

# 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:  $\geq 2$ -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:  $9.2 \pm 4.91$  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 ( $\geq 120$  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 $\pm$ 3	20 $\pm$ 3	20 $\pm$ 3	20 $\pm$ 3
Interval (y)	9,3 $\pm$ 5,06	12,5 $\pm$ 3,56	NA	NA
Height (cm)	170,2 $\pm$ 6,72	164,9 $\pm$ 4,67	171,9 $\pm$ 5,05	165,8 $\pm$ 5,3
BMI (kg/m <sup>2</sup> )	20,0 $\pm$ 2,37	22,3 $\pm$ 3,72	21,3 $\pm$ 2,71	22,3 $\pm$ 3,10
Vitamin D (ng/mL)	21,5 $\pm$ 8,07	24,3 $\pm$ 6,41	23,6 $\pm$ 5,26	21,4 $\pm$ 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 $\pm$ 331,35	0,42 $\pm$ 4,24	528,9 $\pm$ 103,90	0,46 $\pm$ 7,25

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

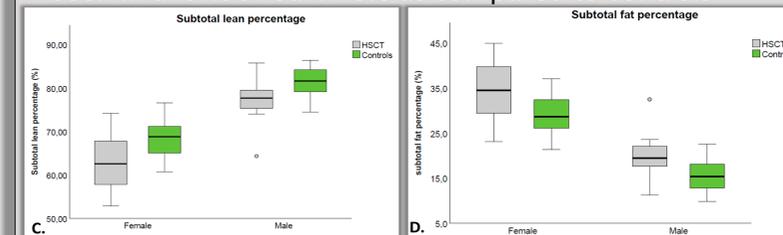
### Dual-energy X-ray absorptiometry

#### 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



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