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Bone mineral density in upper and lower extremities during 12 months after spinal cord injury measured by peripheral quantitative computed tomography

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Objective: To evaluate the loss of trabecular and cortical bone mineral density in radius, ulna and tibia of spinal cord injured persons with different levels of neurologic lesion after 6, 12 and 24 months of spinal cord injury (SCI).
Design: Prospective study in a Paraplegic Centre of the University Hospital Balgrist, Zurich.
Subjects and methods: Twenty-nine patients (27 males, two females) were examined by the highly precise peripheral quantitative computed tomography (pQCT) soon after injury and subsequently at 6, 12 and in some cases 24 months after SCI. Using analysis of the bone mineral density (BMD), various degrees of trabecular and cortical bone loss were recognised. A rehabilitation program was started as soon as possible (1–4 weeks) after SCI. The influence of the level of neurological lesion was determined by analysis of variance (ANOVA). Spasticity was assessed by the Ashworth Scale.
Results: The trabecular bone mineral density of radius and ulna was significantly reduced in subjects with tetraplegia 6 months (radius 19% less, $P<0.01$; ulna 6% less, $P>0.05$) and 12 months after SCI (radius 28% less, $P<0.01$; ulna 15% less, $P<0.05$). The cortical bone density was significantly reduced 12 months after SCI (radius 3% less, $P<0.05$; ulna 4% less, $P<0.05$). No changes in BMD of trabecular or cortical bone of radius and ulna were detected in subjects with paraplegia. The trabecular BMD of tibia was significantly reduced 6 months (5% less, $P<0.05$) and 12 months after SCI (15% less, $P<0.05$) in all subjects with SCI. The cortical bone density of the tibia only was decreased after a year following SCI (7% less, $P<0.05$). No significant difference between both groups, subjects with paraplegia and subjects with tetraplegia was found for tibia cortical or trabecular BMD. There was no significant influence for the physical activity level or the degree of spasticity on bone mineral density in all subjects with SCI.
Conclusions: Twelve months after SCI a significant decrease of BMD was found in trabecular bone in radius and in tibia of subjects with tetraplegia. In subjects paraplegia, a decrease only in tibia BMD occurred. Intensity of physical activity did not significantly influence the loss of BMD in all subjects with para- and tetraplegia. However, in some subjects regular intensive loading exercise activity in early rehabilitation (tilt table, standing) can possibly attenuate the decrease of BMD of tibia. No influence was found for the degree of spasticity on the bone loss in all subjects with SCI.
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Keywords: spinal cord injury; bone mineral density; peripheral quantitative computed tomography; physical activity; spasticity

Introduction

There are many factors influencing bone mineral density namely hormonal[1,2] activity dependent[3,4] or gravity dependent.[5,6] Also spinal cord injury (SCI) is associated with loss of bone mineral density.[7–18]

It is empirically known that osteoporosis below the level of the SCI by far exceeds the normal loss of bone mass associated with many causative factors. These include ageing,[19] bed rest and immobilisation,[3,20,21] absence of gravity during space flights,[5,6] or disuse due to disorders other than paralysis.[22,23] An equilibrium between bone reabsorption and formation is established 2 years after SCI.[8] Common complications of long term SCI are spontaneous or pathological

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fractures of long bones. Such fractures occur in subjects with paraplegia, mostly in lower extremities with an incidence of 2–6 per cent.[24,25] It is poorly understood whether clinical interventions can prevent the decrease of bone mass[26] after SCI and thereby prevent fractures. However, in normal subjects, physical activity is considered as the most important non-hormonal factor influencing bone formation and reabsorption.[20,27] According to the literature, loss of bone mass occurs most rapidly during the first 4 months and reaches a level of two-thirds of original bone mass about 16 months following complete SCI.[8] Other bone density studies have shown that bone mineral content in patients with chronic SCI reaches a level of 75% in the proximal femur and 50% in the proximal tibia of healthy subjects.[9] In some subjects with tetraplegia, during the early phase after SCI the calcium balance can become negative and can lead to a serious hypercalcemia.[28] An increase in bone mineral density resulting from intensive training programs could not feasibly be achieved, but some influence on bone mineral density could be shown by passive weight bearing,[26,29] walking with orthoses[30] or electrically induced ergometry training for lower extremities.[31] The aim of the present study was to evaluate the trabecular and cortical BMD development for upper and lower extremities in subjects with para- and tetraplegia and to obtain more detailed information about the factors influencing this development over the time after SCI.

