

Low bone mineral density in adolescents with leukemia after hematopoietic stem cell transplantation: Endocrinopathy after HSCT and steroid treatment for GVHD might be major concerns ?

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Background: HSCT has improved the prognosis of children with malignant hematologic disease. However, it has had significant adverse effects on the endocrine system, including bone health. limited studies are available to assess osteoporosis in survivors of adolescents after HSCT

Objective and hypotheses: We investigate the bone mineral density (BMD) and endocrinopathy/treatment factors associated with low bone mineral density in adolescents with leukemia treated with hematopoietic stem cell transplantation (HSCT).

Method: Demographic measurements an dual-energy X-ray absorptiometry assessment of Sixty-one adolescents (F=28, M=33; lymphoid=28, myeloid=33) over 14 years of age (16.6 ± 1.3) who were referred to the pediatric endocrinology clinic between September 2009 and September 2014 after HSCT at the Catholic HSCT center were evaluated. Low BMD was classified when lumbar spine (LS)-BMD SDS (standard deviation score) adjusted for age and current height was below -2.0.

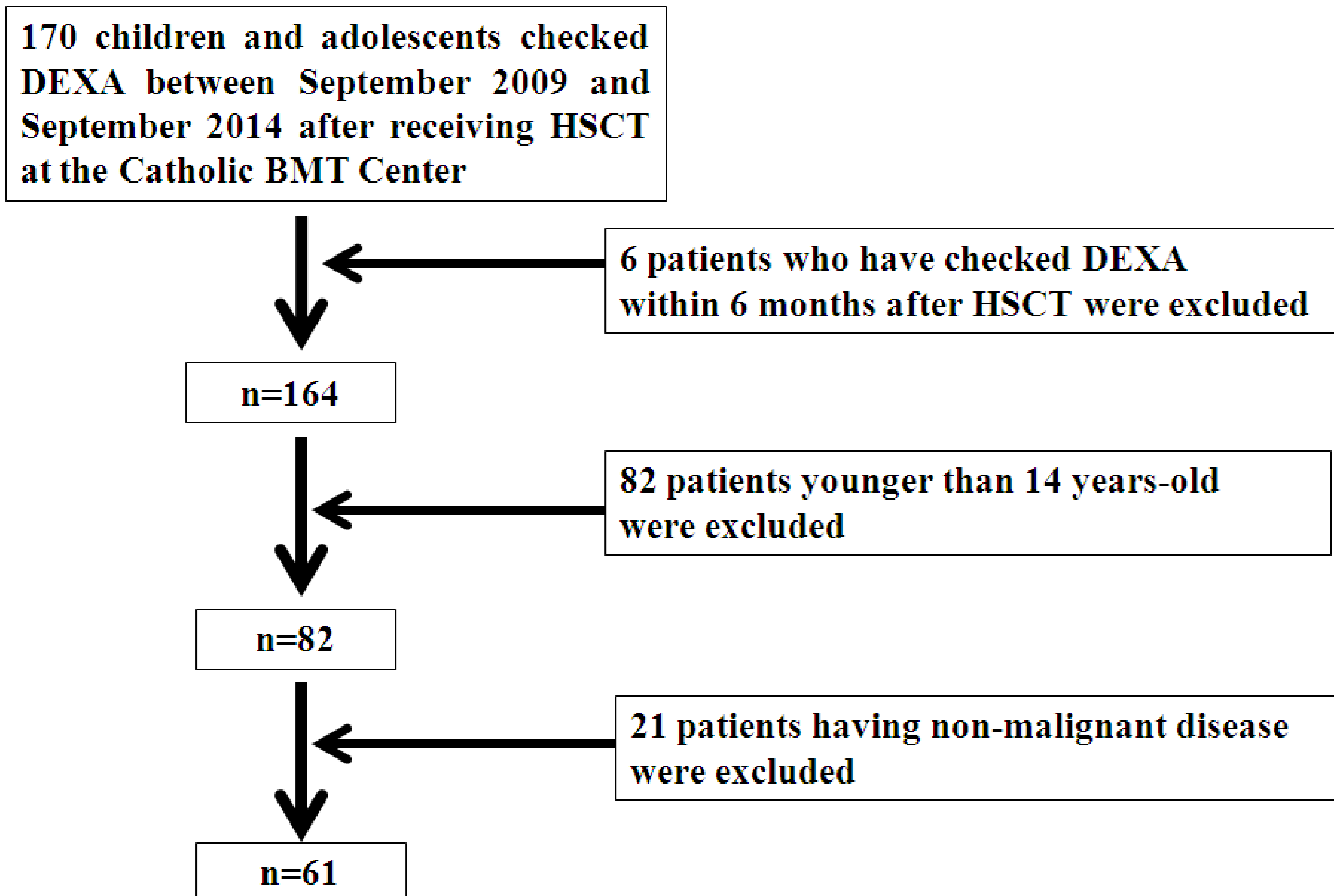


Figure 1. Selection of patient populations

Results: Clinical characteristics were in table 1

Twenty-three (37.7%) out of 61 patients revealed low bone mineral density. In low BMD group, LS-SDS was -3.2 ± 1.1 . In low BMD group, the incidence of chronic graft-versus-host disease (cGVHD) (73.9% vs. 42.1%, $P < 0.019$), and hypogonadism (78.3% vs. 44.7%, $P < 0.016$) were higher than normal BMD group. There were no significant differences of age, sex, weight-SDS, weight-SDS, diagnosis, preparative regimen, acute-GVHD, duration of steroid or cyclosporine treatment for GVHD, growth hormone deficiency (Table 2).

In a multivariate logistic regression analysis, the development of hypogonadism was associated with low BMD (beta=1.371, $P = 0.026$) (Table 3).

Table 1. Patient characteristics and treatment variables

	Total (n=61)
Sex (female)	Female=28 (45.9%)
CA at DEXA (years)	16.6 ± 1.3
BA at DEXA (years)	15.6 ± 2.0
CA at HSCT (years)	12.4 ± 3.8
Interval between DEXA and HSCT (years)	4.2 ± 3.7
