Hemiosteoporosis After Severe Stroke, Independent of Changes in Body Composition and Weight

A. Ramnemark, MD; L. Nyberg, RPT, PhD; R. Lorentzon, MD, PhD; T. Olsson, MD, PhD; Y. Gustafson, MD, PhD

Background and Purpose—Fractures are a serious complication after stroke, and the risk of hip fractures among stroke patients is increased 2 to 4 times versus a reference population. Fractures after stroke are probably caused by the development of hemiosteoporosis and the high incidence of accidental falls. The aim of this study was to investigate the development of hemiosteoporosis in relation to other changes in body composition during the first year after severe stroke.

Methods—The study included 24 patients with extensive paresis after stroke. Bone mineral content (BMC) and fat and lean mass were assessed 1, 4, 7, and 12 months after stroke onset by a dual-energy x-ray absorptiometer.

Results—The loss of total body BMC was significant during the first year after stroke (–1.6%; \( P < 0.05 \)), but there were no significant changes in total lean or fat mass. At inclusion, there were no significant differences between sides in lean or fat mass or BMC, but during follow-up, BMC of the affected side decreased significantly compared with the same side at inclusion (–7.5%; \( P < 0.01 \)). Side differences in fat mass became significant between legs (9.3%; \( P < 0.001 \)) and whole sides (4.8%; \( P < 0.01 \)). There were only minor side changes in lean mass. Loss of BMC was independent of weight changes.

Conclusions—During the first year after severe stroke, patients developed pronounced hemiosteoporosis. This was not associated with general changes in lean or fat mass. The development of hemiosteoporosis was independent of weight changes after stroke. (Stroke. 1999;30:755-760.)

Key Words: body composition ■ bone density ■ complications ■ hemiplegia ■ osteoporosis

Stroke is associated with serious complications, including fractures that usually affect the paretic side. We have previously shown that the risk of hip fracture after stroke is increased 2 to 4 times compared with a reference population and that the hip fractures occurred late after stroke onset (median, 30 months).

Fractures after stroke are probably caused by 2 main factors: a high incidence of accidental falls and a progressing hemiosteoporosis on the paretic side. In a recent prospective study, we found that loss of bone mass in paretic extremities continued throughout the first year after stroke onset and was most pronounced in the humerus (–17.4%) and proximal femur (–12.2%).

Disuse has been suggested as the main cause for loss of bone mass in patients immobilized because of stroke, paraplegia, or fractures. However, this was not confirmed in our recent prospective study, in which we found only weak associations between bone loss and motor function, activities of daily living (ADL), or ambulation. This may be because we selected only severely affected patients, but it does raise questions about other risk factors for the development of hemiosteoporosis apart from paresis and immobilization.

The accuracy and precision of bone mineral measurement by dual-energy x-ray absorptiometry (DEXA), which was originally developed to measure bone mass, has been well validated. Measurement of soft tissue composition by DEXA is also possible. Fat-free mass correlates well with bone mass, mainly in the weight-bearing skeleton, and a change in fat mass has been shown to be associated with a change in bone mass in healthy postmenopausal women. In patients with hip fracture and among patients with paraplegia, loss of bone mass is associated with a decreased lean mass and an increased fat mass. In stroke patients, a previous cross-sectional study found that loss of bone mass on the paretic side after stroke was marked and was associated with a significant difference in body composition according to side, with decreased lean mass and increased fat mass in the paretic as opposed to the nonparetic side. Concomitantly, no correlation was seen between loss of bone mass or change in body composition and the degree of paresis.

The aim of this study was to investigate the development of hemiosteoporosis in relation to other changes in body composition during the first year after severe stroke.

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755
Body Composition After Severe Stroke

Subjects and Methods
Twenty-four stroke patients (13 men and 11 women) from the geriatric rehabilitation ward at Norlands University Hospital, Sweden, were included 1 month after stroke onset and followed up prospectively during the first year after stroke. Patients are admitted to this unit if they need further rehabilitation after treatment at the acute stroke units, and they are admitted within 2 to 4 weeks after stroke onset. Patients were included consecutively if they met the inclusion criteria: unilateral stroke and extensive extremitiy paresis or total paralysis, ie, inability to lift arm and/or leg straight at inclusion. Exclusion criteria were previous osteoporotic fractures or ongoing glucocorticoid or other hormone treatment. None of the subjects had persistent paresis from previous strokes, and all had been independent regarding activities of daily living according to the Barthel ADL index. It was not possible to obtain a detailed nutritional status because several patients had dysphasia and cognitive dysfunction. None of the participants had oral supplementation of calcium or vitamin D. Five subjects could not be followed up throughout the study period (2 patients died and 3 dropped out of the study) and were excluded from the analyses. Body composition for these patients at inclusion did not differ from those of the subjects who took part throughout the study.