Table 1 Subject characteristics

Subject Nr.	*Age at injury (years)*	*Level of lesion*	*Frankel classification*	*Activity** lower extremities*	*Ashworth score*
01	32	C4	B	No	3
06	24	C4	B	No	3
13	38	C4	B	No	3
21	19	C5	B	Yes	2
00	53	C6	C	Yes	2
04*	28	C7	B	interrupted	
09	27	C6	B	Yes	3
15	26	C6	B	No	3
16	57	C6	B	interrupted	
24	32	T4	A	Yes	2
20	40	T4	A	Yes	2
05	32	T5	C	Yes	1
11	26	T5	B	No	2
17	26	T6	A	No	3
14	27	T8	C	Yes	3
22*	29	T8	A	interrupted	
03	34	T9	A	Yes	2
08	48	T10	A	Yes	2
02	25	T11	A	Yes	1
12	22	T12	C	Yes	2
07	43	T12	A	Yes	2
18	59	T12	A	No	3
19	32	T12	C	Yes	2
23	30	T12	C	Yes	1
25	57	T12	B	Yes	2
26	40	T12	C	Yes	1
10	21	L1	A	No	1

*Females; **standing or walking program

Methods

Subjects and protocol

During a period of 2½ years, 29 subjects with SCI were consecutively admitted to the Swiss Paraplegic Centre of the University Hospital Zurich. Subjects were enrolled in the program after receiving oral and written information about the study. Patients signed a statement of informed consent approved by the local ethical committee. All subjects had endured traumatic SCI, 27 were males and two were females. The characteristics of each subject are charted in Table 1. Within 8 h after injury every patient received methylprednisolon adapted to body weight on the basis of the NASCIS protocol.[32] Three patients were treated only non-surgically. In the other patients surgical stabilisation of vertebral fractures was performed. All patients received heparinisation once daily adapted to their body weight, until 8 weeks after full remobilisation. Other administered drugs were stool softeners, muscle relaxants, antispastic drugs and antibiotics. Two drugs (heparin, methylprednisolon), are known to influence bone metabolismus. Medical examination was done for each subject to identify any possible contraindication (metabolic disease, tumour, drug abuse) to participate in this study. The evaluation included neurological examination, X-rays of the spine and chest and blood analysis. Contraindication for participation in the study were previous lower or upper body extremity fractures and serious psychological or internal problems. To evaluate a possible previous bone risk factor a questionnaire about nutritional status,[33] medical history and lifestyle was completed by each subject under supervision of the physician. Only subjects satisfying the medical report participated in the study.

Peripheral quantitative computed tomography

Bone measurements were performed with a low dose pQCT (DENSISCAN 1000, Scanco Medical AG, Zürich, Switzerland) which has a long term reproducibility of only 0.3% in a mixed population of normal individuals and patients with osteopenia or osteoporosis, and lateral picture resolution of 0.2 mm.[34–36] This system enabled us to separately assess trabecular and cortical bone density in the radius (ulna) and tibia and to differentiate between non, slow and fast bone losers within a few months. Fast bone losers are defined as patients who lose more than 3% trabecular bone density in the radius per year.

The measuring procedure used for this study is described as follows: To ensure that the tomograms were continually made at an identical angle relative to

the bone axis, the extremities of the patients were positioned in anatomically formed radiolucent casts. To define the position of the first tomogram relative to the 'endplate' of the distal radius (ulna) or tibia, a scout view was made. The examination site in the ultradistal radius/ulna was then converted with a stack of ten tomograms (slice thickness 1 mm, interslice distance 1.5 mm), and the average bone density over the core volume was calculated. This value corresponded to pure trabecular bone density (mg/cm^3). Cortical BMD was measured in the meta-/diaphysis from six tomograms. Volumes from 3–10 cm^3 were evaluated. The radiation dose per examination was 0.1 mSv. After the last measurements the bone volume common to all measurements in an extremity was selected by superimposing the stack of tomograms and detection of identical cross-sectional areas and contours. Then the trabecular and cortical BMD were calculated from this 'common volume'. Monthly follow-up measurements were performed in each SCI subject for the ulna and tibia bone mineral density during the first 12 months. Several measurements were also taken 18 and 24 months after SCI in some subjects.

Spasticity The clinically defined degree of spasticity was assessed on the Ashworth Scale.[37] The Ashworth Scale was used to assess the degree of muscle tone on lower extremities and was rated from 0 (no increase in muscle tone) to 4 (limb rigid in flexion or extension).

Level of impairment The neurological defined level of injury and the degree of impairment in our patients was assessed by the ASIA impairment scale.[38] Accordingly the patients were graded for their impairment into Frankel classes ranging from A (complete) to B–D (incomplete).

