

Effects of Alendronate on Bone Metabolism in Glucocorticoid-Induced Osteoporosis Measured by ^{18}F -Fluoride PET: A Prospective Study

Kenzo Uchida¹, Hideaki Nakajima¹, Tsuyoshi Miyazaki¹, Takafumi Yayama¹, Hideo Kawahara¹, Shigeru Kobayashi¹, Tatsuro Tsuchida², Hidehiko Okazawa³, Yasuhisa Fujibayashi³, and Hisatoshi Baba¹

¹Department of Orthopaedics and Rehabilitation Medicine, Faculty of Medical Sciences, University of Fukui, Fukui, Japan;

²Department of Radiology, Faculty of Medical Sciences, University of Fukui, Fukui, Japan; and ³Biomedical Imaging Research Center, University of Fukui, Fukui, Japan

Osteoporosis represents a significant side effect of glucocorticoid therapy, and alendronate has been reported to prevent this glucocorticoid-induced osteoporosis. Functional imaging with ^{18}F -fluoride PET allows quantitative analysis of bone metabolism in specific skeletal regions. However, only a few studies have quantitatively determined bone turnover and metabolism in glucocorticoid-induced osteoporosis by radiologic imaging techniques including PET. The aim of this study was to examine changes in regional bone remodeling and turnover as measured by ^{18}F -fluoride PET, the relationship between these measured changes and conventional bone metabolism parameters, and the effect of alendronate treatment. **Methods:** The study group consisted of 24 postmenopausal women (mean age, 59.7 y) who had various diseases, excluding rheumatoid arthritis, and had been treated with 10 mg or more of oral glucocorticoids (prednisolone equivalent) per day for more than 6 mo. Treatment with 5 mg of alendronate per day began at the time of study entry and continued for 12 mo. ^{18}F -fluoride PET was performed at baseline, 3 mo, and 12 mo to determine localized bone turnover, and the results were compared with other bone metabolism parameters. **Results:** Lumbar spine standardized uptake values (SUVs) were significantly lower ($P < 0.05$) in the osteoporotic group (T-score ≤ -2.5) than in the group that was healthy or osteopenic (T-score > -2.5). Patients treated with alendronate for 12 mo exhibited significant decreases in serum bone-specific alkaline phosphate ($P < 0.05$), urinary N-telopeptide for type I collagen ($P < 0.01$), lumbar spine SUV ($P < 0.01$), and femoral neck SUV ($P < 0.01$) in association with a gradual increase in bone mineral density (BMD) of the lumbar spine relative to the baseline value ($P < 0.05$). Although there was a significant correlation between BMD and SUV in the lumbar spine at baseline ($P < 0.05$), there was no correlation between the 2 variables at 12 mo of treatment with alendronate. **Conclusion:** Alendronate treatment resulted in significant decreases in bone metabolism and turnover in the lumbar spine. It also led to an increase in BMD

of the lumbar spine in patients with glucocorticoid-induced osteoporosis. Our findings suggest that antiresorptive therapy has a direct bone-metabolism effect on skeletal kinetics in glucocorticoid-induced osteoporosis at the clinically important site of the lumbar spine.

Key Words: glucocorticoid; osteoporosis; ^{18}F -fluoride positron emission tomography (PET); bone metabolism; alendronate

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The use of glucocorticoids in the treatment of patients with various diseases is associated with increased bone loss and the risk of bone fractures. Glucocorticoid-induced osteoporosis is the result of a combination of systemic effects on mineral metabolism and local effects on bone quality. Glucocorticoids decrease intestinal absorption of calcium and increase renal calcium excretion (1,2). Another important effect of glucocorticoids on bone is inhibition of bone formation by a decrease in the number of osteoblasts and hampering of their function (3). Glucocorticoids also increase the rate of bone resorption by stimulating the formation and action of osteoclasts. Although a daily dose of 7.5 mg or more of prednisone for at least 6 mo can induce osteoporosis (4,5), lower doses of the drug have also been linked to such changes (6). Several international guidelines for the prevention and treatment of glucocorticoid-induced osteoporosis have been developed (7–10). In general, these guidelines recommend the use of bisphosphonate supplementation, in addition to supplementation with calcium and vitamin D₃, especially in patients at high risk of fractures. Alendronate is effective in preventing and treating glucocorticoid-induced osteoporosis (11–13).