Weight-SDS at DEXA	-1.5 ± 2.5
Height-SDS at DEXA	-1.3 ± 1.8
BMI-SDS at DEXA	-0.75 ± 1.8
Diagnosis	
Lymphoid leukemia	28 (45.9%)
Myeloid leukemia	33 (54.1%)
Preparative regimen	
BU based	30 (49.2%)
TBI based	31 (50.8%)
Acute GVHD	35 (57.4%)
Chronic GVHD	33 (54.1%)
Steroid over 6 months	35 (57.4%)
Cyclosporine over 6months	48 (78.7%)
Hypothyroidism	11 (18.0%)
GHD	14 (23.0%)
Hypogonadism	35 (57.4%)

Table 2. Patient characteristics and treatment variables according to low-BMD.

	Total (n=61)		
	Low-BMD (n=23)	Normal (n=38)	P value
Sex (female)	13 (56.5%)	15 (39.5%)	0.289
CA at DEXA (years)	16.7 ± 2.3	16.5 ± 1.5	0.422
BA at DEXA (years)	15.3 ± 1.7	15.8 ± 2.2	0.286
CA at HSCT	13.2 ± 2.3	11.9 ± 4.4	0.474
Interval between DEXA and HSCT (years)	3.5 ± 2.3	4.6 ± 4.3	0.199
Weight-SDS	-1.3 ± 2.7	-1.5 ± 2.4	0.781
Height-SDS	-1.3 ± 1.8	-1.3 ± 1.8	0.986
BMI-SDS	-0.6 ± 2.1	-0.8 ± 1.6	0.633
Diagnosis			0.197
Lymphoid leukemia	8(34.8%)	20(52.6%)	
Myeloid leukemia	15(65.2%)	18(47.4%)	
Preparative regimen			0.434
BU based	13(56.5%)	17(44.7%)	
TBI based	10(43.5%)	21(55.3%)	
Acute GVHD	12(52.2%)	23(60.5%)	0.598
Chronic GVHD	17(73.9%)	16(42.1%)	0.019
Steroid over 6 months	17(73.9%)	18(47.4%)	0.062
Cyclosporine over 6months	19(82.6%)	29(76.3%)	0.749
Hypogonadism	18(78.3%)	17(44.7%)	0.016
GHD	6(26.1%)	8(21.1%)	0.756
Hypothyroidism	4(17.4%)	7(18.4%)	1.000
Adjusted LS BMD SDS	-3.2 ± 1.1	-0.5 ± 1.0	0.000
Adjusted FN BMD SDS	-2.2 ± 1.3	-1.0 ± 1.2	0.000

Table 3. Odds ratios and 95% confidence intervals of low-BMD.

		Univariate		Multivariate	
	61	OR (95% CI)	P - value	OR (95% CI)	P - value
Steroid over 6 months	No	1.0			
	Yes	3.2 (1.0-9.7)	0.046		
Hypogonadism	No	1.0		1.0	
	Yes	4.4 (1.4-14.5)	0.013	3.9 (1.2-13.2)	0.026

Conclusion: One thirds of adolescents with leukemia treated with HSCT showed low BMD. Monitoring these patients at regular intervals may be necessary for improving bone health during adolescence and adulthood.

References : Lim JS, Hwang JS, Lee JA, Kim DH, Park KD, Cheon GJ *et al.* Bone mineral density according to age, bone age, and pubertal stages in Korean children and adolescents. *Journal of clinical densitometry : the official journal of the International Society for Clinical Densitometry* 2010; 13(1): 68-76.

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