Physical activity All patients underwent a physical training program, walking or standing. The early rehabilitation program was started as soon as possible after SCI (1–4 weeks). Patients with incomplete spinal cord lesion participated in the walking program, as used in our centre.[39,40] The stepping movements could be induced on a treadmill moving at slow speed (about 1.3 km/h). Contraindications for participation in walking exercise included lower motoneuron involvement, previous lower extremity fracture, and medical instability. Subjects with complete spinal cord lesion were allocated to a standing training using a standing frame with hip-suspension.

The frequency of physical training (standing and walking) was at least three times per week for 30 min. Because of motivational or health problems, 11 subjects were not able to reach this exercise level during the time of study. These subjects were in the 'inactive group'. All subjects with the full physical training were in the 'active group'.

Statistical analyses
Patients were separated for statistical analysis into two groups, subjects with paraplegia or tetraplegia. Repeated measures analysis of variance was used for the statistical analysis of the time series measurements of the cases, in order to assess the effect of physical training in the two groups of subjects. Statistical analyses were performed using the SAS statistical analysis system. A significance level of $P<0.05$ was chosen for all tests. The difference in measured bone parameters between three measurements (month 1 and month 6, month 1 and month 12) was calculated as percentage difference relative to the initial value of the two measurements.

Results

Upper extremity measurements

Radius/ulna In subjects with paraplegia, no significant changes ($P>0.05$) were found in trabecular or cortical BMD 6 and 12 months. In subjects with tetraplegia for radius trabecular bone BMD losses of 19% and 28% ($P<0.01$) were found 6 and 12 months after SCI, respectively. For ulna trabecular bone BMD losses of 6% and 15% ($P<0.05$) were found for the same time periods. For the cortical bone, BMD losses of 3% and 4% ($P<0.05$) were found for radius and ulna 12 months after SCI (Tables 2 and 3).

Table 2 BMD of radius in trabecular and cortical bone over time for all, para- and tetraplegic subjects

	1 month after SCI ± *SD* (mg/cm^3)		*6 months after SCI* ± *SD* (mg/cm^3)		*12 months after SCI* *SCI* ± *SD* (mg/cm^3)		*Decrease after 6 months* (%)		*Decrease after 12 months* (%)	
Trabecular bone										
All subjects $n=24$	322	(72)	294	(62)	303	(91)	−4**	(13)	−8**	(20)
Paraplegic $n=18$	319	(74)	301	(74)	334	(75)	0	(2)	0	(2)
Tetraplegic $n=6$	331	(70)	267	(71)	223	(85)	−19**	(24)	−28**	(32)
Cortical bone										
All subjects $n=24$	1212	(145)	1207	(147)	1218	(130)	+1	(6)	0	(3)
Paraplegic $n=18$	1207	(152)	1189	(152)	1219	(149)	−2	(6)	+1	(2)
Tetraplegic $n=6$	1226	(134)	1274	(120)	1217	(73)	0	(1)	−3*	(5)

*Significant $P<0.05$, **significant $P<0.01$

Lower extremity measurements

Tibia In all SCI subjects the tibia bone measurements (Table 4) showed a pronounced loss of trabecular compared to cortical bone. For each subject the absolute changes in trabecular and cortical BMD and the relative percentage change from baseline values in BMD per year were calculated. There was a loss of trabecular bone of 5% for all subjects 6 months after SCI and 15% after 12 months after SCI. For the cortical bone losses of 2% and 7% ($P<0.05$) were found for the same time periods. There was no significant difference between subjects with paraplegia (6% and 14% loss for trabecular, 2% and 7% for cortical bone) and tetraplegia (4% and 16% for trabecular, 1% and 8% for cortical bone). The degree of spasticity, assessed by Ashworth scale did not significantly influence the loss of BMD in the tibia. Also the chosen intensity of physical activity did not significantly ($P>0.05$) influence the loss of BMD.

Single cases In one inactive subject with tetraplegia (Figure 1b) the greatest loss of tibia BMD occurred 1 and 2 years after SCI (14% and 80% for trabecular, 2% and 20% respectively for cortical bone). In the same subject loss of radius BMD was 65% and 71% for trabecular and 4% and 11% for cortical bone, respectively (Figure 1a, 2). In two subjects (Figure 3), who performed regular standing activity at least 1 h four times per week over the time, tibia BMD remained stable. The loss for trabecular bone was only 3% and 1.5% respectively after 24 months.

