:307–322
13. Boutin RD, Kaptuch JM, Bateni CP et al (2016) Influence of IV contrast administration on CT measures of muscle and bone attenuation: implications for sarcopenia and osteoporosis evaluation. AJR Am J Roentgenol 207:1046–1054
14. Ritz A, Lurz E, Berger M (2022) Sarcopenia in children with solid organ tumors: an instrumental era. Cells 11:1278
15. Ooi PH, Thompson-Hodgetts S, Pritchard-Wiart L et al (2020) Pediatric sarcopenia: a paradigm in the overall definition of malnutrition in children? JPEN J Parenter Enteral Nutr 44:407–418
16. Orsso CE, Tibaes JRB, Oliveira CLP et al (2019) Low muscle mass and strength in pediatrics patients: why should we care? Clin Nutr 38:2002–2015
17. Ritz A, Froeba-Pohl A, Kolorz J et al (2021) Total psoas muscle area as a marker for sarcopenia is related to outcome in children with neuroblastoma. Front Surg 8:718184
18. Kawakubo N, Kinoshita Y, Souzaki R et al (2019) The influence of sarcopenia on high-risk neuroblastoma. J Surg Res 236:101–105
19. Ritz A, Kolorz J, Hubertus J et al (2021) Sarcopenia is a prognostic outcome marker in children with high-risk hepatoblastoma. Pediatr Blood Cancer 68:e28862
20. Lurz E, Patel H, Frimpong RG et al (2018) Sarcopenia in children with end-stage liver disease. J Pediatr Gastroenterol Nutr 66:222–226
21. Dedhia PH, White Y, Dillman JR et al (2018) Reduced paraspinous muscle area is associated with post-colectomy complications in children with ulcerative colitis. J Pediatr Surg 53:477–482
22. McBee MP, Woodhouse C, Trout AT et al (2022) Skeletal muscle mass as a marker to predict outcomes in children and young adults with cancer. Abdom Radiol 47:452–459
23. Rossi F, Valdora F, Barabino E et al (2019) Muscle mass estimation on breast magnetic resonance imaging in breast cancer patients: comparison between psoas muscle area on computer tomography and pectoralis muscle area on MRI. Eur Radiol 29:494–500
24. Huang WJ, Zhang ML, Wang W et al (2022) Preoperative pectoralis muscle index predicts distant metastasis-free survival in breast cancer patients. Front Oncol 12:854137
25. Ufuk F, Demirci M, Sagtas E et al (2020) The prognostic value of pneumonia severity score and pectoralis muscle area on chest CT in adult COVID-19 patients. Eur J Radiol 131:109271
26. Choong CL, Alias A, Abas R et al (2020) Application of anthropometric measurements analysis for stature in human vertebral column: a systematic review. Forensic Imaging 20:200360
27. Altan M, Nebioğlu Dalcı Ö, İşeri H (2011) Growth of the cervical vertebrae in girls from 8 to 17 years. A longitudinal study. Eur J Orthod 34:327–334
28. Hellsing E (1991) Cervical vertebral dimensions in 8-, 11-, and 15-year-old children. Acta Odontol Scand 49:207–213
29. Krishnamoorthy VV, Parameswaran R, Vijayalakshmi D et al (2016) Assessment of skeletal maturation in concordance to statural height and body weight in 12-year-old children — a cross-sectional study. J Clin Diagn Res 10:Zc51–55