The Determinants Of Skeletal Fragility In Children With Type 1 Diabetes

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Background & Objective

Type 1 Diabetes (T1DM) is associated with increased fracture risk, even in childhood, but the pathophysiology of the skeletal fragility remains unclear. We aim to determine the effects on T1DM on bone health in children, and specifically, its relationship to fracture.

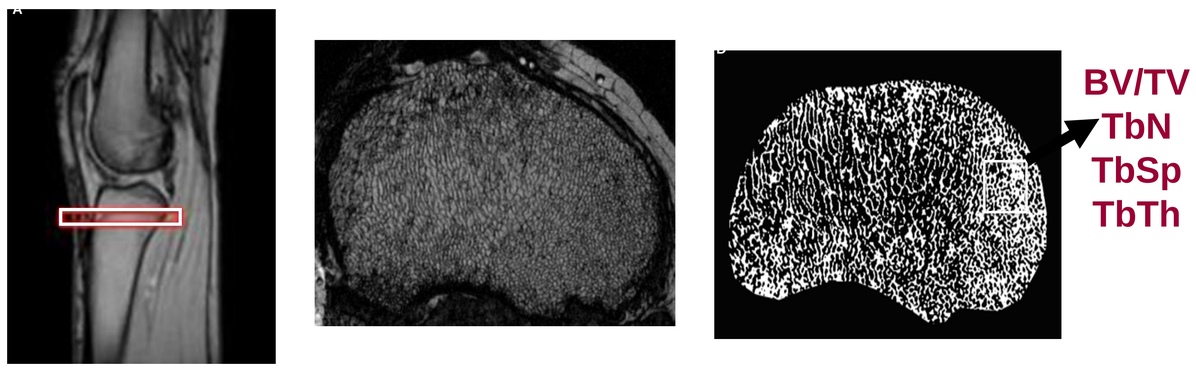

Figure 1. MRI of proximal tibia to assess trabecular bone microarchitecture and image processing using Matlab software.

Methods

Thirty-two children with T1DM at a median (range) age of 13.7 years (10.4,16.7), and median HbA1c 65mmol/mol (27,100) were recruited. Serum bone alkaline phosphatase (BAP) and c-terminal telopeptide type 1 collagen (CTX) as well as DXA total body (TB) and lumbar spine (LS) bone mineral content (BMC) adjusted for bone area were converted to SDS. 3T MRI of the proximal tibia was performed to assess bone microarchitecture (Fig.1), by measuring bone volume/total volume (appBV/TV), trabecular number (appTbN), trabecular separation (appTbSp) and trabecular thickness (appTbTh). MR spectroscopy at lumbar spine was performed to assess bone marrow adiposity, by measuring marrow fat fraction (FF, %). MRI data were compared to 26 age- and sex-matched healthy controls, with median age of 13.8 (10.2,17.8). Values are presented as median (range).

Results

	T1D (n=32)	Control (n=26)	*p*
Age (years)	13.7 (10.4,16.7)	13.8 (10.2,17.8)	0.994
Gender (M/F)	16/16	13/13	0.999
Height SDS	0.3 (-1.5,2.5)	-0.1 (-1.6,2.7)	0.173
Weight SDS	0.8 (-1.3,3.2)	0.6 (-1.2, 3.1)	0.569
BMI SDS	0.5 (-0.6,2.9)	1.0 (-1.6,2.7)	0.798
Tanner stage (Pre/Early/Late) (n)	3/17/12	4/13/9	0.831
BMI SDS	0.5 (-0.6,2.9)	1.0 (-1.6,2.7)	0.798
Age at diagnosis (yr)	5.9 (1.3,10.8)		
Disease duration (yr)	7.2 (3.1,12.4)		
HbA1c (%)*	8.1 (4.6,11.3)		
HbA1c (mmol/mol)*	65 (27,100)		
HbA1c at diagnosis (%)	10.7 (7.3,17.2)		
HbA1c at diagnosis (mmol/mol)	93 (56,164)		
Severity at diagnosis			
- Not DKA/DKA/Unknown (n)	21/10/1		
Insulin dose (unit/kg/day)	1.0 (0.6,1.8)		
Insulin pump/injections	10/22		
Physical activity score	2.4 (1.3,4.1)	2.5 (1.6,4.1)	0.425
Previous fracture(s)(Y/N)	10/22	5/21	**<0.001**

