Osteoporosis Int (1994) 4:138–143

Osteoporosis International

Original Article

Bone Mineral Status in Paraplegic Patients Who Do or Do Not Perform Standing

S. Goemaere[1], M. Van Laere[2], P. De Neve[2] and J. M. Kaufman[1]

[1]Osteoporosis and Bone Metabolism Unit of the Departments of Rheumatology and Endocrinology and [2]Rehabilitation Centre, University Hospital of Ghent, Ghent, Belgium

Abstract. Bone mineral density (BMD) was assessed by dual-photon X-ray absorptiometry at the lumbar spine (L3, L4), the proximal femur and the femoral shaft, and by single-photon absorptiometry at the forearm in 53 patients with complete traumatic paraplegia of at least 1 year's duration and in age- and sex-matched healthy controls. The patients did (n = 38) or did not (n = 15) regularly perform passive weightbearing standing with the aid of a standing device. Compared with the controls, the BMD of paraplegic patients was preserved in the lumbar spine and was markedly decreased in the proximal femur (33%) and the femoral shaft (25%). When considering all patients performing standing, they had a better-preserved BMD at the femoral shaft (p = 0.009), but not at the proximal femur, than patients not performing standing. BMD at the lumbar spine (L3,L4) was marginally higher in the standing group (significant only for L3; p = 0.040). A subgroup of patients performing standing with use of long leg braces had a significantly higher BMD at the proximal femur than patients using a standing frame or a standing wheelchair (p = 0.030). The present results suggest that passive mechanical loading can have a beneficial effect on the preservation of bone mass in osteoporosis found in paraplegics.

Keywords: Bone mineral density; Paraplegia; Spinal cord injury; Standing

Correspondence and offprint requests to: S. Goemaere, Department of Rheumatology, University of Ghent, De Pintelaan 185, B-9000 Ghent, Belgium.

Introduction

Paraplegic patients develop marked osteoporosis below the level of the injury [1]. This sublesional osteoporosis is so striking that it can be visualized by conventional radiography as early as 6 weeks after the injury [2]. Histomorphometric, calcium kinetic and biochemical studies have shown that bone turnover is markedly increased in the first months following a complete spinal cord lesion [3,4]. Initial bone loss is rapid, but bone mass tends to stabilize about 6 months after the injury, at the level of an 'osteoporotic steady state' [4,5]. At that time the trabecular bone mass is reduced by one third [6,7]. Several studies have confirmed the laboratory abnormalities, which indicate an enhanced bone remodelling and reach a maximum between 3 and 10 months [6,8]; after about 1 year bone remodeling has returned to a steady state [8]. The abnormal laboratory values are more pronounced in paraplegia than in other forms of 'disuse osteoporosis', and it has been suggested that denervation and regional changes in blood flow could be important factors in this cause of bone rarefaction [4,8].

The influence of bisphosphonates on the development of osteoporosis during the initial stage has been studied [9], as has the effect of physical activity on calciuria and hydroxyprolinuria [10,11]. A study conducted in 1948 [12] showed a positive effect of ambulation on osteoporosis, but a similar recent study [13] failed to demonstrate any difference in bone mineral content between wheelchair-bound paraplegic patients and patients who used long leg braces for 1 h daily.

Since improvement of vertebral fixation procedures and various standing devices permit early standing, we wished to establish whether early and regular passive