Functional imaging with ^{18}F -fluoride PET allows quantitative analysis of bone metabolism in specific skeletal regions (14). The preferential rapid uptake of ^{18}F -fluoride

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For correspondence or reprints contact: Kenzo Uchida, Department of Orthopaedics and Rehabilitation Medicine, Faculty of Medical Sciences, University of Fukui, Matsuoka Shimoaizuki 23, Eiheiji, Fukui 910-1193, Japan.

E-mail: kuchida@u-fukui.ac.jp

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reflects sites of high osteoblastic activity related to bone remodeling (15,16). Furthermore, ^{18}F -fluoride has been used to measure bone blood flow, and a significant correlation was reported between ^{18}F -fluoride uptake and osteoblastic activity, as determined by bone morphometry (17). Extension of these studies to regional bone metabolism showed significant relationships between regional skeletal kinetic parameters measured by ^{18}F -fluoride PET (18) and the number and activity of osteoblasts, as well as bone formation and mineral apposition rate (19,20). The plasma clearance technique used in these studies has also been used clinically to correlate changes in bone metabolism with the type and severity of metabolic bone disease, such as osteoporosis (21), renal osteodystrophy (19), and Paget disease (22,23). However, only a few studies have quantitatively determined bone turnover and metabolism in glucocorticoid-induced osteoporosis by radiologic imaging techniques including PET (24). To our knowledge, there is no information on regional changes in bone metabolic activity (e.g., lumbar spine) in patients treated with alendronate for glucocorticoid-induced osteoporosis.

The present prospective study was designed to determine the effects of alendronate treatment on regional bone turnover, measured by ^{18}F -fluoride PET and by global biochemical markers and bone mineral density (BMD), in postmenopausal women with glucocorticoid-induced osteoporosis.

MATERIALS AND METHODS

Subjects

The study population consisted of 24 Japanese postmenopausal women (mean age, 59.7y; range, 50–69 y) free of rheumatoid arthritis, who had been treated with at least 10 mg of oral glucocorticoids (prednisolone equivalent) per day for more than 6 mo. The underlying conditions included systemic lupus erythematosus in 5 patients, pemphigus in 4, pemphigoid in 4, polymyositis or dermatomyositis in 3, asthma in 3, multiple sclerosis in 2, malignant lymphoma in 2, and Behçet disease in 1. None had a history of fractures. Excluding these diseases, none of the patients had any other disease or took any medications, including calcium, that affected bone metabolism before baseline measurements.

Treatment with 5 mg of oral alendronate once daily was initiated on the day after the first ^{18}F -fluoride PET scan and continued for the duration of the study (12 mo). All examinations, including ^{18}F -fluoride PET, strictly followed the Ethics Review Committee Guidelines of Fukui University, and written informed consent was obtained from all patients. The ^{18}F -fluoride PET study was undertaken as an Advanced Medical Technology Development Project at Fukui University.

Measurement of BMD

BMD was measured at the time of study entry (baseline), 6 mo, and 12 mo. BMD of the lumbar spine (L1–L4) in the posteroanterior projection and femoral neck (left side), expressed in g/cm^2 , was measured with dual-energy x-ray absorptiometry (QDR 1000; Hologic). In our university, the coefficient of variance at these

sites was less than 2%. The BMD scan was performed within 2 wk of the ^{18}F -PET scan and measurement of biochemical markers.

Measurement of Biochemical Markers

Serum bone-specific alkaline phosphatase (BSALP), a marker of bone formation, was measured in nonfasting patients at baseline and at 3, 6, and 12 mo. Urinary N-telopeptide for type I collagen (NTx), a marker of bone resorption, was measured in fasting patients (morning, second urine) at baseline and at 3, 6, and 12 mo. Blood and urine specimens were collected on the same day as the PET examination and stored frozen (-20°C) until measurement. BSALP and NTx were measured quantitatively using Metra BAP (Quidel Corp.) and Osteomark NTx (Inverness Medical Innovations), respectively, in a fully automated enzyme immunoassay apparatus (plate enzyme immunoassay multisystem EMS-01; Nippon Advanced Technology), and the serum and urinary values were estimated from the respective optical absorption rate.

