

Bone Loss Rate in Adrenal Incidentalomas: A Longitudinal Study

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Although by definition patients with adrenal incidentalomas (AI) do not have evident clinical syndromes, they may frequently suffer from subclinical hypercortisolism (SH). This is of some importance because of evidence that SH may lead to clinical complications, including bone loss. Thus, the understanding of bone involvement due to SH may be extremely important in the management of AI. Unfortunately, the available data on bone mineral density (BMD) in AI patients come from cross-sectional studies, which, to further complicate our understanding, are also conflicting, probably due to a different selection of patients and/or the variability in cortisol secretion (CS) often described in AI. To gain further insight about this topic, we performed a longitudinal study evaluating the rate of spinal and femoral bone loss levels in 24 females with AI.

AI subjects were subdivided in two groups on the basis of the median of urinary cortisol secretion (UFC): group I (n = 12; UFC, <140.4 nmol/24 h) and group II (n = 12; UFC, >140.4

nmol/24 h). Spinal BMD was measured by both single energy quantitative computed tomography (L1-L4) and dual energy x-ray absorptiometry (DXA; L2-L4), and femoral BMD was determined by DXA. Bone loss rate was expressed as the change in z-score per yr.

The spinal bone loss rate was higher ($P < 0.005$) in group II than in group I when measured by both quantitative computed tomography (-0.19 ± 0.14 vs. 0.00 ± 0.15) and DXA (-0.19 ± 0.17 vs. 0.00 ± 0.11). Moreover, CS and spinal bone loss rate were significantly correlated when patients were considered together.

In conclusion, our data show that 1) AI patients with higher CS have increased lumbar trabecular bone loss rate than those with lower CS; and 2) the degree of spinal bone loss rate is related to the degree of CS. Thus, lumbar spine (LS) BMD has to be evaluated for well balanced decision-making on the treatment of choice for AI female patients. (*J Clin Endocrinol Metab* 86: 5337-5341, 2001)

IN THE LAST years incidentally discovered adrenal masses [adrenal incidentalomas (AI)] have been detected with increasing frequency due to the widespread use of abdominal imaging techniques (1-4). Although by definition AI patients do not show evident clinical syndromes, some of these subjects may show a certain degree of cortisol hypersecretion, commonly called subclinical hypercortisolism (SH) (5-13). It is still not clear whether SH may lead to clinical complications, including osteoporosis; the knowledge of bone involvement, if any, in AI may be extremely important in the management of these patients.

While it is well known that overt glucocorticoid excess leads to osteoporosis (14, 15), data on bone involvement in AI patients with SH are conflicting. In fact, previous data suggesting that SH in AI patients may lead to alteration of bone metabolism (16) and bone loss (17) have not been confirmed by other reports (18, 19).

To gain further insight about this topic, a longitudinal study of 24 female AI patients with various degrees of cortisol secretion (CS) was performed, evaluating spine and femoral bone mineral density (BMD) at baseline and after an

average of 29.6 months of follow-up. Only female patients were studied to avoid the confounding factor of the possible gender-dependent effect of high CS on BMD (20).

Subjects and Methods

Subjects

Twenty-four consecutive female patients with AI were longitudinally studied at baseline and after variable follow-up periods (Table 1). Fifteen of these subjects were previously enrolled in a cross-sectional study (17).

Diagnosis of AI was made on the basis of 1) unilateral adrenal mass detected during noninvasive methods of imaging of the abdomen performed for unrelated diseases, and 2) lack of signs and/or symptoms of hormonal hypersecretion.

Taking into account the changeability of hormonal secretion over time, in each subject all hormonal data are reported as the mean of multiple observations (*i.e.* at least two, at the beginning and the end of follow-up). Data for biochemical markers of bone metabolism were obtained at baseline. AI subjects were subdivided into two numerically identical groups on the basis of urinary cortisol secretion (UFC): group I (n = 12) with UFC values less than 135.5 nmol/24 h, and group II (n = 12) with UFC values greater than 145.4 nmol/24 h; the median value of the entire cohort was 140.4 nmol/24 h.