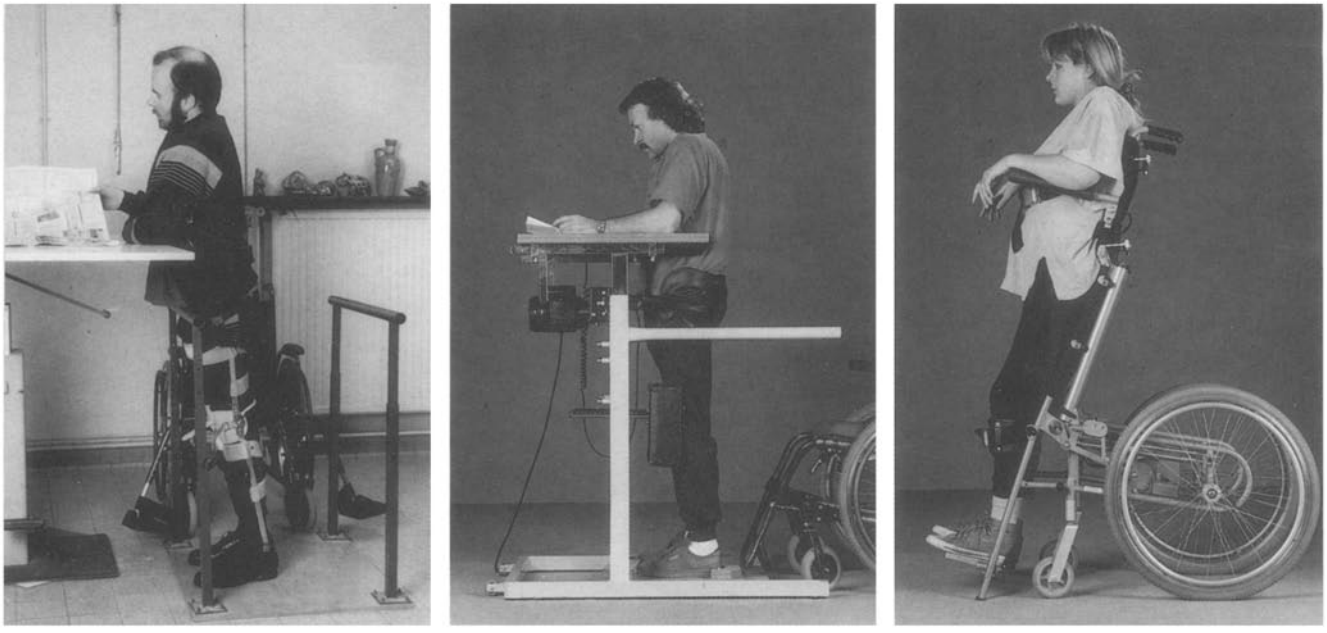

Fig. 1. *Left*: Standing using long leg braces: there is a real axial loading on the lower extremities ($n = 20$). *Middle*: Standing using a standing frame: a hip-suspension band is necessary to maintain the patient in the upright position ($n = 9$). *Right*: Standing using a standing wheelchair: the patient is bending backwards ($n = 9$).

mechanical loading of this type has any long-term effect on bone mineral density (BMD).

Patients and Methods

Patients

Fifty-three patients with complete traumatic spinal cord injury were included in this cross-sectional study. All patients were wheelchair-bound, not bedridden and ambulatory. Disease duration was longer than 1 year, to avoid the period of acute bone loss in paraplegic patients. As early as possible after the traumatic event (usually within 3 months) standing was performed and sustained over the long term if desired by the patient. Postmenopausal women, patients younger than 20 years of age and patients receiving bisphosphonates for periarticular ossification (PAO) were excluded from the study. No diseases or concurrent medications known to interfere with bone metabolism were identified from the history or routine biochemical investigations. The control population ($n = 53$) was recruited from the hospital staff and matched for sex and age (within 1 year of age).

For each patient the following parameters were recorded: the motor and sensory level of the lesion; passive range of motion of the hip and spasticity according to the Ashworth scale [14] (0, no increase in tone; 1, slight increase in muscle tone, giving a 'catch' when the limb is moved in flexion or extension; 2, more marked increase in tone, but the limbs can still be easily moved in flexion or extension; 3, considerable increase in tone, with passive movement being difficult; 4, limbs rigid in flexion or extension). If hip mobility was reduced, radiographs were obtained to establish the presence and degree of PAO according to the Brooker grading system [15].