Nineteen patients remained for the final analyses (12 men [mean age, 73.3±4.3 years] and 7 women [mean age, 76.3±10.4 years]; the age difference between genders was insignificant [P=0.50]). Stroke diagnoses were nonembolic infarction (n=9), embolic infarction (n=5), and intracerebral hemorrhage (n=3). Concurrent diagnoses of interest were diabetes mellitus (n=6); 1 patient was insulin dependent at the time of inclusion. Three patients smoked, all of whom were men. None of the participants had pharmacological treatment for osteoporosis. Bone mass and body composition were measured, and motor function (Motricity Index19; range, 1 to 100) and spasticity (modified Ashworth20; range, 1 to 5) were estimated. Blood samples for analysis of serum calcium and albumin were drawn at inclusion and at each follow-up visit. For 2 patients with paresis in only an arm or a leg, respectively, only the results of the paretic extremity and its contralateral nonaffected extremity were used in analyses. One patient could not be assessed at the 7-month follow-up owing to acute illness. None of the patients developed recurrent stroke during the study period.

Bone mineral density (BMD; g/cm²) and bone mineral content (BMC; g) of the total body were measured with a DEXA (Lunar DPX-L, software version 1.3, Lunar Co). This technique, which uses the different attenuations of a collimated beam of x-rays at 2 different energy levels,21 can also estimate the amount of soft tissue (the difference between the total tissue mass and the BMC), and the amount of fat mass is then derived by use of an algorithm.22 The remaining soft tissue mass, called lean mass, contains muscle, fluids, connective tissue, and other components,23 but in the extremities, lean mass can be approximated as to the skeletal muscle mass.24 Fat mass (g, %), lean mass (g), and BMC (g) were derived from the total body scan for the paretic and nonparetic arm, leg, and total body side by use of the Lunar definition. Z scores, defined as the number of standard deviations from the age-matched reference mean (Lunar reference population), were calculated from the results of the bone measurements. Because it was sometimes difficult to position the stroke patients owing to extremity paresis, painful joints, and spasticity, we evaluated the coefficient of variance (CV; SD/mean) in 2 stroke patients (1 patient early and 1 patient late after stroke onset) who were scanned repeatedly 5 times each after being repositioned between scanings. The CV was estimated at 0.8% for total body BMD and 0.9% to 3.2% in the different locations of BMC, fat mass, and lean mass. To minimize interobserver variation, the majority (94%) of all BMC measurements and analyses were made by the same test assistant.

Height at inclusion was measured on the ward with standardized equipment. Weight, also measured on the ward at inclusion with standardized equipment, did not differ from body weight derived from the DEXA measurements (0.2%; P=0.67). In the statistical analyses, weight derived from the DEXA measurements at each follow-up visit was used. The body mass index (BMI) was also calculated.

Data for parameters of body composition were distributed normally, and parametric tests were used for statistical analysis. Student’s paired t test was used for paired observations, and Student’s unpaired t test was used for independent observations. ANOVA for repeated measures was used for comparison of body composition between more than 2 time points. Statistical correlations were calculated with the Pearson correlation coefficient (r). A P value of <0.05 was considered statistically significant. All calculations were made with the SPSS statistical package.

The study was approved by the Ethics Committee of the Medical Faculty of Umeå University, and all participants gave their informed consent.

Results

Body composition at inclusion is shown in Table 1. Men were taller and heavier and had significantly higher total body BMC and lean mass than women at inclusion. All but 2 of the participants (both men) had age-matched z values for total BMD within 1 SD, ie, the majority had BMD normal for their sex and age.

During follow-up, there was a significant loss of bone mass in the total body (BMD and BMC), but there were no significant changes in total fat or lean mass (Table 2). No significant changes in BMI were found during follow-up for men or women (data not shown). However, individual subjects had pronounced body weight changes, ranging from a loss of 15.9 kg to a gain of 8.6 kg, corresponding to a change in region fat mass of ~55% to 70%.

