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Body composition and phase angle in Russian children in remission from acute lymphoblastic leukemia

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Abstract. Elevated degree of body fatness and changes in other body composition parameters are known to be common effects of treatment for acute lymphoblastic leukemia (ALL) in children. In order to study peculiarities of somatic growth and development in ALL survivors, we describe the results of BIA body composition analysis of 112 boys and 108 girls aged 5-18 years in remission from ALL (remission time range 1-13 years) compared to data from the same number of age- and sex-matched healthy controls (n=220). Detrimental effect on height in ALL boys was observed, whereas girls experienced additional weight gain compared to healthy subjects. In ALL patients, resistance, body fat, and percent body fat were significantly increased. The reactance, phase angle, absolute and relative values of skeletal muscle and body cell mass were significantly decreased. Principal component analysis revealed an early prevalence of adiposity traits in the somatic growth and development of ALL girls compared to healthy controls.

1. Introduction

Acute lymphoblastic leukemia (ALL) represents the most common form of cancer in children having incidence about 3-4 cases per 100.000/year that peaks around 2-5 years of age. The use of modern treatment protocols involving polychemotherapy and prophylactic central nervous system interventions provides cure rate exceeding 80% [1]. So, estimation of the long-term effects of treatment for childhood ALL has become increasingly important. There exist a substantial number of studies on body composition changes in children in remission from ALL [2-4]. In particular, excessive fatness and significant reduction in bone mineral density are reported as frequent late complications of ALL treatment. To our knowledge, in Russia, such studies have not been previously conducted.

Along with BIA estimates of body composition, there is growing interest for direct use of measured BIA parameters, such as resistance, reactance, and phase angle, in epidemiological and clinical investigations [5-7]. In our recent paper we reported data on phase angle and body composition in healthy Russian children aged 10-16 years [8]. Here, we aim at the evaluation of the long-term effects of ALL and its treatment on the somatic growth and development of children in terms of basic anthropometric and BIA parameters, including height, weight, phase angle and body composition.

2. Subjects and methods

220 children (112 males and 108 females) after treatment for acute lymphoblastic leukemia (ALL) were assessed cross-sectionally in 2008-2009 at an average age 10.6 years (range, 5-18 yr). All patients were in first remission, and none had received any hormone replacement therapy. Remission time ranged from 1 to 13 years. Another 220 age- and sex-matched healthy children were measured who comprised a control group.

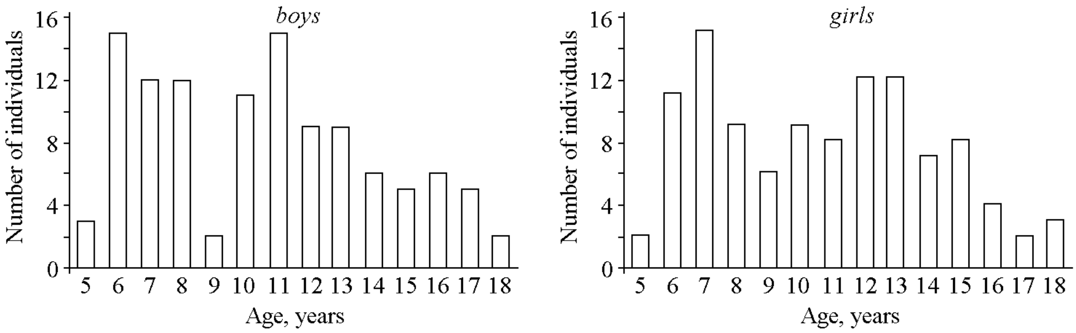

Figure 1. Histograms of ALL patients' and control subjects distribution across age

Table 1. Basic anthropometric characteristics of ALL patients and controls, mean (s.d.)

Parameter	Boys		Girls	
	ALL (n=112)	Controls (n=112)	ALL (n=108)	Controls (n=108)
Age, years	10.5 (3.5)	10.5 (3.5)	10.7 (3.4)	10.7 (3.4)
Body mass, kg	40.1 (15.0)	40.2 (17.7)	40.6 (15.4)	37.8 (14.3)
Body height, cm	143.2 (19.6)	146.8 (22.8)	142.4 (17.1)	144.1 (19.4)
BMI, kg/m^2	18.9 (3.1)*	17.6 (2.8)	19.3 (4.1)*	17.4 (2.6)

* significant difference compared to control group, p<0.01

Table 2. BIA estimates of body composition parameters in ALL patients and controls, mean (s.d.)