After the acute immobilization period, the patients performed standing using various standing devices (Fig. 1): long leg braces ($n = 20$), a standing frame ($n = 9$) and a standing wheelchair ($n = 9$). Standing was continued at home after discharge from the hospital. The main reason for not performing standing ($n = 15$) was mostly the unwillingness of the patient, rather than the functional level. All patients had a score of 6 on the functional independence measurement scale of Granger [16], indicating an independence for activities of daily living (ADL) and transfers. The patients could be divided into three groups based on the frequency of standing: daily standing for at least 1 h, infrequent standing (3 times per week) and no standing.

Bone Densitometry

Bone mineral density (BMD) of the lumbar spine (L3, L4), the hip (neck, trochanter and total hip) and the mid-femoral shaft was assessed by dual photon X-ray absorptiometry (DXA) on a Hologic QDR1000/W (Waltham, MA). The second lumbar vertebra was excluded because of frequent interference from metal fixation devices; in some cases L3 and L4 also had to be excluded for the same reason. Hips with grade II and III PAO (Brooker's scale) were excluded from the analysis ($n = 2$). BMD of the forearm was assessed by single-photon absorptiometry (SPA) (Nuclear Data 1100A; Germany). DXA results are expressed as absolute values (BMD in g/cm^2) and as Z-scores (deviation from

the mean for age- and sex-matched healthy controls expressed as number of standard deviations). For lumbar spine and hip DXA, the reference population provided by the manufacturer was used. For femoral shaft DXA and for SPA measurements at the forearm, a local control population was used to calculate the *Z*-scores. For the forearm measurement we report the values at a cortical site (at the junction of distal and mid third of forearm) after correction for fat (BMC2 in arbitrary units) and after normalization for bone width (BMC2/BW in arbitrary units/mm).

Statistics

Statistical analysis was performed with the SAS statistical package running on a PC. Disease duration in the standing and non-standing group was compared using the non-parametric Wilcoxon rank sum test. Equality of the distributions of spasticity and sex in patient groups was tested using Fisher's exact test. All differences in absolute BMD values and *Z*-scores among the study groups were statistically evaluated using analysis of variance modelling techniques [17] (*t*-test and *F*-test). Influence of disease duration on BMD values was assessed by Spearman correlation testing. All model assumptions were checked by visual inspection for the Pearson residuals. The level of statistical significance was set at $\alpha = 0.05$.

Results

From our traumatic paraplegia population, 53 patients (42 males and 11 females) could be retained for this cross-sectional study after exclusion according to the aforementioned criteria. Clinical data for patients and controls are summarized in Table 1. No statistically significant differences were noted as regards disease duration and degree of spasticity between standing and non-standing paraplegic patients. Body weight was significantly higher in patients not performing standing.

Bone densitometry at the different measurement sites in the controls and the paraplegics showed significantly reduced values for total hip region (decrease of 33%) and the femoral shaft (decrease of 25%); BMD was not significantly different at the lumbar spine (L3 and L4). A non-significant increase in BMD at the proximal forearm was observed.

Comparison among the standing groups showed no differences between the group who stood daily ($n = 20$) and the group who stood three times weekly ($n = 18$) (data not shown). For this reason the data for these two standing groups were pooled ($n = 38$). For the different regions of interest, BMD (absolute values in g/cm^2 and *Z*-scores) in the standing and non-standing groups was compared with the control population and the results are summarized in Table 1 and Fig. 2. In paraplegia BMD was significantly decreased at the proximal femur and femoral shaft.