<table>
<thead>
<tr>
<th>Region</th>
<th>BMI</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total body BMD, g/cm²</td>
<td>1.15±0.09</td>
<td>0.98±0.04</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total body BMC, g</td>
<td>3047±483</td>
<td>2991±296</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total region fat, %</td>
<td>29.9±5.9</td>
<td>38.8±6.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Total fat mass, kg</td>
<td>23.8±7.9</td>
<td>23.9±5.9</td>
<td>NS</td>
</tr>
<tr>
<td>Total lean mass, kg</td>
<td>51.4±6.3</td>
<td>35.1±3.9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are mean±SD.

*P<0.05, †P<0.01, and ‡P<0.001, bivariate analyses compared with inclusion.
nonparetic sides. However, during follow-up, BMC in the affected side decreased significantly overall compared with the same side at inclusion, resulting in significant differences between BMC in the paretic versus nonparetic arm ($P<0.001$ from 4-month follow-up), leg ($P<0.001$ from 7-month follow-up), and side ($P<0.01$ from 7-month follow-up). BMC in the nonparetic arm also decreased significantly between inclusion and the end of the study ($P<0.05$ at 12-month follow-up). Side differences in fat mass became significant in leg and side ($P<0.01$ and $P<0.05$ from 4-month follow-up, respectively), but the increases in fat mass in the paretic leg and side were not significant compared with the same locations at inclusion. Finally, there was a significant loss of lean mass in the nonparetic arm during follow-up ($P<0.05$ from 4-month follow-up) compared with no significant change in lean mass in the paretic arm between inclusion and study end.

Because the interindividual variability in weight was high, changes in body composition were analyzed separately for patients who gained weight ($n=11$, 9 men; mean weight change, $4.5 \pm 2.3$ kg or $6.5 \pm 3.7$% of initial body weight) and patients who lost weight ($n=8$, 5 women; mean weight change $-6.0 \pm 5.5$ kg or $-8.3 \pm 7.8$% of initial body weight). Weight changes were mainly explained by changes in fat mass. Changes in body composition for the 2 subgroups are presented in Table 3, and changes in sides are illustrated in Figure 2. Loss of BMC was extensive in all measurements of the paretic side, independent of weight change.

Motor impairment (degree of paresis) was generally most pronounced in the upper extremity and improved significantly on the paretic side during follow-up ($P<0.001$). There were only a few correlations between motor function and changes of body composition (data not shown). There were no significant changes in spasticity during follow-up and no correlations to changes in body composition were found (data not shown).

At inclusion, 8 of 19 patients had albumin levels below reference values ($<36.6$ g/L; range, 30.6 to 36.3 g/L), but at study end only 1 patient had persisting hypoalbuminemia. Serum calcium levels were within the normal range (2.10 to 2.60 mmol/L) in all but 1 of the participants, a women with

![Figure 1](image-url). Changes in BMC, fat, and lean mass in paretic side the first year after stroke. Differences between inclusion and end of study: BMC, $P<0.01$; fat, $P=NS$; and lean, $P=NS$. Differences between inclusion and end of study in paretic versus nonparetic side (A vs B) were as follows: BMC, $P<0.01$; fat, $P=0.05$; and lean, $P=NS$.

In the patients who completed the study ($n=19$), there were 8 right-sided and 11 left-sided strokes, and all but 1 of the subjects included were right-handed. There were no statistically significant differences in BMC or fat or lean mass between the dominant and nondominant sides at inclusion, and therefore no correction for dominant side was made when body composition for the paretic versus the nonparetic side was analyzed.

At the inclusion and follow-up visits at 4, 7, and 12 months, differences in body composition were calculated between the affected and nonaffected arm and leg (Table 2), and changes in body composition were calculated between body sides (Figure 1). At inclusion, there were no significant differences between BMC or fat or lean mass in paretic versus
slightly elevated calcium throughout the study (range, 2.66 to 2.70 mmol/L).

**Discussion**

We found a rapid and pronounced loss of BMC on the paretic side during the first year after severe stroke. The extensive loss of BMC was not associated with general changes in lean or fat mass. Side difference became significant in fat mass owing to an increase of fat mass on the paretic side. The losses of lean mass were generally small. However, a significant loss was found in the nonparetic arm. There was a major interindividual variability in weight during follow-up, but despite a pronounced difference in fat mass among those who gained weight and those who lost weight, the loss of BMC did not differ between groups.

