

Bone health in adolescents and young adults after allogeneic hematopoietic stem cell transplantation in childhood

A single center cross-sectional study

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KEY MESSAGES

- ✓ Bone geometry and bone strength are impaired in adolescent and young adult males after childhood alloHSCT
- ✓ Both males and females had a disturbed body composition
- ✓ No relation was found between the suboptimal body composition and impaired bone health

INTRODUCTION

It is assumed that bone mass and strength accrual during puberty are impaired after allogeneic hematopoietic stem cell transplantation (alloHSCT) due to toxicity of treatments, prolonged inactivity and disturbed body composition.

OBJECTIVES

Cross-sectional study of bone geometry, bone strength and its relation with body composition.

METHODS

Bone strength, mass, size, density (BMD) and body composition were determined by *dual-energy X-ray absorptiometry* and *peripheral quantitative computed tomography*.

Participants

Inclusion criteria:

- Boys and girls of 15 to 25 years
- AlloHSCT: ≥2-year interval since alloHSCT
- Controls: healthy volunteers

Cases:

- AlloHSCT: n=22 (11 males, 11 females)
- Controls: n=22 (11 males, 11 females)

Diagnosis and treatment:

- Age at alloHSCT: 9.2±4.91 years.
- Diagnosis:
 - Acute lymphoblastic leukemia: n=16
 - Acute & chronic myeloid leukemia: n=2 & n=2
 - Anaplastic large cell lymphoma and myelodysplastic syndrome: n=1 & n=1
- Myeloablative conditioning regimens:
 - Total body irradiation based (1200 cGy): n=15
 - Busulfan based: n=7
 - +Cyclophosphamide (≥ 120 mg/kg): n=10
- Acute GvHD (grade II to IV): n=8
- Chronic GvHD: n=1

RESULTS

Characteristics	AlloHSCT		Controls	
	Males	Females	Males	Females
Age at evaluation (y)	19 ± 3	20 ± 3	20 ± 3	20 ± 3
Interval (y)	9,3 ± 5,06	12,5 ± 3,56	NA	NA
Height (cm)	170,2 ± 6,72	164,9 ± 4,67	171,9 ± 5,05	165,8 ± 5,3
BMI (kg/m ²)	20,0 ± 2,37	22,3 ± 3,72	21,3 ± 2,71	22,3 ± 3,10
Vitamin D (ng/mL)	21,5 ± 8,07	24,3 ± 6,41	23,6 ± 5,26	21,4 ± 5,91
LH (U/L)	9,4 (7,09)*	4,0 (5,25)	5,4 (3,41)*	0,8 (7,13)
Testosterone/estradiol (ng/dL)	525,8 ± 331,35	0,42 ± 4,24	528,9 ± 103,90	0,46 ± 7,25

*: significantly different as compared to controls (p<0,05); y: years; Interval: interval between alloHSCT and evaluation; NA: not applicable

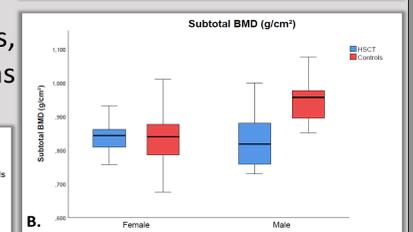
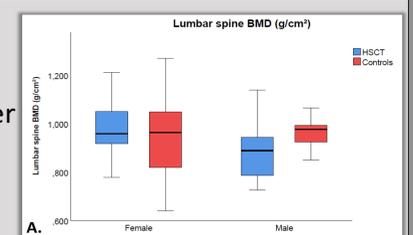
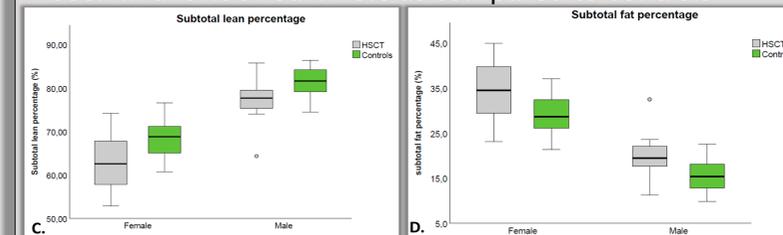
Dual-energy X-ray absorptiometry

Bone

- In males whole body BMD and BMD at spine was lower as compared to controls (p=0,003 & 0,058, respectively)
- In females no difference was seen (p=0,916 & 0,475)

Body composition

- Despite similar BMI, in both males and females, significantly higher fat mass and lower muscle mass was seen in alloHSCT survivors as compared to controls



Figures: Results of DXA scans: A. BMD at lumbar spine; B. BMD of whole body less head; C. Lean mass percentage of whole body less head; D. Fat mass percentage of whole body less head

Peripheral quantitative computed tomography

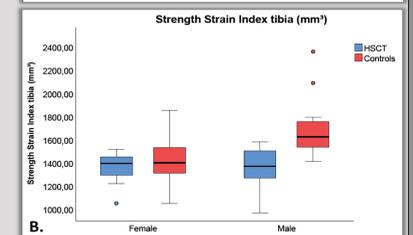
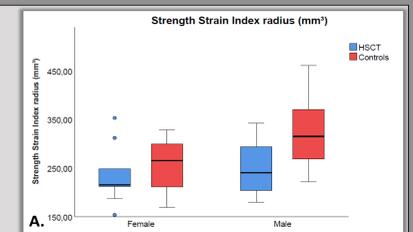
Males:

- Lower trabecular BMD at both radius and tibia (4%)
- Smaller cortical areas at both radius (66%) and tibia (38%)
- Smaller periosteal circumferences were present at tibia
- Lower strength strain at both radius and tibia (Fig A & B)
- No correlations were found with lean and fat mass

Females:

- No significant differences in bone geometry and bone strength as compared to controls

	Radius			Tibia		
	AlloHSCT	Controls	P-value	AlloHSCT	Controls	P-value
BMD						
Trabecular BMD (mg/cm ³)	202,0 ± 45,37	254,1 ± 30,94	<0,001	216,5 ± 39,3	276,9 ± 27,67	0,005
Cortical BMD (mg/cm ³)	1104 ± 59,3	1135 ± 39,7	0,167	1144 ± 45,4	1163 ± 36,3	0,262
Cortical dimensions						
Area (mm ²)	72,1 ± 8,49	86,4 ± 11,60	0,004	247,5 ± 29,98	295,1 ± 32,17	0,002
Periosteal circumference (mm)	42,1 ± 4,24	44,1 ± 3,77	0,246	70,5 ± 4,46	74,5 ± 3,62	0,032
Endosteal circumference (mm)	29,1 ± 5,82	29,3 ± 3,93	0,934	42,7 ± 7,74	42,9 ± 3,78	0,942



CONCLUSIONS

Bone geometry and bone strength are impaired in males. As no relation was found with the suboptimal body composition, a revalidation program must contain specific bone-promoting measures such as weight bearing exercise on top of promoting a healthy diet and life-style.