Table 1. Clinical data and bone densitometry results for paraplegic patients and controls

	Control subjects	Paraplegic patients	
		Standing	No standing
n (female/male)	53 (11/42)	38 (4/34)	15 (7/8)
Age: median and	35.9	34.6	34.7
range, years	21–60	20–60	21–58
Weight:[a] median and	75	68	80
range, kg	48–77	48–83	56–104
Disease duration:			
median and	–	31.7	50.5
range, months	–	12–118	12–180
% with spasticity[b]	–	79.5%	73.2%
Grade 1		31.5%	46.6%
Grade 2		31.5%	6.6%
Grade 3+4		16.5%	20.0%
BMD: Mean ± (SD), g/cm^2			
Mean *Z*-score[c]			
Lumbar spine			
L3	1.08 (0.14)	1.08 (0.24)	1.00 (0.18)
	−0.05	+0.34	−0.76[d]
L4	1.06 (0.17)	1.10 (0.14)	1.01 (0.19)
	−0.27	−0.45	−1.03
Hip[e]			
Neck[a]	0.89 (0.14)	0.67 (0.10)	0.67 (0.13)
	−0.04	−2.10	−2.12
Trochanter[a]	0.77 (0.12)	0.56 (0.10)	0.54 (0.10)
	+0.12	−2.23	−2.34
Total[a]	1.02 (0.14)	0.71 (0.13)	0.70 (0.17)
	−0.03	−2.24	−2.46
Femoral shaft[a]	1.85 (0.17)	1.46 (0.19)	1.31 (0.28)
	+0.04	−3.19	−5.02[d]
Forearm[f]			
BMC2	50.32 (9.15)	53.92 (8.44)	49.88 (7.32)
	+0.17	+0.78	+0.18
BMC2/BW	1.60 (0.20)	1.65 (0.17)	1.62 (0.17)
	−0.23	+0.15	−0.13

[a] Statistically significant difference among groups (*F*-test).
[b] Ashworth scale [14].
[c] *Z*-score: difference in standard deviations from the mean value in the same age class.
[d] Statistically significant difference between standing and non-standing paraplegic patients (*t*-test).
[e] Two patients with periarticular ossification excluded.
[f] BMC2 in arbitrary units, BMC2/BW in arbitrary units/mm.

Comparing controls and standing- and non-standing paraplegics, a statistically significant, partially preventive effect of standing on bone loss was achieved at the femoral shaft, but not at the proximal hip (Fig. 2). Limited bone loss at L3 and L4 was observed in the non-standing group (marginally significant for L3; $p = 040$). Standing did not affect BMD at the forearm.

In Table 2 the methods of standing are compared. Patients who used long leg braces had a significantly higher BMD in two hip subregions (trochanter and total hip) compared with patients using other standing devices.

Correlation between BMD and disease duration was significant only for the femoral shaft (Spearman correlation coefficient = −0.388, $p = 0.004$). The degree of spasticity or the level of the spinal cord injury did not