^{18}F -Fluoride PET

^{18}F -fluoride PET was performed using the Advance system (GE Healthcare). This system allows simultaneous acquisition of 35 transverse slices with interslice spacing of 4.25 mm, with septa (2-dimensional mode). Performance tests showed that the intrinsic resolution of the scanner was 4.0–5.3 mm in the axial direction and 4.6–5.7 mm in the transaxial direction. The field of view and pixel size of the reconstructed images were 512 and 4 mm, respectively. A dose of 185 MBq of ^{18}F ions was injected into the antecubital vein over a period of 10 s. Fifty minutes after the tracer injection, the patient was positioned supine in the PET scanner, and an emission scan was started at a rate of 2 min per bed position from the skull to the mid thigh (7–8 bed positions). After the emission scan, postinjection transmission scanning was performed for 1 min per bed position at the same position as for the emission scan, using a standard $^{68}\text{Ge}/^{68}\text{Ga}$ rod source for correction of attenuation. The acquired data were reconstructed by an iterative method with selection of 14 subsets and 2 iterations. The reconstructed tissue-activity images were converted into standardized uptake value (SUV) images corrected for the injected dose and patient's body weight using the following equation:

$$\text{SUV} = \frac{\text{tissue activity (kBq/mL)} \times \text{body weight (kg)}}{\text{injected } ^{18}\text{F ion dose (MBq)}}$$

The images were processed using Dr. View software (AJS Co. Ltd.) on a Linux workstation. With this software and hardware, ^{18}F -fluoride PET images were visualized and conformed into 3-dimensional sections. A region of interest (18×18 mm) was placed at the center of each vertebral body from L1 to L5 in the sagittal plane (Fig. 1A) and at the center of the left femoral neck in the coronal plane (Fig. 1B). The mean SUVs of the lumbar vertebrae and femoral neck were plotted as localized bone metabolism parameters against the values of BMD or biochemical markers. ^{18}F -fluoride PET images were obtained at baseline, 3 mo, and 12 mo.

Statistical Analysis

All values were expressed as mean \pm SD. The unpaired t test was used to compare differences in bone turnover markers between patients with low and high BMD T-scores at baseline. The paired t test was used to compare differences in bone turnover markers (BSALP, NTx, and SUV) and BMD between baseline and 3,

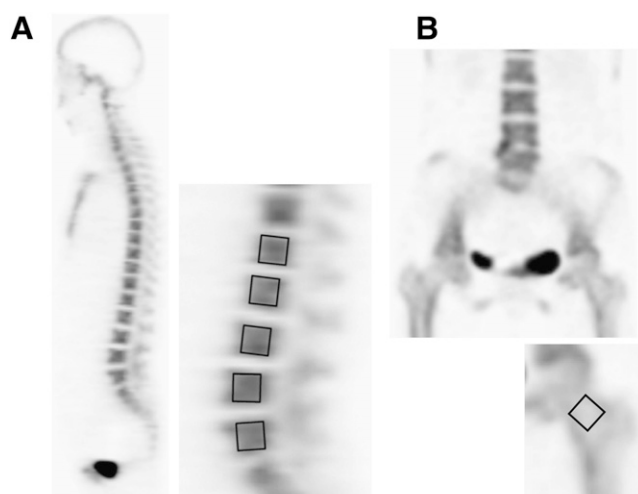


FIGURE 1. (A) Midsagittal ^{18}F -fluoride PET image through lumbar vertebrae showing region of interest within vertebral bodies (at right is magnification of L1–L5 vertebral bodies, with squares indicating regions of interest). (B) Coronal image of pelvis and both proximal femurs (at bottom is magnification of left femoral neck, with square indicating region of interest).

6, or 12 mo of treatment. The correlations between BSALP, NTx, lumbar spine BMD, and lumbar spine SUV at baseline and 12 mo of treatment were examined by Pearson correlation coefficients. A P value of less than 0.05 was considered to represent statistical significance. All statistical analyses were conducted using SPSS software (version 15.0).

RESULTS

Table 1 summarizes the baseline characteristics of the study group. The mean time since menopause was 9.8 y (range, 3–19 y). The mean T-scores of the lumbar spine and the femoral neck were -2.2 (range, -4.43 to -0.16) and -2.9 (range, -4.8 to -0.6), respectively. The mean dose of oral glucocorticoids (prednisolone equivalent) before and

during the study was 13.7 ± 2.3 mg/d. The values of both BSALP and NTx showed marked variability among the subjects, and the mean NTx tended to be higher than the normal value in our institution. The SUVs of the lumbar spine and the femoral neck were 5.2 ± 0.72 and 2.5 ± 0.47 , respectively, and the former was significantly higher than the latter.