No postmenopausal patients were within the first 4 yr after the last menses. Age, years since menopause, body mass index, duration of follow-up, and gonadal status were not different between the two groups (Table 1a). Finally, all eugonadal patients had regular menses for the entire period of the study. Furthermore, we subdivided our sample also according to the commonly used criteria for defining SH: group SH- (n = 17) and group SH+ (n = 7). The diagnosis of SH was made on the presence of two of the following three alterations in the pituitary-adrenal axis: 1) increased UFC levels [>193.1 nmol/24 h, which is the cut-off of both our and international (21) normal reference values], 2)

Abbreviations: AI, Adrenal incidentalomas; BGP, bone GLA protein; BMD, bone mineral density; Cr, creatinine; CS, cortisol secretion; Δ , change; D-Pyr, deoxypridinoline; DXA, dual energy x-ray absorptiometry; F after Dex, serum cortisol levels after 1-mg overnight dexamethasone suppression test; FN, femoral neck; LS, lumbar spine; QCT, quantitative computed tomography; SH, subclinical hypercortisolism; UFC, urinary cortisol secretion.

TABLE 1a. Clinical characteristics of all, group I, and group II patients

	All (n = 24)	Group I (n = 12)	Group II (n = 12)
Age at baseline (yr)	54.9 ± 13.1 (26–77)	55.7 ± 13.0 (38–77)	54.1 ± 13.7 (26–72)
YSM at baseline	13.8 ± 6.7 (70–92)	15.5 ± 7.2 (6–27)	12 ± 6.2 (6–22)
Pre-/postmenopause	8/16	4/8	4/8
Months of follow-up	29.6 ± 14.1 (12–61)	29.0 ± 13.6 (15–61)	30.3 ± 15.3 (12–60)
BMI (kg/m ²)	28.0 ± 3.9 (22.4–37.2)	28.4 ± 4.2 (23.1–35.0)	27.6 ± 3.8 (22.4–37.2)

Data are expressed as the mean ± SD (range). Patients are presented either all together (All) or subdivided on the basis of the median of crescent UFC levels with group I including the first 12 patients, and group B including patients 13–24. YSM, Years since menopause; BMI, body mass index at baseline. No differences were found between the groups I and II for each variable.

TABLE 1b. Clinical characteristics of group SH⁻ and group SH⁺ patients

	Group SH ⁻ (n = 17)	Group SH ⁺ (n = 7)
Age at baseline (yr)	56.0 ± 11.8 (38–77)	42.4 ± 16.7 (26–72)
YSM at baseline	13.9 ± 7.15 (6–27)	13.3 ± 6.2 (8–22)
Pre-/postmenopause	5/12	3/4
Months of follow-up	31.6 ± 16.2 (12–61)	24.8 ± 5.4 (19–33)
BMI (kg/m ²)	28.5 ± 4.5 (22.4–37.2)	26.8 ± 2.0 (23.1–29.4)

Data are expressed as the mean ± SD (range). Patients are subdivided in two groups according with the absence (group SH⁻) or the presence (group SH⁺) of subclinical hypercortisolism (see *Subjects and Methods*). YSM, Years since menopause; BMI, body mass index at baseline. No differences were found between the two groups for each variable.

unsuppressed serum cortisol levels after a 1-mg overnight dexamethasone suppression test (F after Dex; >82.8 nmol/liter), and 3) low ACTH levels (<2.2 pmol/liter). We did not observe any difference in age, years since menopause, body mass index, or duration of follow-up between groups SH⁻ and SH⁺ (Table 1b).

No subject had evidence of neoplastic disease. At computed tomography, all lesions were homogeneous and hypodense and had regular margins; these features are compatible with the diagnosis of adrenocortical adenoma (4). The diameters of incidentalomas were not different between groups I and II at baseline (mean ± SD, 2.4 ± 1.3 vs. 2.1 ± 0.8 cm; *P* = NS; range, 1.0–5.5 and 0.9–3.5 cm, respectively) and at the end of follow-up (mean ± SD, 2.8 ± 1.5 vs. 2.6 ± 1.0 cm; *P* = NS; range, 1.0–5.5 and 0.9–4.7 cm, respectively); similar results were observed after subdividing patients into SH⁻ and SH⁺ [at baseline (mean ± SD), 2.3 ± 1.2 vs. 2.1 ± 0.8 cm (*P* = NS; range, 1.0–5.5) and 0.9–3.0 cm, respectively; at the end of follow-up, 2.7 ± 1.4 vs. 2.7 ± 0.9 cm (*P* = NS; range, 1.0–5.5 and 0.9–3.7 cm, respectively)].