The participants were initially a homogeneous group of stroke patients who had been independent in ADL before the onset of stroke, and at inclusion, all subjects had extensive unilateral paresis in the arm and/or leg. The most common criteria for exclusion were insufficient severity of paresis or prestroke osteoporosis, especially in women. However, the participants were not representative of stroke patients undergoing geriatric stroke rehabilitation, and it might therefore be difficult to draw conclusions about risk factors for hemiosteoporosis in general from this study.

DEXA was originally developed to measure bone mass, and the reproducibility of DEXA in stroke patients has been confirmed, albeit only in the upper extremities. The unit for measuring bone mass in DEXA could be either BMD (g/cm²) or BMC (g). BMD is useful for the prediction of risk for fractures, but BMC is preferred when body composition, measured in grams, and fat and lean mass are analyzed. BMC is also less affected by weight changes than BMD, which is dependent on bone area.

There is not yet any completely established standard for measuring body composition, but DEXA is generally accepted. DEXA measures fat by use of an algorithm, and its precision for measuring total body fat is good, although its precision for measuring fat mass in subregions is reduced, especially in obese people. The majority of body fluids are contained in lean mass, making measures of lean mass more sensitive to changes in hydration than BMC and fat mass. The precision of DEXA measurement of body composition is affected by weight changes, especially total body bone mass, but subregions are less affected by weight changes, and there are no systematic errors of measurements related to weight changes.

As expected, the male subjects included in the present study had greater bone mass than the female subjects. The absolute majority of the included patients were normal for their age regarding body composition and bone mass, although the men may have had a slightly higher fat mass than would be expected.

The losses of bone mass in the total body were significant during follow-up but were normal for the age group if our follow-up period (11 months) is approximated to the known 1-year rate loss. The progressing hemiosteoporosis has been identified previously and described in detail. The average change in total body fat mass was insignificant during follow-up, as was BMI, but the major interindividual variability in weight change was explained mainly by changes in fat mass. One might expect fat loss to have an effect on BMC measurements in patients who lost weight, resulting in an underestimated loss of bone mass in these patients. This is probably of minor importance in the present study because the loss of bone mass in the nonparetic side was independent of fat changes in patients who lost weight. Therefore, the changes shown are
obviously genuine bone mass reductions and not likely to be artifacts due to a change in body water, for example. Malnutrition and weight loss are common after stroke, and therefore the great variability in weight change was unexpected. Substantial loss of fat mass may increase risk for fractures due to decreased energy absorption in accidental falls. On the other hand, the changes in lean mass were less than expected. Reduced muscle function should result in atrophy, although an upper motor-neuron injury, such as a stroke, results in considerably less loss of muscle mass than a peripheral neuron lesion. Accordingly, there were only minor changes in lean mass after stroke, and the changes were similar between the paretic and nonparetic sides in this respect. The nonaffected arm lost even more lean mass than the affected arm. However, a potential confounding factor is interference of measurements from edema. A change in hydration may theoretically interfere with the measurement of lean mass, because lean mass contains fluid as well as skeletal muscle. Inactivity edema is a well-known clinical complication after severe stroke, and the interference of edema in the paretic leg with bone mass estimation after stroke has been reported. Thus, we may have underestimated the actual loss of muscle mass after stroke. However, measurement of BMC is more sensitive to a change in hydration in the chest and abdomen than in the extremities.

The low serum albumin levels at inclusion in half of the patients might indicate protein malnutrition early after stroke. However, because albumin levels normalized in the great majority of these patients during follow-up, protein malnutrition is considered to have had a minor impact on the loss of lean mass.

Our results concerning hemiosteoporosis fit well with findings from cross-sectional studies. However, the changes in fat mass and lean mass after stroke that were found in our prospective study do not correspond completely with results from a previous cross-sectional study of soft tissue composition after stroke. In that study, a significant difference in body composition between sides 23 to 38 weeks (mean, 29 weeks) after stroke was found, which was due to a decreased lean mass and an increased fat mass in the paretic side. The differences between those results and our results might be explained in part by the selection of patients (our participants were 10 years older) and by the study design, because our data were collected prospectively.

There were only a few statistically significant correlations between bone loss and motor function and no correlations with the presence of spasticity. This might be explained by the fact that the participating subjects were a selected group of stroke patients with pronounced functional disabilities.

In summary, bone mass reduction is pronounced in the paretic extremities after stroke and progresses during the first year after stroke. Hemiosteoporosis after stroke seems to be a process independent of changes in fat or lean mass and weight. Other mechanisms must be identified before successful intervention can be made available. Finally, the great interindividual changes in fat mass found in the present study may be of major importance for pharmacokinetics in stroke patients.

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References


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