

The relationship between bone mineral density and immobilization duration in hemiplegic limbs

Derya DEMIRBAG,* Ferda OZDEMIR,* Siranus KOKINO* and Sakir BERKARDA**

*Physical Medicine and Rehabilitation Department, Trakya University Medical Faculty, Edirne, Turkey

**Nuclear Medicine Department, Trakya University Medical Faculty, Edirne, Turkey

Objective: Prolonged immobilization in stroke is known to result in hypercalciuria, hypercalcemia, accelerated bone resorption, and osteoporosis. Furthermore, bone mineral loss accelerated with increasing duration of hemiplegia. Although stroke is a common disease that causes sudden immobilization, relatively few investigations of bone metabolism in stroke have been reported. The aim of this study was to investigate the changes in bone mineral density of the forearms and legs related to duration of hemiplegia-induced immobilization after stroke. **Methods:** Forty-one hemiplegic patients with stroke were evaluated. The patients' age, gender and duration of hemiplegia-induced immobilization were recorded. The measurements of bone mineral density (BMD) in all patients were evaluated with DEXA using the Norland apparatus. The BMD values (g/cm^2) were determined by measurements made in the lumbar vertebrae, both forearm and legs (femoral neck and trochanter). **Results:** We found that bone mineral density was decreased in the affected extremities relative to the intact contralateral side on measurements by dual energy x-ray absorptiometry in bones such as forearm, femoral neck and trochanter. There was a significant difference between bone mineral density of paretic and nonparetic forearms and legs. Bone mineral density of the upper limbs was lower than that of the lower limbs. There was a negative correlation between duration of hemiplegia and BMD values. **Conclusions:** Bone mineral loss may be related to the duration of hemiplegia-induced immobilization. Bone mineral loss is accelerated when the duration of hemiplegia is prolonged.

Key words: bone mineral density, the duration of hemiplegia, stroke

INTRODUCTION

REDUCTION of mechanical stress on bone inhibits osteoblast-mediated bone formation and accelerates osteoclast-mediated bone resorption, leading to what has been called disuse osteoporosis. Prolonged therapeutic bed rest, immobilization due to motor paralysis from injury of the central nervous system or peripheral nerves, application of cast to treat fractures are common causes of disuse osteoporosis.¹ Mechanical stress on bone is one of the determinants of bone morphology, BMD and bone

strength. Therefore, disuse accelerates bone resorption and depresses bone formation and consequently bone becomes atrophic and fragile.^{2,3}

Hemiplegia (paralysis) or hemiparesis (weakness) of one side of the body contralateral to the site of the lesion are the classic signs of stroke, or cerebrovascular accident.⁴ Demineralization and muscle atrophy are common in patients with hemiplegia.⁵ Osteoporosis in patients with hemiplegia of more than 1 month duration occurs as a result of immobilization, during the 1st year particularly.^{6,7} Several longitudinal studies showed that, there is increased bone loss, especially on the hemiplegic side, in stroke patients.⁷⁻⁹ However, only limited information is available about changes in bone mineral after stroke and few studies have been conducted on the possible associations between changes in bone mineral and duration of hemiplegia-induced immobilization. Thus, the aim of the

Received March 22, 2005, revision accepted August 22, 2005.

For reprint contact: Ferda Ozdemir, M.D., Trakya University School of Medicine, Physical Medicine and Rehabilitation Department, 22030 Edirne, TURKEY.

E-mail: ferdadr@yahoo.com

present prospective study was to illustrate the potential for accelerated bone loss following hemiplegia in patients with stroke.

MATERIALS AND METHODS

Patients with left hemiplegia admitted to our University Hospital were considered for this study. All eligible patients (n = 41) (28 men and 13 women) agreed to participate. In our study, the patients were hospitalized for rehabilitation for the first time.

Exclusion criteria were: right and bilateral hemiplegia, no motor involvement, ataxia, dominant left hand, previous strokes affecting the sensorimotor system, unconsciousness or terminal illness, chronic renal failure, significant liver dysfunction, early oophorectomy, presence of mental, cognitive and speech problems, presence of osteosynthetic material in the femoral neck, a history of hip fracture, unilateral bone diseases such as osteosarcomas and osteomyelitis or systemic bone diseases and medical treatment affecting bone mineral density.