Table 1: Clinical characteristics of all children with T1D. Children with T1D are significantly more likely to fracture compare to healthy controls. *Average over last 12m

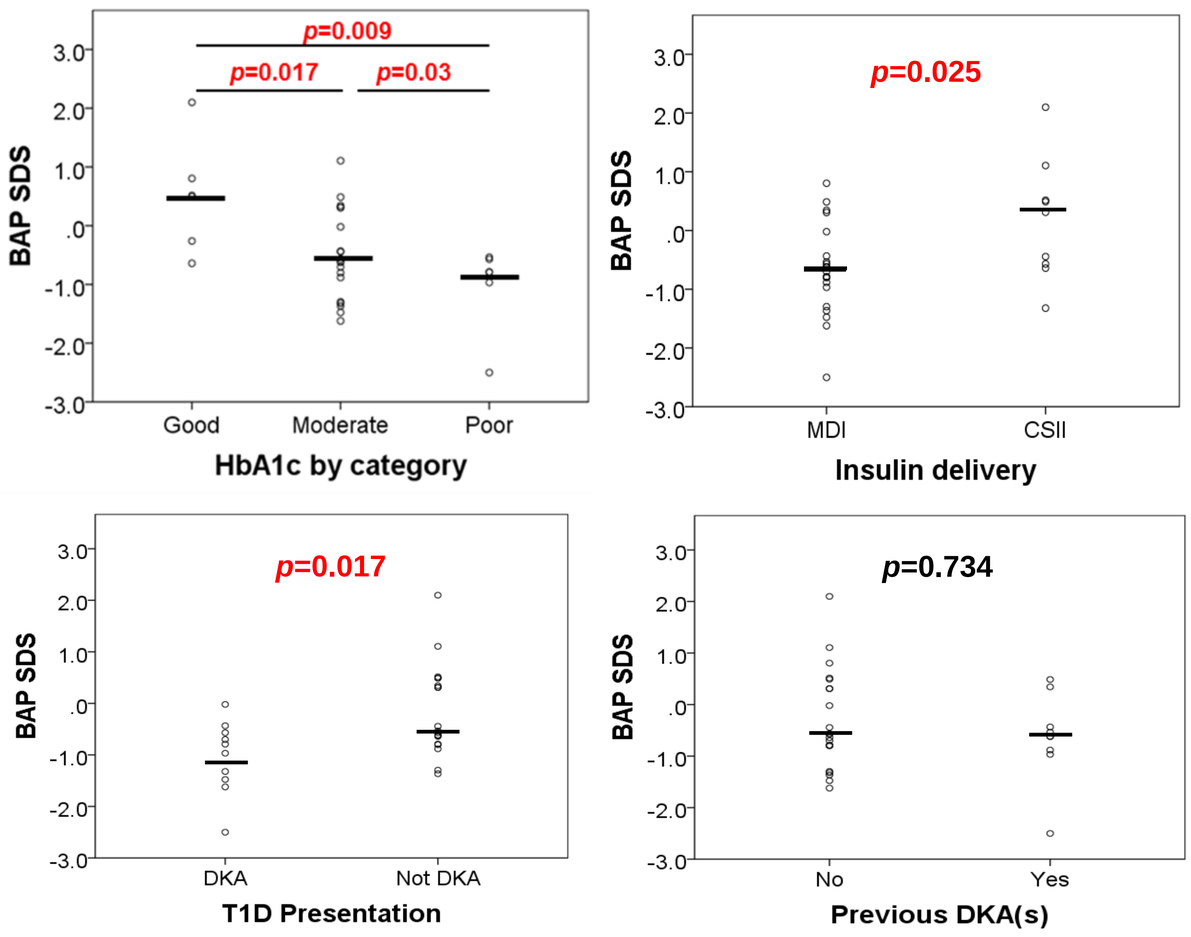

Figure 2: The relationship between T1D characteristics and bone formation markers. Children with poor glycaemic control had significantly lower bone formation marker. Children who presented in DKA at the time of T1D diagnosis also had reduced bone formation marker although subsequent number of DKAs did not affect BAP SDS. T1D children on CSII (insulin via pump) had higher BAP SDS than those on MDI (insulin via injection).