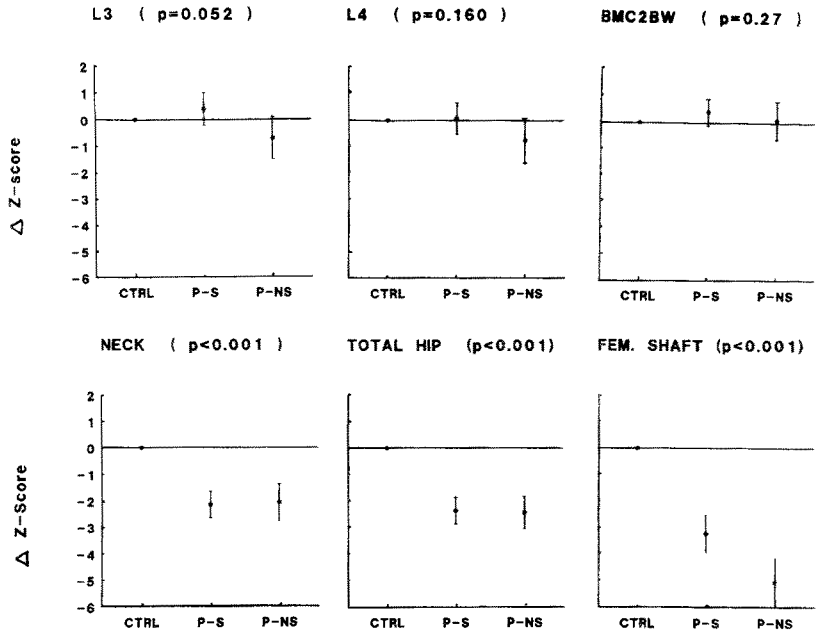

Fig. 2. Differences in mean bone mineral density (Δ *Z*-scores) and 95% confidence intervals between paraplegic patients (standing and non-standing group) and the matched controls at different regions of interest. The *p* value (*F*-test) indicates the statistically significant difference among the three groups. CTRL, control population (n = 53); P–S, paraplegic patients in standing group (n = 38); P–NS, paraplegic patients in non-standing group (n = 15).
Ordinate, difference in *Z*-scores from matched controls.

Table 2. Bone mineral densities expressed as mean absolute values and SD and mean *Z*-scores in patient groups according to the method of standing

	Long leg braces	Standing frame	Standing wheelchair
n (female/male)	20 (5/15)	9 (2/7)	9 (1/8)
Age: median and range, years	34 20–60	24 20–50	35 26–60
Weight:[a] median and range, kg	66 48–80	65 56–72	75 60–83
Disease duration: median and range, months	34 12–118	33 14–84	48 27–100
BMD: Mean ± (SD), g/cm^2 Mean *Z*-score[c]			
Lumbar spine			
L3	1.04 (0.30) +0.28	1.07 (0.10) −0.13	1.15 (0.21) −0.26
L4	1.08 (0.10) −0.39	1.05 (0.10) −0.63	1.15 (0.20) +0.27
Hip[b]			
Neck	0.71 (0.09) −1.70	0.63 (0.10) −2.70	0.62 (0.09) −2.75
Trochanter[a]	0.59 (0.10) −1.52	0.54 (0.09) −2.05	0.48 (0.08) −2.53
Total[a]	0.76 (0.13) −1.73	0.67 (0.11) −2.73	0.59 (0.09) −3.22
Femoral shaft	1.48 (0.18) −3.76	1.45 (0.25) −3.82	1.43 (0.17) −3.56
Forearm[c]			
BMC2[a]	51.64 (8.02) +0.56	55.19 (7.62) +1.19	58.36 (9.71) +0.91
BMC2/BW	1.64 (0.15) +0.25	1.69 (0.20) +0.45	1.60 (0.20) −0.41

[a] Statistically significant difference among groups (*F*-test).
[b] Two patients with periarticular ossification were excluded.
[c] BMC2 in arbitrary units, BMC2/BW in arbitrary units/mm^3.

affect BMD (data not shown). The lesion involved the lumbar region in four cases; all other patients had lesions of the thoracic spine.

Discussion

This cross-sectional study of wheelchair-bound paraplegic patients confirms the decrease in BMD in the non-weightbearing areas (hip and femoral shaft) also reported in previous studies [12]. The present study also illustrates the much better preservation of bone mass at the lumbar spine (L3, L4) in contrast to the markedly decreased BMD values at the hip and the femoral shaft. In this respect the term 'sublesional osteoporosis' should be used cautiously when referring to the bone loss in paraplegia. A possible explanation for this finding could be the 'bone-preserving' effect of weightbearing in these wheelchair-bound patients. Also, more mechanical stress could be transmitted to these areas due to the presence of internal bone fixation material.

The preventive effect of standing on bone loss at the femoral shaft contrasts with the absence of such an effect at the proximal femur. Possibly, the transmission of force through trabecular and cortical bone differs, so that the minimal effective strain for initiating bone remodeling [18] is reached more rapidly in cortical bone. Another possibility is that there exist different strain thresholds to control bone modeling and remodeling [18].