The detailed demographic characteristics of all the cases were noted and the physical examination was evaluated. Motor recovery status in the upper, lower extremities and hands was categorized according to the Brunnstrom motor evaluation scale as identified by 7 stages after physical examinations. Brunnstrom stages of recovery of hemiplegia are: *Stage 1*: Presynergy, flaccid, no active movement, *Stage 2*: Resistance to passive movement, no voluntary movement, *Stage 3*: Marked spasticity, synergistic voluntary movement, *Stage 4*: Spasticity decreases, synergies begin to wane and weakest synergies can be overcome, *Stage 5*: Isolated movements, stronger synergies can be overcome, waning spasticity, *Stage 6*: Isolated joint movement freely performed, normal to near normal movements, no spasticity, *Stage 7*: Normal.¹⁰

In addition, spasticity was assessed according to the modified Ashworth scale of upper and lower extremities,

which ranges from 0 (no increase in muscle tone) to 5 (affected part rigid in flexion or extension).¹¹

The patients' onset to rehabilitation admission interval (duration of hemiplegia) (month) was recorded. The BMD measurements of all the patients were measured on admission to the hospital.

Bone mineral density (BMD g/cm²) was measured using dual-energy X-ray absorptiometry (DEXA; Norland XR 36, Norland Medical Systems Inc., Fort Atkinson, USA). Total BMD of the lumbar 2nd, 3rd and 4th vertebrae and femoral neck, trochanter and each forearm was derived directly from the total body scan using Norland definitions. All measurements were performed in a supine position to enable relaxed and stable positioning of the patients.

To minimize interobserver variation, all scans were done by the same investigator and all were analyzed by the same technician, who, at the time of the analysis, was not aware of the patient's paralyzed side or disability.

Statistical methods

Data were analyzed using the Windows 11.0 version of the Statistical Package for the Social Sciences (SPSS). Descriptive statistics were expressed as mean ± SD. All variables were tested for normal distribution by the Kolmogorov-Smirnov test. All variables were found normally distributed. Paired-samples t test was used for continuous variables. Statistical correlations between the BMD and duration of hemiplegia were evaluated using Pearson correlation test. The correlation between the Brunnstrom values, the modified Ashworth scale and BMD was also investigated. P values less than 0.05 were considered statistically significant.

Informed consent was obtained from each participant according to the Second Helsinki Declaration, and the trial was approved by the Ethical Committee of the Trakya University Medical Faculty.

Table 1 Mean bone mineral density (BMD) of the total leg and forearm and demographic features (n = 38)

	Mean ± SD		
	Female (n = 13)	Male (n = 25)	Total (n = 38)
Age	63.30 ± 7.20	62.32 ± 9.29	62.65 ± 8.55
BMI (kg/m ²)	30.90 ± 4.81	25.95 ± 2.92	27.65 ± 4.32
BMD (g/cm ²)			
L2	0.885 ± 0.239	0.907 ± 0.287	0.899 ± 0.269
L3	0.882 ± 0.226	0.915 ± 0.276	0.903 ± 0.257
L4	0.859 ± 0.228	0.927 ± 0.277	0.904 ± 0.260
Femur neck (paretic)	0.628 ± 0.106	0.649 ± 0.173	0.642 ± 0.152
Femur neck	0.736 ± 0.090	0.779 ± 0.198	0.765 ± 0.169
Trochanter (paretic)	0.644 ± 0.245	0.756 ± 0.222	0.718 ± 0.233
Trochanter	0.689 ± 0.271	0.772 ± 0.214	0.744 ± 0.235
Distal radius (paretic)	0.359 ± 0.088	0.356 ± 0.131	0.357 ± 0.117
Distal radius	0.398 ± 0.101	0.413 ± 0.121	0.408 ± 0.113