Parameters	T1D (n=32)	Controls (n=26)	*p*
Bone turnover markers			
BAP SDS	-0.57 (-2.50,2.10)		**0.002**
CTX SDS	-1.05 (-2.49,0.51)		**<0.001**
DXA			
TB BMC for BA SDS	-0.1 (-1.1,0.9)		**0.018**
LS BMC for BA SDS	-0.3 (-1.0,1.8)		**0.011**
MRI			
AppBV/TV	0.55 (0.47,0.63)	0.59 (0.47,0.63)	**0.024**
AppTbN (mm^{-1})	1.67 (1.56,1.93)	1.82 (1.56,1.99)	**0.004**
AppTbSp (mm)	0.27 (0.21,0.32)	0.24 (0.20,0.33)	**0.001**
AppTbTh (mm)	0.32 (0.27,0.39)	0.32 (0.25,0.38)	0.954
Marrow Adiposity (FF, %)	23.1 (11.0,66.0)	20.0 (8.0,61.1)	0.250

Table 2: Biochemical, DXA and MRI-based Measures of Bone turnover markers, Bone Density, Bone Microarchitecture and Vertebral Bone Marrow Adiposity. Children with T1D have low bone turnover, with reduced bone mineralisation and impaired bone microarchitecture.

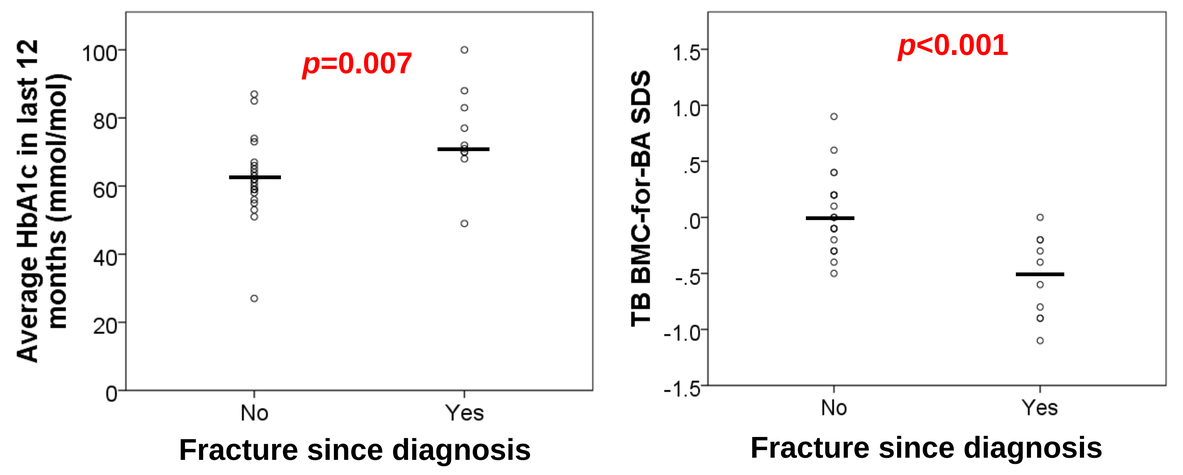

Figure 3: Subanalysis of children with T1D depending on fracture status. In the T1D children with fracture, glycaemic control was significantly higher with lower total body bone mineral density

Conclusion

Children with T1D display a low bone turnover state which is associated with a deficit in bone mineralisation and microarchitecture.

Fractures were more likely in those with poorer glycaemic control and bone mineral status.