According to the baseline BMD T-score of the lumbar spine, based on the World Health Organization criteria (25) for the diagnosis of osteoporosis, patients were categorized into a healthy/osteopenic group (T-score > -2.5) or an osteoporotic group (T-score ≤ -2.5) (Table 2). The mean values of BSALP, NTx, and femoral neck SUV at baseline tended to be higher in the osteoporotic group, but the differences were not significant. On the other hand, the lumbar spine SUV was significantly lower in the osteoporotic group ($P < 0.05$).

Table 3 shows the serial changes in BSALP, NTx, SUV, BMD, and T-score at 3, 6, and 12 mo of alendronate treatment. Treatment for 12 mo tended to reduce BSALP, NTx, lumbar spine SUV, and femoral neck SUV but gradually increased BMD and the T-score of the lumbar spine and femoral neck, relative to baseline values. Although alendronate treatment over a span of 12 mo significantly increased the level of BMD of the lumbar spine ($P < 0.05$), such treatment significantly reduced BSALP ($P < 0.05$), NTx ($P < 0.01$), and SUV levels of both the lumbar spine ($P < 0.01$) and the femoral neck ($P < 0.01$) during the same period. Figure 2 shows percentage changes in these parameters at 3, 6, and 12 mo. The percentages for BSALP were 76.8% and 73.1% at 6 and 12 mo, respectively ($P < 0.05$), whereas those for NTx were 53.7%, 44.2%, and 40.5% at 3, 6 and 12 mo, respectively ($P < 0.01$). The percentages for lumbar spine SUV were 92.4% and 85.6% at 3 and 12 mo, respectively, and the percentages for femoral neck SUV were 90.4% and 75.7% at 3 and 12 mo, respectively. The percentage changes in lumbar spine SUV were significant at 3 mo ($P < 0.05$) and 12 mo ($P < 0.01$), as was the percentage change in femoral neck SUV at 12 mo ($P < 0.01$). The increase in BMD for the lumbar spine at 12 mo was 8.2%, which was significant relative to baseline ($P < 0.05$).

At 12 mo of alendronate treatment, lumbar spine SUV was decreased in all patients. BSALP decreased in 19 patients (79%) but increased in 5 patients, and NTx decreased in all 24 patients (100%). On the other hand, femoral neck SUV decreased in 20 patients but increased in 4 patients. Of the 20 patients who showed a decrease, 17 (85%) showed a decrease in BSALP and 20 (100%) showed a decrease in NTx. Of the 4 patients who showed an increase in femoral neck SUV, 2 showed a decrease in BSALP and 4 showed a decrease in NTx.

Figure 3 shows the correlations between BSALP, NTx, lumbar spine BMD, and lumbar spine SUV at baseline and at 12 mo of treatment with alendronate. BSALP correlated significantly with SUV at baseline ($P < 0.05$) but not at

TABLE 1. Baseline Characteristics

Characteristic	Mean	SD	Range
Age (y)	59.7	6.3	50–69
Time since menopause (y)	9.8	6.0	3–19
Weight (kg)	53.0	8.5	40–70
Height (cm)	153.0	4.7	144–164
Prednisolone equivalent (mg/d)	13.7	2.3	11–18
Lumbar spine BMD (g/cm^2)	0.78	0.08	0.56–0.91
Lumbar spine T-score	2.2	0.90	4.43–0.16
Femoral neck BMD (g/cm^2)	0.72	0.09	0.54–0.95
Femoral neck T-score	2.9	0.88	4.8–0.6
BSALP (U/L)	27.0	11.3	9.6–56.7
NTx (nmol BCE/nmol Cr)	56.5	22.3	20.1–97
Lumbar spine SUV	5.2	0.72	4.23–6.95
Femoral neck SUV	2.5	0.47	1.58–3.35

BCE = bone collagen equivalent; Cr = creatinine.