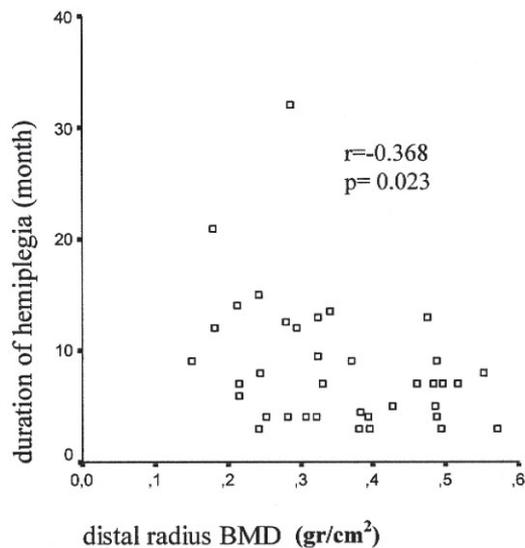


Fig. 1 Correlation between BMD at the distal radius on the paretic side and duration of hemiplegia in all patients (n = 38).

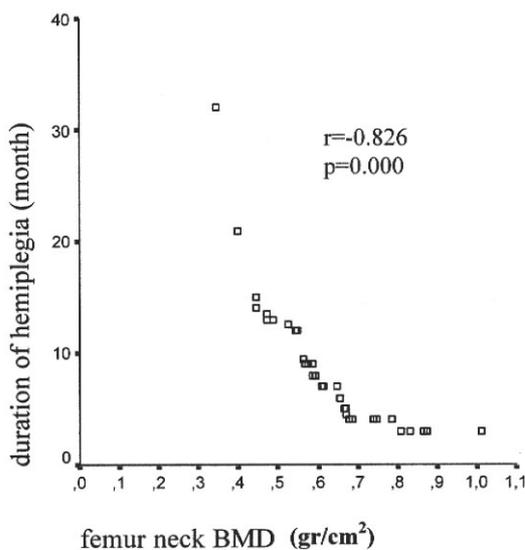


Fig. 2 Correlation between BMD at the femur neck on the paretic side and duration of hemiplegia in all patients (n = 38).

RESULTS

A total of 38 patients of whom 25 were male (65.8%) and 13 female (34.2%), with an average age of 62.65 ± 8.55 (min = 48, max = 78) were prospectively included in the study. BMD values of the spine, legs and forearm and demographic features in the 38 patients were presented in Table 1.

There was no statistically significant correlation between the age of the patients and BMD at any of the regions in stroke patients.

BMD of all paretic sides was significantly different

Table 2 Correlations among the Brunnstrom values of upper extremity and hand and the BMD at the distal radius on the paretic side and duration of hemiplegia in all stroke patients

	Hand BR		Upper extremity BR	
	r	p	r	p
Distal radius BMD	0.759	0.000	0.735	0.000
Duration of hemiplegia	-0.244	0.140	-0.349	0.032

Table 3 Correlations among the Brunnstrom values of lower extremity and the BMD at the femur neck and trochanter on the paretic side and duration of hemiplegia in all stroke patients

	Lower extremity BR	
	r	p
Femur neck BMD	0.431	0.007
Trochanter BMD	0.752	0.000
Duration of hemiplegia	-0.381	0.018

from that of the nonparetic sites in all stroke patients (femur neck $t = -8.157$, $p = 0.000$; distal radius $t = -10.238$, $p = 0.000$). In addition, the loss on the paretic side was significantly greater than that on the nonparetic side. On the paretic side, a significant amount of bone mineral was lost.

There was a statistically significant difference between BMD values at the distal radius and femur neck of the paretic and the nonparetic side (femur neck $z = -3.180$, $p = 0.001$; distal radius $z = -2.900$, $p = 0.004$) in female patients.

There was a statistically significant difference also between BMD values at the distal radius and femur neck of the paretic and the nonparetic side in male patients (femur neck $z = -4.372$, $p = 0.000$; distal radius $z = -4.372$, $p = 0.000$).

We found a statistically significant difference between BMD values of the upper extremity and the lower extremity on the paretic side in all stroke patients (femur neck $t = 11.722$, $p = 0.000$; trochanter $t = 10.992$, $p = 0.000$). BMD values at the lower extremity were significantly greater than those at the upper extremity on the paretic side.

