Impact of haematopoietic stem cell transplantation with total body irradiation on apparent bone mineral density in childhood leukaemia survivors

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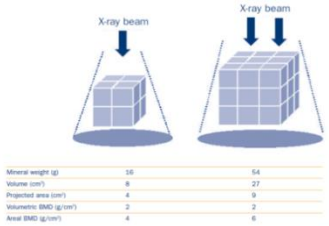
Background

- Childhood HSCT/TBI survivors have multiple risk factors for reduced bone mineral density (BMD) and poor growth.
- Reduced Z-scores from Dual energy X-Ray absorptiometry (DEXA) have been reported.
- However, smaller bones have apparently lower areal BMD than larger ones (figure 1). DEXA measurements may be difficult to interpret in childhood HSCT/TBI survivors who are often short.
- Bone mineral apparent density (BMAD) allows correction of BMD for size in patients with short stature.

Figure 1: *DEXA BMD does not take into account of the depth of the bone. The smaller bone has an apparently lower areal BMD than the larger one despite having the same volumetric density (Carter et al).*



Aim

To investigate the influence of HSCT/TBI on size-corrected BMD in childhood leukaemia survivors

Method

Participants 2 Groups (all post-pubertal):

- Group 1: BMT/TBI ALL survivors diagnosed at <18 yrs, in remission ≥3 yrs
- Group 2: Standard chemotherapy treated ALL survivors diagnosed at <18 yrs in remission ≥3 yrs

Exclusion:

- Currently on steroids, untreated endocrinopathies, pregnancy

Assessments & definitions

- Auxology: height, weight
- DEXA scanning(Lunar Prodigy® fan beam): BMD-Z-scores, bone mineral content (BMC), bone area (BA), bone width
- Vitamin D levels

Definition of size-corrected BMD using BMAD:

- Total-BMAD ($BMAD_T$)=BMC/total body BA^2/ height
  (Ref: Katzman et al.J Clin Endocrinol Metab 1991:73:1332-1339)
- Lumbar spine-BMAD ($BMAD_{L2-4}$)=BMD_{L2-4} x[4/(π x width)]
  (Ref: Carter et al. Bone Miner Res. 1992; 7: 137–145.)

Analysis: Student's t-tests, Pearson's correlations

Approval: Regional Research Ethics Committee

Results

Table 1: Demographics

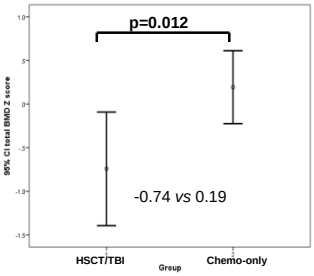
	HSCT/TBI (n=21,11M)	Chemo-only (n=31, 13M)
Current age (years)*	21.5(16.2-26)	21.5(16.2-26)
Age at primary diagnosis (years) *	5.3 (1.0-10.8)	7.0 (1.6 -18.0)
Age of HSCT/TBI (years)*	9.3 (2.6-16.7)	NA
Endocrinopathies:		
Growth hormone Deficiency	12	0
Hypothyroidism	10	0
Hypogonadism	17	0

* Median (range)

Table 2. Baseline measurements: HSCT/TBI survivors compared with are shorter with lower lean mass than chemotherapy-only survivors

Group(s) Variable	HSCT/TBI (n=21)	Chemo-only (n=31)	t-test p
Height SDS	-1.4 (1.5)	0.2 (0.9)	<0.001
Weight SDS	-1.6 (2.5)	1.1 (1.3)	<0.001
Fat Mass (kg)	15.1 (10.1)	21.6 (10.4)	0.06
Lean mass (kg)	36.9 (10.2)	45.0 (10.8)	0.009

Figure 2. HSCT/TBI survivors had lower total-BMD Z scores



However, size corrected is needed for interpretation as total-BMD correlated positively with height-SDS, weight-SDS, fat and lean masses (all p≤0.001).

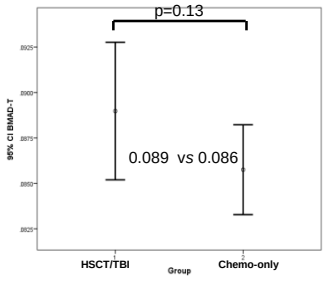


Figure 3. Total BMAD-Z scores

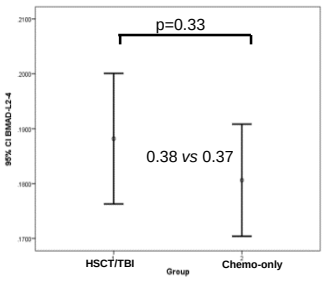


Figure 4. Lumbar spine BMAD Z scores

There were no mean(SD) differences in size-corrected BMD between HSCT and chemotherapy-only patients (Figures 3 and 4).

Table 3. BMAD was not associated with treatment factors, vitamin D levels or endocrinopathies in HSCT survivors identified

	$BMAD_T$ p-value	$BMAD_{L2-4}$ p-value
Age of primary treatment	0.36	0.67
Age of HSCT/TBI	0.23	0.68
HSCT before or after 8 years	0.35	0.75
Vitamin D levels	0.13	0.21
Endocrine disorders:		
Growth hormone deficiency	0.16	0.46
Hypothyroidism	0.53	0.58
Gonadal failure	0.33	0.43

Summary and Conclusions

- Size of patient must be taken into account to avoid over diagnosis of osteopenia when assessing BMD in cancer survivors.
- Treatment effects on peak bone mass in survivors need further evaluation.

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