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Fracture predictors in patients with endogenous cortisol excess

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The objective of this study was to investigate the factors influencing fractures in endogenous Cushing's syndrome (CS) of various etiologies
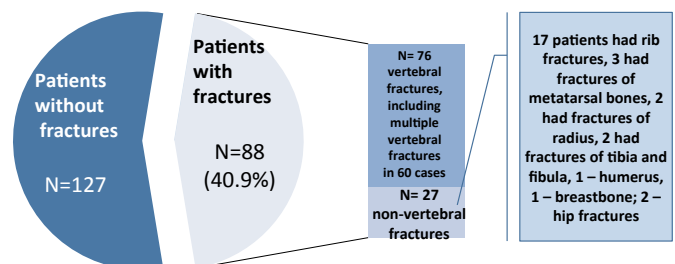
Materials and methods:

Patients: the retrospective data of patients, who had received treatment due to endogenous CS, (2001 to 2011) was evaluated. All enrolled patients underwent standard spinal radiographs in the lateral positions of the vertebrae Th4-L4. Recent low traumatic non-vertebral fractures were recorded in the medical cards. Bone mineral density (BMD) was measured by DXA GE Lunar Prodigy. 24h urinary free cortisol (24hUFC) was measured by an immunochemiluminescence assay (extraction with diethyl ether).

Assay: Serum samples on octeocalcin (OC), carboxyterminal cross-linked telopeptide of type I collagen (CTx)), late-night cortisol in serum, adrenocorticotropin (ACTH) were assayed by electrochemiluminescence (ECLIA). Cobas e601 Roche.
24hUFC was measured by an immunochemiluminescence assay (extraction with diethyl ether) on a Vitros ECi

Results:

N= 215 patients, 178 were female and 37 male, median age 35 (Q25-Q75 27-48) years old

Patients without fractures N=127

Patients with fractures N=88 (40.9%)

N= 76 vertebral fractures, including multiple vertebral fractures in 60 cases

N= 27 non-vertebral fractures

17 patients had rib fractures, 3 had fractures of metatarsal bones, 2 had fractures of radius, 2 had fractures of tibia and fibula, 1 – humerus, 1 – breastbone; 2 – hip fractures

The similarities and differences of patients with CS with and without low-traumatic fractures

	Cushing's syndrome with low-traumatic fractures (n=88)	Cushing's syndrome without low-traumatic fractures (n=127)	P
Sex F: M(%)	65 : 23 (26,1%)	113 : 14 (11%)	0,004
Diagnosis: Cushing's disease: Adrenal CS :ACTH-ectopic CS	70 : 1 : 17	108 : 6 : 13	0,232
Age (years)	38 (27-50) 18-77	33 (27-46) 18-71	0,324
Body mass index (kg/м²)	28,1 (25,3 – 33,5) 19,2 – 50,6	30,1 (26,1- 33,9) 19,7 – 48,1	0,283
Serum calcium (mmol/l)	2,37 (2,27-2,43) 2,02-2,59	2,37 (2,29 – 2,46) 1,97 – 2,73	0,339
24 h urinary free cortisol (nmol/24 hours)	2348,4 (1060,0 – 4000,0) 192,0 -8720,0	1450,5 (872,1 – 2569,5) 138,0 – 10212,0	0,005
23:00 serum cortisol (nmol/l)	720,0 (519,0 – 1020,0) 216,0 – 1585,0	562,0 (407,9 – 757,0) 140,0 – 2430,0	0,001
8:00 ACTH (pg/ml)	101,9 (66,1 – 141,0) 1,0 – 499,0	88,2 (57,2 – 119,0) 1,0 – 631,3	0,095
23:00 ACTH(pg/ml)	86,3 (56,3 – 125,6) 1,0 – 508,0	68,5 (36,6 – 101,3) 1,0 – 800,5	0,007
Osteocalcin (ng/ml)	6,0 (3,0 -7,8) 1,5 – 47,9	8,4 (5,6 – 13,1) 1,5 – 36,9	<0,001
Serum CTx (ng/ml)	0,41 (0,2 -0,51) 0,01 – 1,72	0,38 (0,24 -0,63) 0,01 – 1,38	0,518
Neck Z-score	-1,1 (-1,9 - -0,6) -2,7 – 1,8	-0,9 (-1,4 - -0,6) -4,0 – 1,0	0,281
Total Hip Z-score	-1,0 (-1,8 – 0,3) -3,9 – 1,6	-0,5 (-0,9 – 0,0) -2,2 – 2,6	0,042
L1-L4 Z-score	-1,8 (-2,7 - -0,7) -4,5 -2,1	-1,7 (-2,3 - -0,8) -3,8 – 1,6	0,626

After applying the logistic regression analysis (adjusted for sex, age, BMI, BMD, OC), the main predictor of fractures was 24h UFC level (p=0,02) and a separately analyzed late-night serum cortisol level (p=0,001).
Patients with late-night serum cortisol higher than 597 nmol/l were more likely to have low traumatic fractures (Odds ratio 2.86 (95%CI 1.55-5.28) p= 0.001)

Conclusions: The severity of hypercortisolemia is the best predictor of low traumatic fractures in patients with CS. Patients with higher levels of late-night serum cortisol might need earlier preventive treatment for osteoporosis