Discussion

The aim of the present study was to evaluate the BMD development over time after SCI for upper and lower extremities in subjects with para- and tetraplegia. The main results were a significant loss of trabecular BMD in the radius and tibia in subjects with tetraplegic and a significant loss of trabecular BMD only in the tibia in subjects with paraplegia. These results are in agreement with other studies which confirm the development of bone mineral loss dependent on the level of lesion.[7,9,10,18,41,42] Our results show a clear dissociation of BMD loss between the trabecular and cortical compartments, which was found in all subjects. All BMD values were within the normal range at the beginning of measurements. In trabecular bone considerable loss of BMD occurred very rapidly after SCI. In contrast, loss of cortical BMD began later, and was significant

Table 3 BMD of ulna for trabecular and cortical bone over time in all, para- and tetraplegic subjects

	1 month after SCI $\pm SD$ (mg/cm^3)	*6 months after SCI* $\pm SD$ (mg/cm^3)	*12 months after SCI* $SCI \pm SD$ (mg/cm^3)	*Decrease after 6 months* (%)	*Decrease after 12 months* (%)
Trabecular bone					
All subjects $n=24$	374 (79)	364 (70)	360 (81)	−1 (7)	−4* (13)
Paraplegic $n=18$	378 (83)	372 (75)	390 (61)	0 (6)	0 (6)
Tetraplegic $n=6$	364 (70)	332 (40)	284 (57)	−6 (8)	−15* (20)
Cortical bone					
All subjects $n=24$	1195 (156)	1183 (170)	1176 (148)	0 (1)	−1* (4)
Paraplegic $n=18$	1188 (175)	1178 (185)	1185 (170)	0 (1)	0 (2)
Tetraplegic $n=6$	1217 (80)	1206 (103)	1153 (67)	0 (1)	−4* (6)

*Significant $P<0.05$, **significant $P<0.01$

Table 4 BMD of tibia for trabecular and cortical bone over time in all, para- and tetraplegic subjects and in active and inactive subjects

	1 month after SCI $\pm SD$ (mg/cm^3)	*6 months after SCI* $\pm SD$ (mg/cm^3)	*12 months after SCI* $SCI \pm SD$ (mg/cm^3)	*Decrease after 6 months* (%)	*Decrease after 12 months* (%)
Trabecular bone					
All subjects $n=24$	310 (67)	276 (58)	262 (65)	−5 (9)	−15* (15)
Paraplegic $n=16$	314 (70)	284 (64)	261 (63)	−6 (11)	−14* (16)
Tetraplegic $n=6$	299 (64)	258 (42)	265 (74)	−4 (4)	−16* (8)
Active $n=13$	316 (72)	283 (64)	277 (47)	−7 (12)	−8* (18)
Inactive $n=11$	302 (64)	269 (55)	249 (78)	−3 (4)	−20* (14)
Cortical bone					
All subjects $n=24$	924 (129)	903 (132)	855 (114)	−2 (3)	−7 (5)**
Paraplegic $n=18$	936 (136)	907 (137)	876 (120)	−2 (3)	−7 (5)**
Tetraplegic $n=6$	893 (113)	896 (133)	811 (95)	−1 (0)	−8 (4)**
Active $n=13$	935 (136)	900 (126)	889 (116)	−2 (4)	−6 (5)**
Inactive $n=11$	910 (126)	908 (147)	827 (112)	−1 (2)	−8 (4)**

*Significant $P<0.05$, **significant $P<0.01$

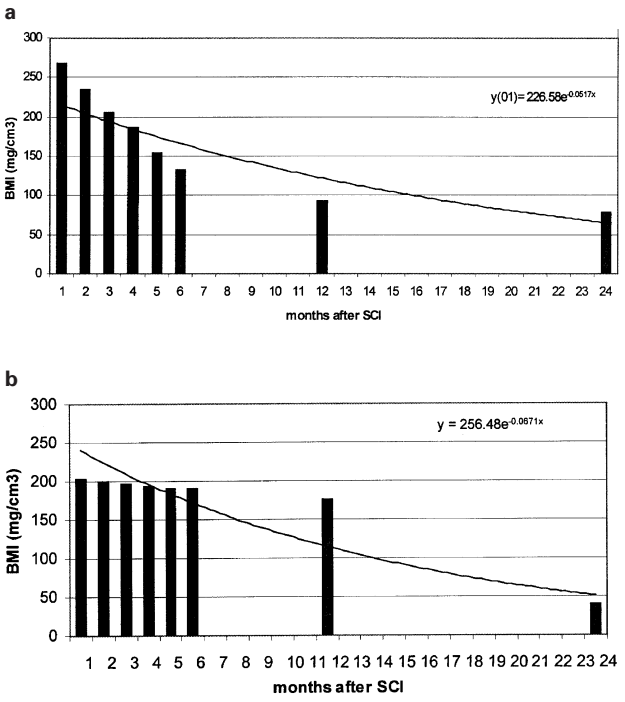

Figure 1 (a) BMD development of trabecular bone of radius. Single case: Patient No. 01. (b) BMD development of trabecular bone of tibia. Single case: Patient No. 01