Previous studies [11,12,19] also demonstrated beneficial effects of weightbearing and activity on bone metabolism. In a recent study, Biering-Sörensen et al. [13] could not demonstrate a positive effect of standing on bone mineral content (BMC), which is in contrast to the findings in the present study. Differences in study design may account for this apparent discrepancy. In the

present study standing was performed as early as possible after the traumatic event. Patients were only included in the study if the disease duration was at least 1 year, which should avoid the period of acute bone loss and allow the study of the 'osteoporotic steady-state' situation, as has been demonstrated in several studies [2,8].

Although our patients had been paraplegic for more than 1 year, the influence of disease duration was significant at the femoral shaft, which might indicate that loss of cortical bone continues for more than 1 year after the injury. There were no significant differences in disease duration among patient groups in the present study. However, data of a cross-sectional study should be interpreted with caution in this regard.

Whether a patient did or did not perform standing depended primarily on the motivation of the patient. Not performing standing was not correlated with a lesser degree of activity or a more sedentary life in our patients; all patients were ambulatory and functionally independent as measured by the functional independence measurement scale of Granger [16]. However, the limitations inherent in a cross-sectional study design must be borne in mind here also. Except for body weight, no significant differences between subgroups could be identified in the patient characteristics (Table 1). The known positive correlation between body weight and BMD [20] does not confound our results as patients performing standing had a lower mean body weight compared with controls and non-standing patients.

The existence of a mechanical influence on bone metabolism is known from many studies [18,21–23]. In the present study the type of standing may be important, as is suggested by the higher BMD values at the proximal femur in the patients using long leg braces than in those using a standing wheelchair or a standing frame. Again, body weight (see Table 2) cannot confound these results because the body weight was significantly higher in the patients using a standing wheelchair as compared with patients performing standing with the aid of long leg braces or a standing frame. When long leg braces are used, axial loading on the hip is higher than with standing wheelchairs as a consequence of the more vertical standing position. Patients using a standing frame need suspension at the gluteal region, which diminishes the load transfer to the hip.

In contrast to the bone loss in the lower extremities, a non-significant increase of BMD in the forearm was noted. In analogy with the calcium redistribution according to a gravity gradient that is seen in other forms of immobilization osteoporosis [24,25], bone repartition may be influenced by factors such as regional changes in blood circulation. However, in ambulatory wheelchair-bound paraplegic patients the increased force on the forearm during transfers might be a significant contributory factor.

Lower extremity fracture in paraplegic patients [26] has been reported to occur in 7% of the cases with complete lesions. Femoral fractures are more frequently located in the supracondylar (33%) and midfemoral regions 30%, which is in contrast with the more proximally located femoral fractures seen in involutional osteoporosis. These fractures usually occur spontaneously or after only minimal trauma. One patient in the present study had a history of a supracondylar femoral fracture. His axial bone mass was within normal limits (Z-score -1.4), while bone density at the femoral neck and shaft was markedly reduced (Z-scores of -4.1 and -8.5, respectively).

Daily standing has proven to be effective in maintaining an adequate range of motion and diminishing the spasticity [27]. The present study suggests an additional beneficial effect on bone mass of the proximal femur and femoral shaft, which might be of clinical importance in reducing the risk of femoral fractures in paraplegic patients.