Two patients (no. 3 and 6 from group I in Table 2), who displayed diameters of AI greater than 4 cm, had previously refused surgery. Four patients from group I (no. 3, 9, 11, and 12 in Table 2) and five patients from group II (no. 2, 3, 6, 7, and 8 in Table 2) showed an increase in diameter of AI greater than 20% with respect to baseline. The percent increase in AI diameter was not different between groups I and II (mean ± SD, 13.7 ± 18.9% vs. 18.5 ± 16.8%; *P* = NS; range, 0–50% and 0–52.7%, respectively) and between groups SH⁻ and SH⁺ (mean ± SD, 14.9 ± 17.8% vs. 18.9 ± 18.1%; *P* = NS; range, 0–50% and 0–52.7%, respectively).

Pheochromocytoma and aldosteronoma were excluded by appropriate hormonal measurements (24-h urinary catecholamines, PRA and aldosterone in the recumbent position and after 3 h of orthostatic posture).

Pre-menopausal women were studied in the early follicular phase (d 3–7) of the menstrual cycle.

All subjects gave informed consent before the study. None of them was given medications known to affect bone metabolism, including E replacement therapy. In the last 3 yr all patients had been given 1 g/d calcium and 880 IU/d vitamin D₃, orally, to avoid bone metabolism alterations due to possible subclinical vitamin D deficiency. Vertebral fractures were excluded in all subjects by lateral x-ray of the spine.

Methods

In all subjects serum total calcium, phosphorous, and creatinine were determined by a multichannel autoanalyzer to exclude concomitant diseases that could affect bone metabolism. In all patients serum determinations of ACTH (mean of three determinations at 20-min intervals), cortisol, intact PTH, and bone GLA protein (BGP) levels were

performed at 0800 h, and total deoxypyridinoline (D-Pyr/Cr) levels were measured in fasting spot urine, then corrected for creatinine excretion. Serum and urinary samples were collected and stored at -70 C until assayed.

Cortisol and UFC levels (after dichloromethanol extraction) were measured immunofluorimetrically by kits (TDX-FLX Abbott, GmbH, Diagnostika, Wiesbaden-Delkenheim, Germany); serum ACTH levels were measured by IRMA (BRAHMS Diagnostica GmbH, Berlin, Germany). Serum intact PTH levels were measured by a two-site immunochemiluminometric assay (Chiron Corp., East Walpole, MA). BGP was assayed by IRMA for the intact molecule (ELSA-OST-NAT, Cis Biointernational, Gif-sur-Yvette, France; intra- and interassay coefficients of variation, 3.8% and 4.7%, respectively), and D-Pyr/Cr was assayed fluorometrically, after reverse phase HPLC, by kits from Bio-Rad Laboratories, Inc. (Segrate, Italy; intra- and interassay coefficients of variation, 6.6% and 12.3%, respectively).

BMD was evaluated at both axial and appendicular skeletal sites, as previously described (22). Spinal BMD was measured by both single energy quantitative computed tomography (QCT; L1–L4; Toshiba CT Xpeed, Toshiba Medical Systems Division, Tokyo, Japan), which is able to detect selectively trabecular true density (*in vivo* precision, 1.8%), and dual energy x-ray absorptiometry (DXA; L2–L4; Norland XR-26, Norland Instruments, Fort Atkinson, WI), which assesses the BMD of total vertebral bodies (*in vivo* precision, 1.0%). BMD was also evaluated by DXA at the femoral neck (FN; *in vivo* precision, 2.4%). Individual BMD values were expressed as SD units (z-scores) in relation to reference population of our center (23) and as the change in (Δ) z-scores per yr between baseline and the end of follow-up.

Statistical analysis

The results are expressed as the mean ± SD. For each variable, normality of distribution was tested by the W statistic of Shapiro-Wilk. Comparison between groups of patients was performed using unpaired *t* test or Mann-Whitney *U* test as appropriate. To compare different subgroups (eumenorrhic and postmenopausal patients in groups I and II), two-way ANOVA and Student-Newman-Keuls *post-hoc* analysis were performed. Fisher's exact test was used to evaluate the difference in the ratio of eu-/hypogonadal patients in the SH⁺ and SH⁻ groups. The associations between variables were tested by either Pearson or Spearman correlation, as appropriate. *P* < 0.05 was considered significant.