TABLE 2. Bone Turnover Markers According to BMD T-Score at Baseline

Marker	T-score > -2.5	T-score ≤ -2.5	P
Number of patients	14	10	—
Lumbar spine BMD (g/cm ²)	0.88 (0.14)	0.71 (0.07)	<0.01
Lumbar spine T-score	-1.2 (1.2)	-3.0 (0.59)	<0.01
Femoral neck BMD (g/cm ²)	0.77 (0.07)	0.63 (0.06)	<0.01
Femoral neck T-score	-2.4 (0.64)	-3.7 (0.67)	<0.01
BSALP (U/L)	24.2 (9.0)	32.0 (13.7)	0.160
NTx (nmol BCE/nmol Cr)	53.8 (21.8)	56.2 (21.1)	0.802
Lumbar spine SUV	5.9 (1.3)	4.9 (0.46)	<0.05
Femoral neck SUV	2.4 (0.60)	2.6 (0.58)	0.641

BCE = bone collagen equivalent; Cr = creatinine.
Data are mean followed by SD in parentheses.

12 mo. NTx did not correlate significantly with SUV at baseline or at 12 mo. BMD and SUV showed a significant correlation at baseline ($P < 0.05$) but not at 12 mo.

DISCUSSION

The skeletal effects of glucocorticoids are observed mainly in regions with a high content of trabecular bone, particularly the ribs and spine, and seem to depend on the duration and dosage of therapy (26). A prednisone dosage exceeding 7.5 mg daily for at least 6 mo is associated with an increased risk of bone loss and fractures (4,5), and even lower doses of the drug have also been linked to such changes (6). A metaanalysis report of 23 studies indicated that the cumulative glucocorticoid dose was consistent with doses that produced bone loss (27); however, the correlation between a specific daily dose or cumulative dose and bone loss or risk of fractures was inconsistent in several individual studies (26). Patients in the present study had been treated with oral glucocorticoids at more than 10 mg/d for more than 6 mo but had no history of fractures. Patients were also selected on the basis of not being on any medications, including calcium, that could have affected bone metabolism. Because of this strict criterion for this pro-

spective study, and because treatment guidelines in Japan call for treating most osteoporotic patients with bisphosphonate-containing medications at 3 mo after the initiation of glucocorticoids, only 24 patients could be enrolled. The mean BMD of the lumbar spine at baseline (0.78 g/cm²) for our patients was below the cutoff for fracture-prone Japanese individuals (0.82 g/cm²). These individuals represented glucocorticoid-treated osteoarthritic patients free of rheumatoid arthritis who were treated with more than 5.0 mg of glucocorticoids per day (10).

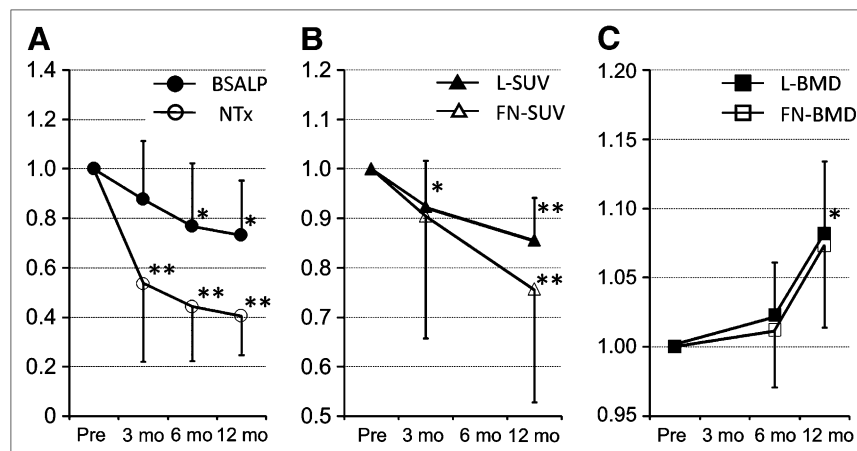
Patients with glucocorticoid-induced osteoporosis are reported to have abnormalities in global biochemical markers of bone turnover and metabolism, although the reported changes have been inconsistent (28,29). Theoretically, the use of glucocorticoids is associated with reductions in markers of bone metabolism reflecting decreases in bone formation, although markers of bone resorption show inconsistent changes during the same treatment. In a report of a randomized placebo-controlled trial, prednisone rapidly and significantly decreased both markers of bone formation and markers of bone resorption (30). In the present study, the mean baseline BSALP of our postmenopausal women was within the reference range; however, the mean baseline NTx tended to be above the reference range though a