References

1. Chantraine A. L'ostéoporose et les para-ostéo-arthropathies au cours de la paraplégie. Brussels: Editions Arscia, 1979.
2. Chantraine A. Actual concepts of osteoporosis in paraplegia. Paraplegia 1978;16:51–8.
3. Klein L, Van De Noort S, Dejak JJ. Sequential studies of urinary hydroxyproline and serum alkaline phosphatase in acute paraplegia. Med Serv J Can 1966;22:524–33.
4. Chantraine A, Nusgens B, Lapiere CM. Bone remodeling during the development of osteoporosis in paraplegics. Calcif Tiss Int 1986;38:323–7.
5. Privat C, Martinazzo J, Ohanna F. Physiopathologie: 'os, peau, contractures'. In: Actes des Seconds Entretiens de la Fondation Garches, 6–7 October 1989:27–45.
6. Chantraine A. Clinical investigation of bone metabolism in spinal cord lesions. Paraplegia 1971;8:253–9.
7. Minaire P, Meunier PJ, Edouard C, et al. Quantitative histological data on disuse osteoporosis. Calcif Tissue Res 1974;17:57–73.
8. Bergmann P, Heilporn A, Schoutens A, et al. Longitudinal study of calcium and bone metabolism in paraplegic patients. Paraplegia 1977;15:147–59.
9. Minaire P, Berard E, Meunier PJ, et al. Effects of disodium dichloromethylene diphosphonate on bone loss in paraplegic patients. J Clin Invest 1981;68:1086–92.
10. Naftchi NE, Viau AT, Sell GH, et al. Mineral metabolism in spinal cord injury. Arch Phys Med Rehabil 1980;61:139–42.
11. Kaplan PE, Roden W, Gilbert E, et al. Reduction of hypercalciuria in tetraplegia after weight-bearing and strengthening exercises. Paraplegia 1981;19:289–93.
12. Abramson AS. Bone disturbances in injuries to the spinal cord and cauda equina (paraplegia). J Bone Joint Surg [Am] 1948;30:982–7.
13. Biering-Sörensen F, Bohr H, Schaadt O. Bone mineral content of the lumbar spine and lower extremities years after spinal cord lesion. Paraplegia 1988;26:293–301.
14. Ashworth B. Preliminary trial of carisoprodol in multiple sclerosis. Practitioner 1964;192:540–2.
15. Keith R, Granger C, Hamilton B, Sherwin F. The functional independence measure: a new tool for rehabilitation. Adv Clin Rehabil 1987;1:6–18.
16. Brooker A, Bowerman J, Robinson R, et al. Ectopic ossification following total hip replacement. J Bone Joint Surg [Am] 1973;55:1629–39.
17. Glantz SA, Slinker BK. Primer of applied regression and analysis of variance. New York: MacGraw-Hill, 1990.
18. Frost HM. Perspectives: bone's mechanical usage windows. Bone Miner 1992;19:257–71.
19. Kaplan E, Gandhavadi B, Richars L, et al. Calcium balance in

paraplegic patients: influence of injury duration and ambulation. Arch Phys Med Rehabil 1978;59:447–50.
20. Martin P, Verhas M, Als C, Geerts L, Paternot J, Bergmann P. Influence of patient's weight on dual-photon absorptiometry and dual-energy X-ray absorptiometry measurements of bone mineral density. Osteoporosis Int 1993;3:198–203.
21. Whalen RT, Arnaud SB, Grindeland RE. Proceedings of the NASA symposium on the influence of gravity and activity on muscle and bone. J Biomech 1991;24:1–178.
22. Gutin B, Kasper MJ. Can vigorous exercise play a role in osteoporosis prevention? A review. Osteoporosis Int 1992;2:55–69.
23. LeBlanc AD, Schneider VS, Evans HJ, Engelbretson DA, Krebs JM. Bone mineral loss and recovery after 17 weeks of bed rest. J Bone Miner Res 1990;5:843–50.
24. Arnaud SB, Morey-Holton E. Gravity, calcium, and bone: update 1989. Physiologist 1990;33:S65–68.
25. Schneider V, Oganov A, LeBlanc A, Rakhmanov A, Bakulin A, Grigoriev A, Varonin L. Space flight bone loss and change in fat and lean body mass. J Bone Miner Res 1992;7:S122.
26. Ragnarsson KT, Seel GH. Lower extremity fractures after spinal cord injury: a restrospective study. Arch Phys Med Rehabil 1981;62:418–23.
27. Oden I, Knutsson E. Evaluation of the effects of muscle stretch and weight load in patients with spastic paraplegia. Scand J Rehabil Med 1981;13:117–21.

Received for publication 12 May 1993
Accepted in revised form 3 September 1993