Results

Hormonal and BMD data for patients in groups I and II are summarized in Table 2. By selection criterion, UFC levels

TABLE 2. Gonadal status, biochemical indexes of adrenal function, and BMD at different skeletal sites of group I and group II patients

Patient no.	YSM	UFC	ACTH	F after dex	SH	ΔDXA	ΔQCT	ΔFN	PTH
Group I									
1	10	55.2	2.2	55.2	–	–0.03	–0.03	–0.03	53.0
2	20	64.6	2.6	46.9	–	–0.06	–0.13	0.09	57.5
3	14	91.9	3.0	22.1	–	–0.02	–0.04	0.03	25.1
4	11	101.3	1.9	55.2	–	0.07	0.13	0.41	70.1
5	23	102.4	2.4	41.4	–	0.02	–0.26	0.03	47.8
6	4	105.4	5.3	33.1	–	–0.07	0.03	0.08	33.9
7	27	110.4	2.6	55.2	–	–0.03	–0.03	–0.04	45.0
8	13	114.5	5.6	46.9	–	0.06	0.07	0.09	59.9
9	0	130.8	5.3	66.2	–	0.15	0.00	–0.06	31.5
10	0	132.2	1.2	22.1	–	0.04	0.20	0.10	32.8
11	0	135.0	2.6	49.7	–	0.15	–0.18	–0.22	39.8
12	0	135.5	2.8	38.6	–	–0.25	0.27	0.11	57.6
Mean ± SD		106.5 ± 26.2	3.1 ± 1.4	44.2 ± 13.8		0.00 ± 0.11	0.00 ± 0.15	0.04 ± 0.15	45.8 ± 13.7
Group II									
1	4	145.4	1.4	60.7	–	–0.25	–0.14	–0.04	57.3
2	21	162.3	5.4	46.9	–	–0.08	–0.13	–0.08	43.7
3	0	175.0	2.2	38.6	–	0.05	–0.03	0.08	32.3
4	10	177.5	2.0	82.8	+	–0.45	–0.15	0.29	64.3
5	9	190.4	1.9	58.0	–	0.02	–0.24	–0.01	38.4
6	8	196.0	0.8	74.5	+	–0.39	–0.29	–0.04	55.3
7	0	200.9	1.7	44.2	+	–0.25	–0.28	–0.01	52.5
8	7	220.8	2.6	41.4	–	–0.24	–0.23	–0.03	55.0
9	13	223.8	1.2	88.3	+	–0.30	–0.14	–0.03	90.0
10	0	248.7	2.2	35.9	+	–0.01	–0.08	–0.21	38.0
11	22	267.7	1.5	138.0	+	–0.30	–0.31	–0.03	50.0
12	0	297.5	1.9	77.3	+	–0.04	–0.46	–0.08	53.3
Mean ± SD		208.9 ± 45.0	2.1 ± 1.1 ^a	65.1 ± 30.4 ^a		–0.19 ± 0.17 ^b	–0.19 ± 0.14 ^b	–0.03 ± 0.13	51.6 ± 11.4

Data are expressed as the mean ± SD. Group I, Patients 1–12; group II, patients 13–24, ordered on the basis of crescent UFC levels. YSM, Years since menopause at baseline; UFC, urinary free cortisol (normal values, <193.1 nmol/24 h); ACTH, mean of three determinations at 0800 h (normal values, >2.2 pmol/liter); F after Dex, Serum cortisol at 0800 h after 1 mg overnight dexamethasone (normal values, <82.8 nmol/liter); PTH, normal values, 10–70 ng/liter; SH, subclinical hypercortisolism (–, absent; +, present; see *Subjects and Methods*); ΔDXA, change per yr of z-values of lumbar vertebral integral spine L2–L4 bone mineral density; ΔQCT, change per yr of z-values of lumbar trabecular vertebral spine L1–L4 bone mineral density; ΔFN, change per yr of z-values of femoral neck bone mineral density.

^a $P < 0.05$ vs. group I.

^b $P < 0.005$ vs. group I.

were significantly higher in group I. ACTH and F after Dex levels were significantly different, being respectively lower and higher in group II than in group I (Table 2). PTH levels were not different between the two groups.

The mean Δz-scores per yr of lumbar BMD measured by both QCT and DXA were significantly lower in group II than in group I (Table 2). The mean Δz-score per yr of FN BMD in group II tended to be lower, although not statistically ($P = 0.12$), than that in group I subjects.

When comparing by ANOVA, mean DXA and QCT Δz-scores per yr of eu- and hypogonadal patients from group I (eugonadal, $n = 4$; hypogonadal, $n = 8$) and group II (eugonadal, $n = 4$; hypogonadal, $n = 8$), no statistically significant difference was observed after allowing for the difference in CS, whereas the difference between mean DXA and QCT Δz-scores per yr in group I compared with group II was confirmed after allowing for the difference in gonadal status.