TABLE 3. Serial Changes in Bone Turnover Markers and BMD During Treatment with Alendronate

Marker	Baseline	Treatment with alendronate		
		3 mo	6 mo	12 mo
BSALP (U/L)	27.0 (11.3)	22.6 (8.7)	19.7 (9.0)*	18.5 (6.6)*
NTx (nmol BCE/nmol Cr)	56.5 (22.4)	26.2 (8.4) [†]	22.3 (8.0) [†]	20.5 (6.2) [†]
Lumbar spine SUV	5.2 (0.72)	4.8 (0.48)*		4.4 (0.48) [†]
Femoral neck SUV	2.5 (0.47)	2.2 (0.53)		1.8 (0.51) [†]
Lumbar spine BMD (g/cm ²)	0.78 (0.079)		0.80 (0.076)	0.84 (0.077)*
Lumbar spine T-score	-2.2 (0.90)		-2.0 (0.73)	-1.6 (0.75)*
Femoral neck BMD (g/cm ²)	0.72 (0.093)		0.72 (0.090)	0.77 (0.084)
Femoral neck T-score	-2.9 (0.88)		-2.7 (0.85)	-2.3 (0.74)

* $P < 0.05$.
[†] $P < 0.01$ vs. baseline.
 BCE = bone collagen equivalent; Cr = creatinine.
 Data are mean followed by SD in parentheses.

FIGURE 2. Percentage changes in BSALP and NTx (A), SUV of lumbar spine and femoral neck (B), and BMD of lumbar spine and femoral neck (C) after alendronate treatment relative to baseline values. Percentage change in BSALP was significant at 6 and 12 mo; that of NTx was significant at 3, 6, and 12 mo. Percentage change in lumbar spine SUV was significant at 3 and 12 mo; that of femoral neck SUV was significant at 12 mo. Percentage change in BMD of lumbar spine was significantly different only between baseline and 12 mo of treatment. * $P < 0.05$. ** $P < 0.01$. FN = femoral neck; L = lumbar spine; Pre = pretreatment.



statistical comparison of our patients and controls without glucocorticoid therapy was not performed. It is possible that certain factors such as age, sex, time since menopause, and background disease may affect the level of bone resorption.

Bisphosphonates induce apoptosis of osteoclasts and inhibit bone resorption (13,31). Randomized clinical trials showed that treatment with bisphosphonates prevents corticosteroid-induced bone loss (32). Alendronate, a member of the bisphosphonate family, is effective in the prevention and treatment of glucocorticoid-induced osteoporosis (11–13,32) and has been reported to prevent bone loss and improve the BMD of lumbar vertebrae by reducing both bone formation and resorption and suppressing bone metabolism (13). Similarly, alendronate treatment in the present study significantly reduced the levels of both biochemical markers (bone formation and resorption), and the decrease in urinary NTx (a marker of bone resorption) was significant; the suppression effect was approximately 60% after 12 mo. Furthermore, dual-energy x-ray absorptiometry measurement of the lumbar spine showed that 12 mo of alendronate treatment increased BMD by 8.2%. A previous study in postmenopausal women with osteoporosis indicated that the alendronate-induced change in BMD was primarily due to changes in bone resorption (33). Considered together, these results suggest that alendronate treatment prevented further reduction in lumbar BMD by reducing bone resorption.

Several studies have examined the feasibility of ^{18}F -fluoride PET for direct assessment of bone turnover in clinically important skeletal sites such as the lumbar spine. Previous studies of patients having disease with high bone turnover showed a significant relationship between bone turnover and biochemical markers (19,22). Brenner et al. (34) reported that the SUV of ^{18}F -fluoride PET correlated well with markers of bone metabolism; the net uptake of fluoride into the mineral compartment (K_i) was measured using arterial blood sampling and kinetic analysis. We also obtained similar results with 8 postmenopausal women, who showed a significant correlation between K_i and SUV (data not shown). On the other hand, there are some reports of a

