Volumetric BMD and bone strength on QCT-based finite element analysis are impaired in patients with Cushing's syndrome in long-term remission

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INTRODUCTION

Cortisol excess in active Cushing's syndrome (CS) is associated with bone loss and skeletal fragility. Although bone mineral density (BMD), as measured using dual-energy X-ray absorptiometry (DXA), may partly recover within few years after remission, fracture risk remains elevated.

OBJECTIVE

To evaluate volumetric BMD and mechanical properties in patients with long-term remission of CS.

DESING AND METHODS

Thirty-six women with CS in remission were included. Subjects were matched by body mass index and menopausal status with 36 controls. Quantitative computed tomography (QCT) was used to assess volumetric BMD (vBMD) at total hip (TH), femoral neck (FN), trochanter (TR) and intertrochanteric (IT) as well as mechanical properties (buckling ratio, cross sectional area and average cortical thickness) at FN. A finite element model was generated from QCT images to calculate tissue stiffness and principal stress. A patient-specific sideways-fall impact was simulated using the patient mass and height.

RESULTS

Table 1 Baseline characteristics in 36 female patients with Cushing's syndrome (CS) and 36 age- and BMI-matched female controls

	CS patients	Controls	p-value
Age (years)	51 ± 15	50 ± 20	0.7150
BMI (Kg/m^2)	27 ± 4	26 ± 4	0.575
Time of remission (years)	13 ± 8	-	
Pituitary adenoma (n,%)	28 (78)	-	
Adrenal Adenoma (n,%)	8 (22)	-	
Hydrocortisone replacement (n,%)	3 (8)	-	
GH replacement (n,%)	2 (5)	-	
Menopause (n,%)	21 (58)	21 (58)	0.835
Duration of menopause (months)	96 ± 61	102 ± 62	

BMI, Body Mass Index; GH growth hormone. Data are expressed as mean±SD or median (interquartile range) depending on the distribution

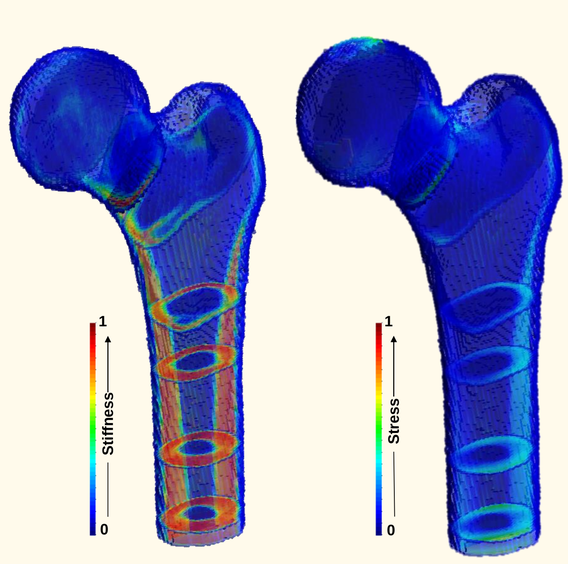

Figure 1 3D Stress and Stiffness Bone distribution for a control case.

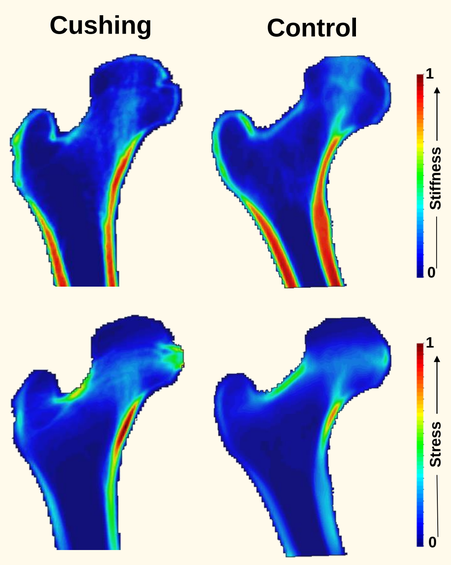

Figure 2 Normalized Stress and Stiffness distribution for a longitudinal cross sectional plane of CS and control case.

Table 2 Densitometric, volumetric, and biomechanical bone parameters in CS patients and healthy controls

Bone parameters	CS patients	Controls	p-value
DXA			
Total hip T-score	-0.75 ± 1.55	-1.03 ± 1.15	0.404
Total hip aBMD (mg/cm^3)	0.91 ± 0.23	0.91 ± 0.11	0.955
Femoral neck T-score	-0.77 ± 0.98	-0.63 ± 1.12	0.613
Femoral neck aBMD (mg/cm^3)	0.75 ± 0.09	0.81 ± 0.15	0.063
QCT			
Total hip-vBMD			
Trabecular	131.73 ± 16.39	127.79 ± 42.59	0.609
Cortical	827.89 ± 266.97	973.6 ± 117.3	**0.004**
Femoral neck-vBMD			
Trabecular	138.98 ± 20.93	165.28 ± 59.98	**0.014**
Cortical	867.8 ± 309.03	1073.177 ± 265.17	**0.003**
Trocantheric-vBMD			
Trabecular	130.47 ± 16.86	160.15 ± 63.99	**0.016**
Cortical	849.59 ± 349.91	1087.31 ± 622.19	0.46
Intertrochanteric vBMD			
Trabecular	131.56 ± 17.56	221.2 ± 239.46	**0.030**
Cortical	815.85 ± 282.52	931.85 ± 50.45	**0.019**
QCT biomechanical properties			
Cross-sectional area (cm^2)	7.58 ± 1.27	7.54 ± 1.3	0.919
Avarage cortical thickness (cm)	0.24 ± 0.54	0.30 ± 0.08	**0.001**
Buckling ratio	6.81 ± 1.92	5.60 ± 1.61	**0.006**
Finite Element Analysis			
Total hip-Stiffness (Young Modulus)			
Cortical	14934.09 ± 330	16186 ± 660.08	**0.03**
Trabecular	288.18 ± 58.24	344.71 ± 29.07	**0.009**
Total hip-Max principal stress	135.28 ± 25.74	115.48 ± 21.79	**0.025**

Variables are expressed as mean ±SD

After adjusting for menopause, diagnosis of CS was the main predictor of all the parameters examined ($p<0.05$ for all correlations), except trabecular vBMD at TH.

CONCLUSIONS

CS female patients in remission have reduced vBMD, and impaired mechanical properties and strength regardless of the menopausal status. These abnormalities may contribute to persistently elevated fracture risk long-term after resolution of cortisol excess.