

CORRELATES OF INSULIN RESISTANCE AMONG ADULT SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

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Preferred presentation: Oral

Category: Other

Background: Following our previous reports of an increased prevalence of insulin resistance and adiposity among ALL survivors, particularly women treated with cranial radiotherapy (CRT), we aimed to (1) assess the relationship between adipokines (leptin and adiponectin) and CRT and (2) determine correlates of insulin resistance, by gender.

Methods: Cross-sectional evaluation of 116 ALL survivors (median age, 23.0 years; range, 18-37) was conducted and included fasting laboratory testing (adiponectin, leptin, insulin, glucose), anthropometric measurements (weight, height, waist circumference), DXA (total body fat, truncal-to-lower-body-fat ratio), and abdominal CT (visceral fat). Insulin resistance was estimated using the homeostatic model assessment for insulin resistance (HOMA-IR). Analytic approach included Spearman correlation coefficients, regression models, and Wilcoxon RankSum testing.

Results: CRT was associated with a higher leptin:adiponectin ratio among both women (CRT 3.0 ± 2.1 , no CRT 1.7 ± 1.7 , $P < 0.01$) and men (CRT 2.2 ± 3.0 , no CRT 0.8 ± 1.1 , $P = 0.01$) and this ratio was associated with HOMA-IR (females $\beta = 0.15$, 95%CI=0.09-0.21, $P < 0.01$; males $\beta = 0.17$, 95%CI=0.11-0.22, $P < 0.01$). However, visceral adiposity and truncal-to-lower-body-fat ratio were more strongly associated with HOMA-IR than leptin:adiponectin ratio (or BMI, waist circumference, waist:height ratio). When assessing HOMA-IR, there was not a significant interaction between CRT and the adipokines.

Conclusions: Among ALL survivors, visceral adiposity and truncal-to-lower-body-fat ratio are superior to serum adipokines and anthropomorphic measures in predicting insulin resistance. Importantly, though the cross-sectional design limits inferences regarding causality, it appears that the relationship between CRT and insulin resistance is largely accounted for by increased adiposity and not via other factors.

Table 1. Serum adipokines and measures of body fatness, stratified by treatment with cranial radiotherapy (CRT), among 116 adult survivors of childhood acute lymphoblastic leukemia (ALL).

	CRT N=39		No CRT N=77		p
	Mean	(SD)	Mean	(SD)	
Leptin: adiponectin ratio	2.6	2.5	1.2	1.5	<0.01
Adiponectin per kg fat mass (mcg/mL/kg)	0.5	0.5	0.8	0.6	<0.01
Leptin per kg fat mass (mcg/L/kg)	0.7	0.4	0.5	0.5	<0.01
Percent total body fat	37.0	8.8	28.1	10.3	<0.01
Truncal-to-lower-body-fat ratio	1.5	0.4	1.2	0.3	<0.01
Visceral fat (kg)	0.38	0.21	0.22	0.16	<0.01
Body mass index (m/kg ²)	30.2	8.3	26.6	5.8	0.01
Waist circumference (cm)	95.8	16.3	89.5	14.3	0.04
Waist:height ratio	59.4	10.4	52.6	8.5	<0.01
HOMA-IR	5.1	3.0	3.8	2.1	0.01