significant correlation between K_i and the histomorphometric parameters (19,20). It is possible that tubular reabsorption of fluoride is affected by patient hydration, which could theoretically affect SUVs. None of our patients presented with renal dysfunction during the course of this study. Therefore, SUVs were substituted for markers of regional bone turnover or bone metabolism because of the simplicity of data acquisition and calculation. However, further research is required to investigate the relationship between regional SUV and histomorphometric parameters. Previous studies of osteoporosis in postmenopausal women with ^{18}F -fluoride PET indicated that such patients exhibit low regional bone formation activity, a good relation between bone turnover and changes in BMD, and a risedronate-related decrease in levels of global markers of bone formation, compared with untreated groups (21,35). Although our osteoporotic patients on glucocorticoid treatment did not show a significant change in BSALP and NTx (used as global markers of bone turnover) as measured at baseline, such treatment significantly reduced lumbar spine SUV in the osteoporotic patients, compared with healthy or osteopenic patients. These findings indicate that the decrease in bone turnover in the lumbar spine measured by SUV reflects the degree of osteoporosis. In this regard, it was reported previously that fluoride clearance relative to bone minerals depends not only on the rate of bone metabolism but also on the area available for tracer clearance (36). It is possible that a reduction in bone mass, as is often seen in patients with osteoporosis, also reduces the number of sites available for bone remodeling activity, which could indirectly influence the measured SUV in our study (22). Accordingly, further studies involving measurements of PET parameters (such as K_i and SUV) and various bone histomorphometric parameters, particularly in trabecular bones, are necessary to determine the relationships between the measured PET values and the bone surface area and volume of such bones.

Follow-up studies have demonstrated that bone resorption significantly decreases within 1 mo of the commencement of antiresorptive therapy, and consequent to the coupling