Mean values of BGP and D-Pyr/Cr at baseline were not different between groups I and II [BGP, 1.48 ± 0.45 pmol/liter (range, 0.89–2.34) vs. 1.24 ± 0.44 pmol/liter (range, 0.79–2.13; $P = \text{NS}$); D-Pyr, 22.3 ± 9.0 pmol/pmol (range, 11.1–35.5) vs. 19.9 ± 6.4 pmol/pmol (range, 11.7–29.5; $P = \text{NS}$), respectively].

As far as the correlations between BMD and markers of disease activity are concerned, in the whole group of patients a significant correlation was found between QCT Δ z-scores

per yr and UFC ($r = 0.52$; $P < 0.01$), F after Dex ($r = 0.49$; $P < 0.02$), and ACTH ($r = -0.44$; $P < 0.05$) and between DXA Δ z-scores per yr and UFC ($r = 0.47$; $P < 0.05$).

Although the normal distribution of UFC levels suggests that CS in AI is a continuum trait in our cohort, we reevaluated our data by categorizing CS on the basis of commonly used criteria for SH diagnosis (13). No difference was found between SH– and SH+ patients in gonadal status (Table 2). Hormonal and BMD data from groups SH– and SH+ are summarized in Table 3. According to the selection criteria, UFC, F after Dex, and ACTH levels were different between the two groups, being respectively higher (UFC and F after Dex) and lower (ACTH) in group SH+ compared with group SH–. Mean z-scores at baseline and mean Δz-scores per yr of lumbar BMD measured by both QCT and DXA were significantly lower in group SH+ than in group SH–, whereas mean z-scores at baseline and mean Δz-scores per yr of FN BMD were not significantly different between the two groups. PTH levels tended to be higher in group SH+ than in group SH–, although the difference was not statistically significant ($P = 0.06$; Table 3). Finally, mean values of BGP and D-Pyr at baseline were not different between group SH– and group SH+ [BGP (mean ± SD), 1.41 ± 0.45 pmol/liter (range, 0.82–1.99) vs. 1.22 ± 0.41 pmol/liter (range 0.79–2.34; $P = \text{NS}$); D-Pyr/Cr (mean ± SD), 22.1 ± 8.22 pmol/pmol

TABLE 3. Biochemical indexes of adrenal function and BMD z-scores at baseline and Δ z-scores per yr at different skeletal sites in group SH⁻ and group SH⁺ patients

	Group SH ⁻ (n = 17)	Group SH ⁺ (n = 7)
UFC	127.8 ± 42.8	230.5 ± 43.1 ^a
ACTH	2.97 ± 1.4	1.6 ± 0.5 ^b
F-after Dex	44.1 ± 13.8	77.3 ± 33.1 ^c
DXA	0.64 ± 1.3	-0.67 ± 0.32 ^c
Δ DXA	-0.03 ± 0.13	-0.25 ± 0.16 ^b
QCT	0.26 ± 0.98	-0.71 ± 0.63 ^c
Δ QCT	-0.04 ± 0.15	-0.22 ± 0.17 ^c
FN	0.35 ± 1.0	-0.37 ± 0.60
Δ FN	0.03 ± 0.13	-0.02 ± 0.15
PTH	45.6 ± 12.5	56.2 ± 10.2

Data are expressed as the mean ± SD. Patients are subdivided in two groups according with the absence (group SH⁻) or presence (group SH⁺) of subclinical hypercortisolism (see *Subjects and Methods*). UFC, Urinary free cortisol (normal values, <193.1 nmol/24 h); ACTH, mean of three determinations at 0800 h (normal values, >2.2 pmol/liter); F after Dex, serum cortisol at 0800 h after overnight 1 mg dexamethasone (normal values, <82.8 nmol/liter); PTH, normal values, 10–70 ng/liter; DXA, Δ DXA, mean z-scores at baseline and mean Δ z-scores per yr, respectively, of lumbar vertebral integral spine L2–L4 bone mineral density. QCT, Δ QCT, mean z-scores at baseline and mean Δ z-scores per yr, respectively, of lumbar trabecular vertebral spine L1–L4 bone mineral density; FN, Δ FN, mean z-scores at baseline and mean Δ z-scores per yr, respectively, of femoral neck bone mineral density.

^a $P < 0.0001$.

^b $P < 0.01$.

^c $P < 0.05$.

(range, 11.1–35.5) vs. 18.6 ± 6.31 pmol/pmol (range, 11.7–28.0; $P = \text{NS}$), respectively].