Parameter	Boys		Girls	
	ALL	Controls	ALL	Controls
R, Ohm	677 (79)*	626 (99)	715 (86)*	678 (84)
X_C, Ohm	62.3 (7.0)*	69.6 (10.0)	65.3 (7.5)*	74.7 (9.4)
PA, grad	5.3 (0.7)*	6.4 (0.7)	5.3 (0.6)*	6.3 (0.7)
TBW, l	22.7 (7.9)	25.2 (10.9)	21.7 (6.4)	22.3 (7.5)
FM, kg	18.9 (3.1)*	17.6 (2.8)	19.3 (4.1)*	17.4 (2.6)
%FM	22.1 (6.5)*	14.1 (4.0)	25.5 (6.8)*	18.0 (5.0)
FFM, kg	30.9 (10.9)	34.4 (14.9)	29.4 (8.9)	30.4 (10.3)
SMM, kg	16.5 (7.3)*	22.5 (7.2)	14.1 (4.7)*	16.8 (4.6)
BCM, kg	15.6 (6.5)*	19.3 (9.1)	14.7 (5.1)*	16.9 (6.1)

* significant difference compared to control group, p<0.01

Standing height in ALL patients was measured using a stadiometer, and weight was measured on a digital scale. In a control group, standing height was determined using the GPM anthropometer. Body mass index (BMI) was calculated as body mass (BM) divided by standing height (Ht) squared. Age distributions and basic anthropometric characteristics of patients and controls are shown in Figure 1 and Table 1, respectively. The whole-body impedance was measured on the right side of the body by the bioimpedance analyzer ABC-01 'Medass' (SRC Medass, Russia) according to a conventional tetrapolar scheme at a constant frequency 50 kHz. Phase angle (PA) was calculated as $\arctan(X_C/R)\times180°/\pi$, where X_C is reactance and R the whole-body electric resistance. Fat-free mass (FFM) was assessed using Houtkooper equation [9]: $FFM=0.61\times(Ht^2/R)+0.25\times BM+1.31$, where Ht is measured in cm. Fat mass was calculated as the difference between BM and FFM, and %FM as (FM/BM)×100. Body cell mass (BCM) and skeletal-muscle mass (SMM) were determined using the formulae provided by the manufacturer. Two-sample rank (Mann-Whitney) test of the equality of two population medians was used. A p value of 0.05 was used to define significance.

3. Results

Body mass index was significantly compromised in ALL patients (Table 1). In ALL boys, this effect was observed due to changes in body height only, while in girls both Ht and Wt were affected compared to healthy controls.

Table 3. Correlations between anthropometric and BIA parameters, boys. Above and below the diagonal are the data on ALL patients and controls, respectively

	Age	Ht	Wt	BMI	R	X_C	PA	FM	%FM	FFM
Remission time	0.34	0.39	0.43	0.28	-0.43	n.s.	0.44	0.25	n.s.	0.47
Age	•	0.90	0.82	0.38	-0.44	n.s.	0.54	0.56	n.s.	0.85
Ht	0.89	•	0.94	0.39	-0.47	n.s.	0.46	0.60	n.s.	0.93
Wt	0.85	0.89	•	0.75	-0.64	n.s.	0.50	0.83	0.41	0.96
BMI	0.65	0.69	0.87	•	-0.60	-0.31	0.31	0.87	0.69	0.60
R	-0.68	-0.75	-0.86	-0.89	•	0.40	-0.59	-0.32	n.s.	-0.72
X_C	-0.46	-0.56	-0.63	-0.64	0.72	•	0.48	n.s.	n.s.	n.s.
PA	0.42	0.37	0.46	0.48	-0.52	0.21	•	0.20	n.s.	0.58
FM	0.68	0.76	0.87	0.86	-0.65	-0.49	0.34	•	0.83	0.65
%FM	n.s.	n.s.	0.22	0.38	n.s.	n.s.	n.s.	0.63	•	n.s.
FFM	0.86	0.95	0.99	0.84	-0.88	-0.63	0.47	0.80	n.s.	•