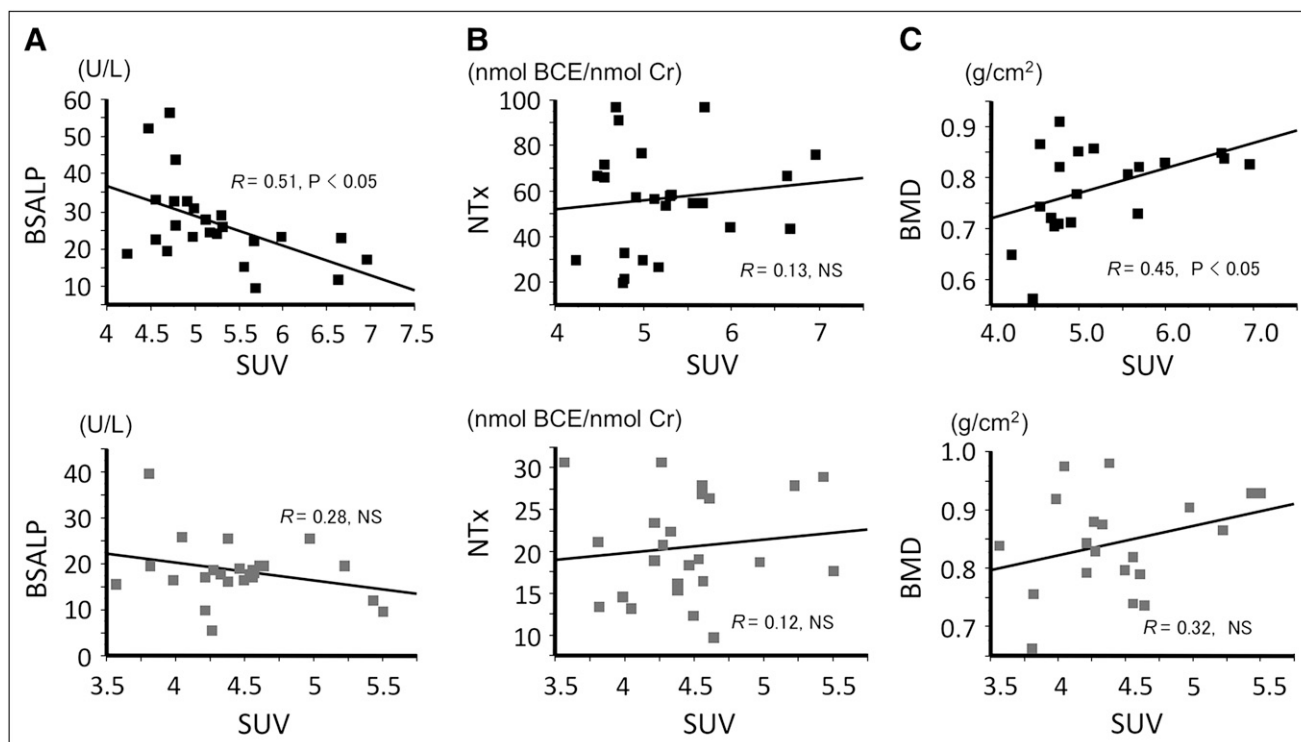


FIGURE 3. Correlations with lumbar spine SUV at baseline (top) and after 12 mo of treatment with alendronate (bottom). (A) BSALP correlated with SUV significantly at baseline ($y = 68.7 - 8.0x$, $R = 0.51$, $n = 24$, $P < 0.05$) but not at 12 mo. (B) No significant correlation was found between NTx and SUV either at baseline or at 12 mo. (C) A positive correlation that was found between BMD and SUV at baseline ($y = 0.5 + 0.05x$, $R = 0.45$, $n = 24$, $P < 0.05$) disappeared after treatment with alendronate for 12 mo. BCE = bone collagen equivalent; Cr = creatinine.

between resorption and formation, a secondary suppression of bone formation occurs within 3 mo (37). In a quantitative study of regional bone metabolism using ¹⁸F-fluoride PET, K_i decreased significantly after 6 mo of risedronate therapy in postmenopausal women (38). In the present prospective study, BSALP and NTx started to decrease within 3–6 mo of alendronate treatment; they had decreased by 27% and 60%, respectively, from baseline at 12 mo of alendronate therapy. These changes in global bone turnover markers were also coupled with similar decreases in SUV in both the lumbar spine and the femoral neck, reflecting regional bone turnover or metabolism, although not similarly so in all patients. Interestingly, there was a significant correlation between BSALP at baseline and the SUV, but not at 12 mo. Changes in NTx at baseline and 12 mo were not significant relative to SUV; for BSALP, the slope of the negative line tended to decrease after treatment, and for NTx, the slope of the positive line tended to decrease after treatment (Figs. 3A and 3B). These results suggest that the rate of decrease of both BSALP and NTx was more than that of regional SUV after alendronate treatment. The decreases in SUV were accompanied by a small but significant increase in lumbar spine BMD at 12 mo after treatment, though no such change was noted for femoral neck BMD. Interestingly, larger studies of antiresorptive therapy tend to report weaker correlations between biochemical markers and changes in BMD for

the femoral neck than for the lumbar spine (39). On further consideration, our patients with higher baseline regional SUV and biochemical markers did not show the greatest increases in BMD in response to alendronate, although there have been some reports that subjects with higher global bone turnover and suppressive effects of biochemical markers show greater increases in BMD (40). It could be that for some reason their regional or global bone turnover at baseline had been influenced by glucocorticoid treatment, background disease, or other factors and tended to be insensitive to alendronate. In general, alendronate exerts a potent inhibitory effect on bone resorption without interfering with bone calcification. Its effect is associated with increased BMD and decreased bone resorption markers, and a secondary decrease in bone formation including osteoblastic activity, thus producing normalization of bone metabolism. Although we cannot ignore the fact that both SUV and BMD could be associated with relatively large measurement errors and that the mechanism of action and potency of alendronate may differ in terms of BMD in each patient, our results indicate that alendronate treatment caused a further decrease in SUV with a subsequent increase in BMD at the same level in the lumbar spine, though it was not significant at 12 mo of treatment, and that SUV and BMD correlate significantly in postmenopausal osteoporotic women on steroid therapy before antiresorptive therapy.

CONCLUSION

To our knowledge, this was the first study of regional bone metabolism in the lumbar spine measured using ^{18}F -fluoride PET in patients with glucocorticoid-induced osteoporosis. The study also examined various bone metabolism markers before and after alendronate treatment. The results demonstrated decreased bone turnover in the lumbar spine, represented by SUVs, and a correlation between these changes and the severity of osteoporosis. Furthermore, the results showed a significant decrease in bone metabolism associated with increased BMD in the lumbar spine after 12 mo of treatment with alendronate. These results suggest that antiresorptive therapy has a direct bone-metabolism effect on skeletal kinetics in glucocorticoid-induced osteoporosis at the clinically important site of the lumbar spine.

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