Discussion

This study was aimed at understanding whether different degrees of CS in AI patients could affect bone tissue. For this purpose we performed a longitudinal study on 24 female patients quantitatively ordered on the basis of the median of UFC values into groups of 12 patients with lower CS (group I) and 12 patients with higher CS (group II). The 2 groups of patients also had different ACTH and F after Dex levels, thus confirming that they were truly different as far as the degree of CS was concerned.

Our data show that AI patients with higher levels of CS have higher bone loss rates, and these two parameters are significantly correlated in the whole cohort studied. This finding is compatible with and reinforces our previous cross-sectional data (17), showing a reduction in BMD in AI patients with SH compared with those without SH. In contrast, no BMD reduction in AI patients with SH has been reported in other cross-sectional studies (18, 19). These discrepancies among cross-sectional studies may be due to different causes. Firstly, different cut-off values for the diagnosis of SH may justify the different results. In fact, it is still not clear which are the best hormonal tests and their best cut-off values to identify AI patients with SH (11, 24). Secondly, previous negative studies involved both male and female subjects (18, 19), at variance with our antecedent (17) and present investigations, in which only females were evaluated. In fact, a gender-dependent sensitivity of bone tissue to glucocorticoid excess has been reported (20), with males being much less

sensitive than females. This may well explain the lack of glucocorticoid effect in those studies comprising both male and female patients. Finally, as bone mass is the result of different genetic (25), metabolic (26), and hormonal (27) factors, and cortisol hypersecretion, if present, is subtle in AI patients, it is possible that a cross-sectional evaluation in a small series may not always be able to detect small differences in a wide range of BMD distributions. To overcome the two latter potential pitfalls, we designed the present longitudinal study carried out only in female patients. The results obtained clearly demonstrated that BMD loss is increased in AI female patients with higher CS.

Patients with higher cortisol secretion had higher trabecular bone loss rate as measured at LS regardless of gonadal status, as suggested by ANOVA. These data were indirectly confirmed by the correlation between disease activity parameters (UFC, F after Dex, ACTH) and rate of trabecular bone loss at LS. A similar, although not significant, difference was found at FN. This is partly at variance with our previous cross-sectional study, in which a statistically significant reduction of bone mass was observed at both LS and FN. Even if the two studies are not comparable because of the different designs, we believe that this seeming discrepancy may be due to the lower disease activity of AI subjects in this investigation compared with those in the previous one (17), as indicated by lower mean values of UFC in SH patients in the present report (230.5 vs. 332.9 nmol/24 h). Finally, we found that PTH levels were higher, although not statistically so, in patients with SH compared to those without SH. This is in line with previous reports by us (17) and others (18) and suggests the state of altered bone turnover in patients with AI and SH. Nevertheless, at variance with our previous study in which we found comparable D-Pyr/Cr levels and reduced BGP levels in SH+ compared with SH- patients (17), in the present investigation markers of bone turnover (BGP and D-Pyr/Cr) at baseline were comparable between SH- and SH+ patients. Although entirely speculative, we believe that this discrepancy may be due to the lower disease activity of AI subjects with SH in this investigation compared with those in the previous study (17).

In conclusion, our data 1) confirm our previous observation that AI patients with higher CS have reduced lumbar trabecular BMD; 2) show that among AI patients, those with higher CS have increased lumbar trabecular bone loss rate; and 3) show that the degree of spinal bone loss rate is directly related to the degree of CS. Based on these results, the need for BMD evaluation at the spine in all female AI patients is strongly suggested. In fact, the knowledge of reduced bone mass may help in making decisions about the need for surgical excision in AI tumors smaller than 4 cm (4, 7).

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IOF-Servier Young Investigator Fellowship

The International Osteoporosis Foundation is pleased to announce the joint winners of the first IOF-Servier Young Investigator Fellowship: Dr. Freda Wynne of the University College of Cork and Dr. Luigi Gennari of the University of Florence.

Call for applications: The next Fellowship will be awarded during the IOF-World Congress on Osteoporosis in Lisbon, May 2002. Financed by an unrestricted grant offered by Servier Research Group, the IOF-Servier Young Investigator Research Fellowship is an award of 40,000 Euros to encourage young scientists under the age of 40 to engage in high-quality research in the field of osteoporosis.

Deadline for submission of applications: January 15, 2002. For eligibility criteria and application forms please see the IOF web site at www.osteofound.org or contact the IOF secretarial office (info@ioflyon.org) at: International Osteoporosis Foundation, 71 cours Albert Thomas, 69447 Lyon Cedex 03 France. Phone: 33 4 72 91 41 77.