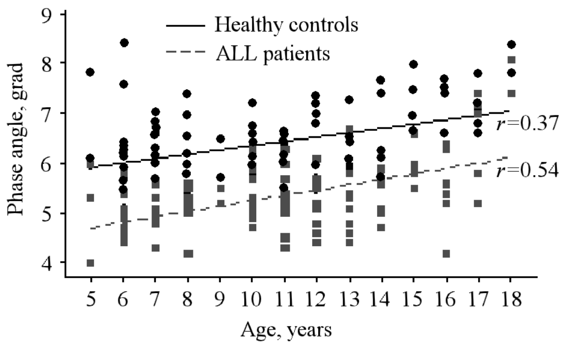

Figure 2. Scatter plots of phase angle across age: remission for acute lymphoblastic leukaemia (■) vs. healthy controls (•), boys

In ALL, the resistance, body fat, and percent body fat were significantly increased (Table 2). The reactance, phase angle, absolute and relative values of skeletal muscle and body cell mass were significantly decreased. Fat-free mass and total body water (TBW) did not differ significantly between groups. Table 3 shows correlations between anthropometric and BIA parameters in boys. BIA estimates of SMM and BCM in children highly correlated with FFM and were excluded from the analysis. One can see stronger associations of BMI with Age, Ht, and FFM in healthy boys compared to ALL patients. Stronger associations are also present for resistance and reactance of healthy controls with the majority of parameters shown in Table 3 compared to ALL subjects. Unlike this, BMI correlates better with %FM in ALL boys. Similar results were obtained for girls (data not shown).

Phase angle (PA) is increasingly used in clinical studies as an indicator of nutritional status, disease severity and life expectancy [6, 10]. In ALL, PA was significantly decreased compared to healthy children and positively correlated with age in both ALL and control groups (see Fig. 2 for boys). After controlling for age, PA was only weakly associated with the remission time (partial r=0.19 for boys).

In boys, principal component analysis with varimax rotation of phase angle with the selected anthropometric and BIA parameters returned two factors responsible for 75% and 71% of the total variance in patients and controls, respectively (Table 4). Factor 1 had maximal loadings on Ht, Wt, and FFM reflecting a principal role of skeletal and muscular traits in the somatic development of boys. In ALL boys, this factor had lesser, but still prevalent, extent. Factor 2 ('adiposity') had maximal loadings on %FM and FM. In girls, the above two factors have changed together with the prevalence of adiposity traits in ALL, and skeletal and muscular traits in healthy controls, respectively. Our previous data showed that the transition to prevalence of adiposity factor is characteristic for healthy girls of more advanced age [8]. Also, unlike healthy boys and girls, in ALL patients, BMI had much greater impact on adiposity rather than on skeletal and muscular development.

Table 4. The results of factor analysis of phase angle with selected anthropometric and body composition parameters

Variable	Boys				Girls			
	ALL		Healthy		ALL		Healthy	
	Factor 1	Factor 2	Factor 1	Factor 2	Factor 1	Factor 2	Factor 1	Factor 2
PA	0.315	-0.056	0.231	0.031	0.191	-0.190	0.113	-0.037
Ht	0.969	0.148	0.982	-0.086	0.242	-0.961	0.933	-0.335
Wt	0.834	0.404	0.905	-0.151	0.605	-0.700	0.830	-0.399
BMI	0.293	0.706	0.603	-0.290	0.776	-0.260	0.553	-0.423
FM	0.496	0.826	0.691	-0.586	0.795	-0.510	0.667	-0.639
%FM	0.055	0.986	0.063	-0.990	0.946	-0.289	0.374	-0.906
FFM	0.899	0.148	0.920	-0.047	0.419	-0.807	0.874	-0.287
Proportion of variance	0.411	0.338	0.504	0.206	0.395	0.359	0.461	0.252

4. Conclusion

Long-term remission represents a common consequence of treatment for acute lymphoblastic leukemia in children. So, the assessment of nutritional status of such children has become a question of significant interest. In this study, we described peculiarities of growth, development and body composition changes in Russian children after treatment for ALL. Taken together, our results show that many anthropometric and BIA parameters of body composition in children in remission of ALL, change significantly compared to healthy ones. The presence of ALL weakens associations of BMI, as well as of resistance and reactance, with Ht, Wt, and other parameters of body composition that reflect the state of an organism's skeletal and muscular development. Phase angle was significantly decreased in ALL, and, after controlling for age, only weakly correlated with the remission time. In ALL girls, we observed early prevalence of adiposity traits in their somatic growth and development compared to healthy controls. Further studies are needed to elucidate other health-related consequences of treatment for ALL in Russian children aimed at optimization of the disease management and rehabilitation strategy.

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