There was also a statistically significant difference in BMD values at the upper extremity when compared with the values obtained in the lower extremity on the paretic side in both genders (femur neck $z = -4.372$, $p = 0.000$; trochanter $z = -4.345$, $p = 0.000$ for male and femur neck $z = -3.180$, $p = 0.001$; trochanter $z = -3.181$, $p = 0.001$ for female).

The mean value of the onset to rehabilitation admission interval (duration of hemiplegia) (month) of the patients with stroke was found to be 8.28 ± 5.81 (min: 3, max: 32). There was no significant correlation between BMD at any spine sites and duration of hemiplegia. We found a

significant negative correlation between BMD at the femur neck and distal radius and duration of hemiplegia on the paretic side in all stroke patients (femur neck $r = -0.826$, $p = 0.000$; distal radius $r = -0.368$, $p = 0.023$) (Figs. 1, 2). However, there was no significant correlation between BMD at the trochanter and duration of hemiplegia on the paretic side.

We found a statistically significant negative correlation only between BMD at the femur neck and duration of hemiplegia on the paretic side in both genders (femur neck $r = -0.944$, $p = 0.000$ for female, femur neck $r = -0.825$, $p = 0.000$ for male).

There was a statistically significant positive correlation between the Brunnstrom values and BMD at the distal radius, femur neck and trochanter on the paretic side in all stroke patients (Tables 2, 3). There was no significant correlation between BMD values of the spine and the Brunnstrom values.

We found a significant negative correlation between the duration of hemiplegia and the Brunnstrom values of the upper extremity and lower extremity. However, no significant correlation was observed between Brunnstrom values of hand and the duration of hemiplegia (Table 2).

We could not find any significant association between the duration of hemiplegia and spasticity, or between the changes in BMD and spasticity.

DISCUSSION

This study showed that BMD of patients will be decreased if the duration of hemiplegia is increased.

Loss of BMD, the result of an imbalance between bone resorption and bone formation, is a potential problem for patients with hemiplegia because of the immobility commonly associated with this impairment.

The changes in BMD of the total leg are in agreement with the results of previous studies.^{8,12} The present study provides further data with regard to changes in BMD related to the duration of hemiplegia induced immobilization in stroke patients.

Immobilization due to several causes induces abnormal bone metabolism and severe decalcification of bone. Palle performed that a histomorphometric analysis on iliac crest biopsies from eight healthy male volunteers submitted to a 4-month antiorthostatic bed rest. Their results suggested that bone architecture might be more affected by the reduction of mechanical forces than the bone mass. These modifications were supposed to be the result of an accelerated bone turnover in the early stage of immobilization.¹³ Fukuoka showed that bone did not show consistent BMD alterations, partially increasing and partially decreasing, and both lumbar and metacarpal bone showed similar rapid BMD changes in the patients with bed rest immobilization as well.¹⁴

Elias reviewed the pathophysiology of osteoporosis as it relates to immobilization or disuse osteoporosis in

paraplegics. The physiology of bone formation and resorption was discussed, and the influence of piezoelectric forces on bone integrity and the consequences of the loss of this effect in paraplegics were addressed. When bone is stressed, negative charges accumulate on the side from which the stress is applied and positive charges accumulate on the opposite side. Presumably the collagenous component of bone plays the major role in the generation of electrical potentials. Another mechanism which is important in the generation of electrical potentials is created by liquid planes streaming past solid planes.¹⁵ Ott also emphasized that decreased bone density and increased fracture risk are seen in patients with SCI.¹⁶

Immobilization due to motor paralysis from stroke causes disuse osteoporosis. Jorgensen investigated changes in lean (muscle) mass and bone mineral density of the legs during the first year after stroke according to the patient's ambulatory level and suggested that lean muscle mass is rapidly lost and may be regained shortly after stroke, whereas loss of BMD appears difficult to prevent, especially on the paretic side.⁵ We measured BMD with DEXA in stroke patients admitted for rehabilitation and compared BMD of the paretic and nonparetic sides at multiple sites. The study also confirmed that DEXA is important to identify the status of high bone resorption. This assay should be measured to the bone health assessment of individuals with risk factors such as impaired physical mobility.

