Relationship between Bone Turnover and Bone Density at the Proximal Femur in Stroke Patients

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Objective: To investigate the relationship between the rate of bone turnover and bone loss at the proximal femur in stroke patients. *Methods:* This study was performed between January 1, 2005 and August 31, 2006 at the Stroke Rehabilitation Unit, Istanbul Physical Medicine and Rehabilitation Training Hospital, Istanbul, Turkey. One hundred six patients who had a stroke for the first time were included in the study. The control group consisted of 33 age- and gender-matched healthy subjects. Bone mineral density (BMD) was measured at the proximal hip region by dual energy X-ray absorptiometry (DXA). Serum osteocalcin (OC) and C telopeptide of type 1 collagen (CTX) levels were measured. Barthel Index (BI) was used for the evaluation of daily activities. Ambulation status of the patients was recorded. *Results:* Mean age was 65.1 ± 9.8 years in the patient group and 51% were male. Mean disease duration was 16.9 ± 9.1 months. Mean BI score was 60.5 ± 25.8 on admission. Femoral neck BMD values were 0.873 ± 0.95 g/cm^2 and 0.816 ± 0.180 g/cm^2 for control subjects and hemiplegic sides of the patient group, respectively. Femur total BMD values were 0.948 ± 0.119 g/cm^2 and 0.872 ± 0.187 g/cm^2 for control group and hemiplegic sides of the patients, respectively. Femoral neck and femur total BMD values in the hemiplegic side were lower than those of controls' ($P < .05$). There was no statistically significant difference between the proximal femur BMD values of the intact and hemiplegic sides. Negative correlation was found between the proximal femur BMD values of both the intact and hemiplegic sides, and serum OC and CTX levels. Bone resorption rate was higher among the patients with stroke; however, bone formation rate was normal in this group. Serum CTX levels showed correlation with ambulation status. Femoral neck BMD values on the intact side were lower in the patient group with disease duration of more than 1 year compared to those with shorter disease duration. *Conclusion:* As a result of this study bone turnover was inversely correlated with bone density at the hip of both hemiplegic and intact sides in stroke patients. Evaluation of bone turnover might be helpful to predict bone loss and to find out the stroke patients with bone loss who can not be decided to begin antiresorptive treatment with bone density measurement. **Key Words:** Bone mineral density—bone turnover—C telopeptide of type 1 collagen, DXA—osteocalcin—stroke.

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Risk of bone loss, falls, particularly to the hemiplegic side, and hip fracture at the hemiparetic side have been reported in patients after stroke.[1-6] Mechanisms for bone loss in hemiplegic extremities has been related to various factors. Motor deficiency and the level of functional dependency at the time of hospitalization have been suggested to be the determinants of increased bone loss.[4] Increased bone resorption attributable to immobilization in the early phase of post-stroke period might be responsible for bone loss.[7-9] Bone loss on the paretic side begins

soon after the stroke incident, and decreases in time.[10] Nevertheless, long-term results of bone loss in stroke patients are not satisfactory.[11]

Previous studies showed the relationship between bone turnover and bone mineral density (BMD) in peri- and postmenopausal women.[12,13] Accelerated bone turnover as shown by biochemical markers has been suggested as an independent risk factor for fractures in postmenopausal osteoporosis.[14] Bone turnover markers are thought to be beneficial following the response to treatment as well.[15] Increased bone resorption has been reported after stroke.[8, 23] The serum pyridinoline crosslinked carboxy terminal telopeptide of type 1 collagen (ICTP), which is a bone resorption marker, has been reported to be one of bone density determinants in the first year after the stroke.[8]

The aim of this study was to investigate the relationship between the bone turnover markers and the proximal femur BMD values of hemiplegic and unaffected sides in stroke patients.

Methods

This study was performed between January 1, 2005 and August 31, 2006 at Istanbul Physical Medicine and Rehabilitation Training and Research Hospital with hemiplegia attributable to stroke were included in this study. Diagnosis was made according to the World Health Organization (WHO) stroke definition by a neurologist. Patients were all assessed in terms of age, gender, body mass index, duration of illness, hemiplegic side, Brunnstrom stage, and ambulation levels. Patients with recurrent stroke, taking medicines that affect BMD, with diseases affecting bone metabolism, with hepatic and renal disorders, and previously rehabilitated were excluded. The hospital ethics committee approved this study. Control group consisted of age and gender matched healthy subjects.

Measurements

Bone densitometry

Dual energy X-ray absorptiometry (DXA) (Lunar model Dpx pro; Lunar Corp, Madison, WI) was used to measure the bone density of both proximal femurs. BMD values were recorded. T score is defined as standard deviation on the basis of mean values of young healthy adult levels.

A T score between the -2.5 and -1 level indicates osteopenia or bone loss. A T score less than or equal to -2.5 is defined as osteoporosis. All measurements were performed by the same experienced technician. The calibration of DXA was performed by phantom scans every 3 weeks.

Biochemical bone turnover markers

The levels of osteocalcin (OC) and C telopeptide of type-1 collagen (CTX) were measured in fasting venous blood samples, which were collected before 9 a.m. The serum intact OC and CTX levels were assessed via micro enzyme-linked immunoabsorbent assay (ELISA). Standard laboratory reference values were 10-20 ng/mL for OC, and less than 0.75 ng/mL for CTX. Serum and urinary calcium (Ca) and phosphorus (P) levels were measured.

Ambulation

Functional ambulation was assessed at four levels. (1) Non-ambulatory; (2) nonfunctional ambulation; (3) household ambulation; and (4) community ambulation.

Barthel Index (BI)

BI is useful for assessing the mobility and self-care activities. BI consists of 10 items, including feeding, transfer, self-care, toilet usage, bathing, mobility, going up and down the stairs, dressing, and bowel and bladder control. The total score is between 0 and 100. The validity and reliability study of BI for the Turkish population has been performed.[17] SPSS version 13.5 (Chicago, IL) was used for statistical data analyses. Paired *t*-test was used for intragroup comparisons, whereas Pearson correlation test was used for intergroup comparisons. Differences were assumed to be significant if *P* value was less than .05.

Results

One hundred six patients, 54 (51%) males and 52 (49%) females, were included in this study. The mean age of the participants was 65.14 ± 9.8 years, whereas the mean age of the control group was 62.6 ± 8.5 years. Mean body mass index of patient group was 25.9 ± 3.9 kg/m^2. Duration of illness was 16.9 ± 9.1 months.

In the patient group, 59 were right hemiplegic, whereas 47 were left hemiplegic. The mean Brunnstrom stage and mean BI score of patients on admission were 3.7 ± 1.4 and 60.5 ± 25.8, respectively.

The BMD values of the hip are shown in Table 1 for both stroke patients and control group. Proximal femur BMD values and T scores of the hemiplegic side were significantly lower in the patient group compared with control group ($P < .05$). Although BMD values of the unaffected hip side were lower in the patient group, the difference was not statistically significant ($P > .05$).

While BMD values of the proximal femur in the hemiplegic side were lower than the values of the unaffected side in the patient group, there was no statistically significant difference in the BMD values between them ($P > .05$). Femur neck T scores of the hemiplegic side were significantly lower than the scores of the unaffected side ($P < .05$). Bone loss and osteoporosis rates for hemiplegic patients and control group were 70.6% and 51.5%, respectively.

Laboratory findings of the patient group are summarized in Table 2. The OC values of the patient group