The function reduction in stroke patients is associated with significant bone loss occurring over prolonged periods.¹⁷⁻¹⁹ We included patients, after prolonged duration of stroke, in the study in order to investigate the relationship between immobilization period and bone loss. These patients had been referred to rehabilitation clinic late due to their lower socialcultural levels and economic limitations. Furthermore, none of the patients performed regular exercise program within this period. Therefore, immobilization period of patients in the study was as long as 3-32 months and this duration was convenient to determine the effect on bone tissue. We believe that the negative correlation we found between immobilization period and BMD is an important observation indicating that bone loss will be increased if the duration of hemiplegia is increased.

Liu found that both at admission and at discharge, BMD of the affected side was lower for the upper and lower limbs. The already lowered admission BMDs might reflect the relatively long time from onset to the first measurement (median 104 days). The affected/unaffected ratio was the lowest for humeral BMD.²⁰ Iversen and et al. noted more pronounced demineralization in the upper limbs as compared with the lower ones.²¹ Hamdy reported that the mean percentage side difference was 7.95% for arms and 3.42% for legs.²² In fact, BMD values were lower for the upper than for the lower limbs in our series as well. This finding might indicate more pronounced

weakness in the upper limbs than the lower limbs.

Hamdy and et al. found that demineralization in the affected limbs started during the first month and gradually progressed. The BMDs decreased by a mean of 9.3% in the upper and 3.7% in the lower limbs by the fourth month and no further loss was observed thereafter. They observed no significant change in the unaffected side and concluded that demineralization occurred only in the affected limbs.⁷ In contrast to Hamdy's findings, we found significant negative correlations between both paretic and non paretic side BMD at the femur neck, distal radius and duration of hemiplegia. The finding of the present study shows that an increase in duration of hemiplegia contributes significantly to a decrease in BMD values on both sides.

The bone loss is dependent on the patient's motor function level at baseline after stroke.^{6,8} Initial neurologic deficits in hemiplegic patients show some improvement in the course of time. This condition is related to neural plasticity. The rate of improvement is superior in rehabilitated patients.^{23,24}

In a study carried out by Jorgensen et al. in which the effects of walking and asymmetrical weight bearing on the loss of bone mineral in the upper and lower femoral neck were investigated, it was stated that the reduction in BMD in the femoral neck occurs mainly in the lower part of the neck and on the paretic side. The BMD loss depended on when or if the patients relearned to walk, but also on the amount of body weight born on the paretic leg. Thus, measuring the lower part of the femoral neck gives a better estimate of the impact of gait and weight bearing than measuring the total femoral neck.¹⁹ In our study, some amount of spontaneous motor recovery had occurred because some time after stroke had elapsed in these patients. According to the results of the present study, statistically significant positive correlations were found between Brunnstrom values of upper extremity and hand and the BMD at the distal radius. In addition, significant positive correlations were found between Brunnstrom values of lower extremity and the BMD at the femur neck and trochanter. Furthermore, we found a significant negative correlation between the duration of hemiplegia and Brunnstrom values of upper extremity and lower extremity.

We conclude that BMD decreases rapidly in immobilized stroke patients with time. Therefore rehabilitation programs for preventing bone loss should be instituted early in the course of stroke disease.

REFERENCES

1. Takata S, Yasui N. Disuse osteoporosis. *J Med Invest* 2001; 48: 147–156.
2. Lanyon LE. Osteocytes, strain detection, bone modeling and bone remodeling. *Calcif Tissue Int* 1993; 53: 102–107.
3. Cowin SC, Moss-Salentijn L, Moss ML. Candidate for the mechanosensor system in bone. *J Biomech Eng* 1991; 113: 191–197.
4. Ryerson SD. Hemiplegia. In: *Neurological rehabilitation*, Umphred DA (ed), St. Louis; Mosby, 1995: 681–721.
5. Jorgensen L, Jacobsen BK. Changes in muscle mass, fat mass, and bone mineral content in the legs after stroke: a 1 year prospective study. *Bone* 2001; 28: 655–659.
6. Sato Y, Fujimatsu Y, Kikuyama M, Kaji M, Oizumie K. Influence of immobilisation on bone mass and bone metabolism in hemiplegic elderly patients with long standing stroke. *J Neurol Sci* 1998; 156: 205–210.
7. Hamdy RC, Moore SW, Cancellaro VA, Harvill LM. Long-term effects of strokes on bone mass. *Am J Phys Med Rehabil* 1995; 74: 351–356.
8. Jorgensen L, Jacobsen BK, Wilsgaard T, Magnus JH. Walking after stroke: Does it matter? Changes in bone mineral density within the first 12 months after stroke. A longitudinal study. *Osteopor Int* 2000; 11: 381–387.
9. Ramnemark A, Nyberg L, Lorentzon R, Englund U, Gustafson Y. Progressive hemiosteoporosis on the paretic side and increased bone mineral density in the nonparetic arm the first year after severe stroke. *Osteopor Int* 1999; 9: 269–275.
10. Dewald JP. Sensorimotor neurophysiology and the basic of neurofacilitation therapeutic techniques. In: *Stroke rehabilitation*, Brandstater ME, Basmajian JV (eds), Baltimore; Williams & Wilkins, 1987: 109–183.
11. Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. *Phys Ther* 1987; 67: 206–207.
12. Karlsson M, Nilsson JA, Sernbo I, Redlund-Johnell I, Johnell O, Obrant KJ. Changes of bone mineral mass and soft tissue composition after hip fracture. *Bone* 1996; 18: 19–22.
13. Palle S, Vico L, Bourrin S, Alexandre C. Bone tissue response to four-month antiorthostatic bedrest: a bone histomorphometric study. *Calcif Tissue Int* 1992; 51: 189–194.
14. Fukuoka H, Nishimura Y, Haruna M, Suzuki Y, Oyama K, Igawa S, et al. Effect of bed rest immobilization on metabolic turnover of bone and bone mineral density. *J Gravit Physiol* 1997; 4: 75–81.
15. Elias AN, Gwinup G. Immobilization osteoporosis in paraplegia. *J Am Paraplegia Soc* 1992; 15: 163–170.
16. Ott SM. Osteoporosis in women with spinal cord injuries. *Phys Med Rehabil Clin N Am* 2001; 12: 111–131.
17. Prince RL, Price RI, Ho S. Forearm bone loss in hemiplegia: a model for the study of immobilization osteoporosis. *J Bone Miner Res* 1988; 3: 305–310.
18. del Puente A, Pappone N, Mandes MG, Mantova D, Scarpa R, Oriente P. Determinants of bone mineral density in immobilization: a study on hemiplegic patients. *Osteopor Int* 1996; 6: 50–54.
19. Jorgensen L, Crabtree NJ, Reeve J, Jacobsen BK. Ambulatory level and asymmetrical weight bearing after stroke affects bone loss in the upper and lower part of the femoral neck differently: bone adaptation after decreased mechanical loading. *Bone* 2000; 27: 701–707.
20. Liu M, Tsuji T, Higuchi Y, Domen K, Tsujiuchi K, Chino N. Osteoporosis in hemiplegic stroke patients as studied with dual-energy x-ray absorptiometry. *Arch Phys Med*

- Rehabil* 1999; 80: 1219–1226.
21. Iversen E, Hassager C, Christiansen C. The effect of hemiplegia on bone mass and soft tissue composition. *Acta Neurol Scand* 1989; 3: 305–310.
 22. Hamdy RC, Krishnaswamy G, Cancellaro V, Whalen K, Harvill L. Changes in bone mineral content and density after stroke. *Am J Phys Med Rehabil* 1993; 72: 188–191.
 23. Stein J. Motor recovery strategies after stroke. *Top Stroke Rehabil* 2004; 11: 12–22.
 24. Nelles G. Cortical reorganization—effects of intensive therapy. *Restor Neurol Neurosci* 2004; 22: 239–244.