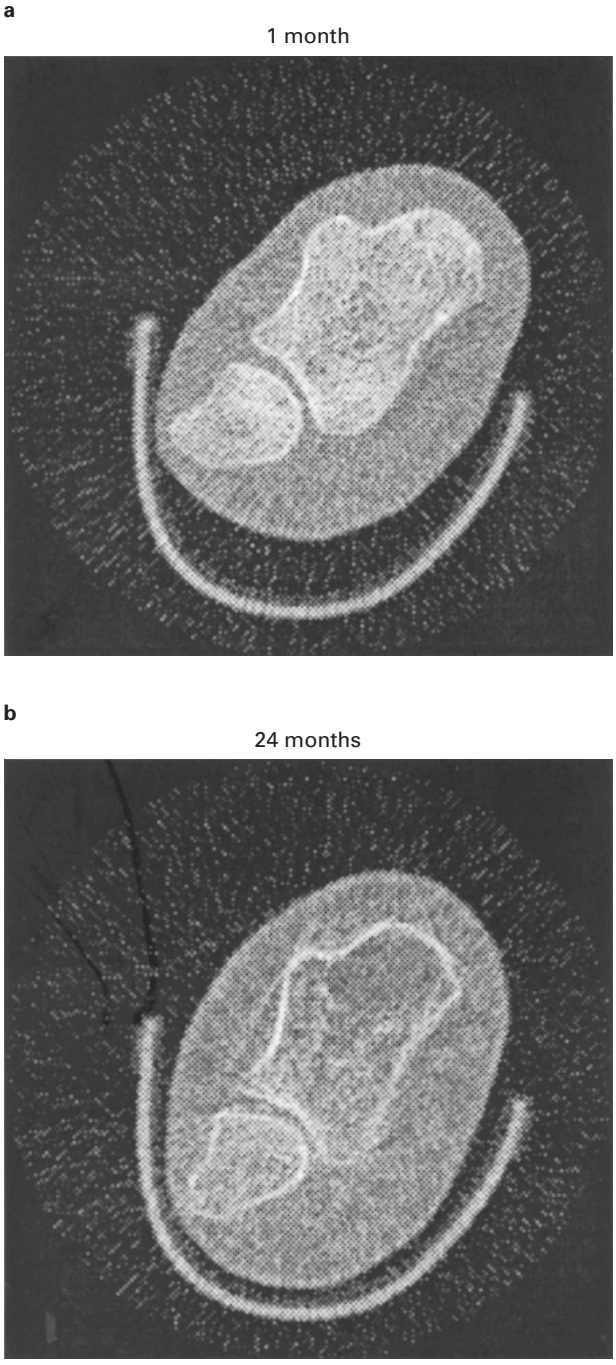

Figure 2 BMD development of trabecular bone of radius. Single case: Patient No. 01 1 and 24 months after SCI

only 12 months after SCI. Neither biochemical bone markers nor the majority of non-invasive bone densitometry methods can differentiate between cortical and trabecular bone. Even substantial loss of trabecular bone compartment can be masked by an unchanged cortical bone mass. This 'bimodal' bone loss primarily of trabecular bone compartment and the relative stability of the cortical bone in subjects with SCI supports the concept of type II osteoporosis[19] in SCI. This observation could have important implications for the early recognition of SCI-induced osteoporosis and consequent pharmaceutical treatment[43] in the future. In this context it should be considered that the risk of osteoporotic fractures in lower extremities is higher for paralysed people compared to healthy people.[24,25]

Further follow-up studies are needed to monitor the bone structure (cortical and trabecular) after SCI. The physical activity chosen here cannot prevent bone loss after SCI. Because of motivational problems, it was frequently difficult to enhance physical activity every day. Despite the obvious demands for an intensive body loading in order to maintain bone mass, there is some evidence that not only active but also passive training can be useful to prevent bone loss: In a study by Goemare *et al*[26] the BMD of the femoral shaft was higher in subjects with paraplegia who performed passive weight bearing (standing) than in those without this training. Also in our study in two exceptionally active subjects, who performed standing activity over the course of rehabilitation, the bone loss depleted slower, than would be expected from the other subjects. Higher risk of lower extremities fractures has to be taken into consideration when standing or non-standing is used as a rehabilitation means in persons with SCI.[26] Studies with a different duration of daily standing training are needed to see the exact effect of axial weight loading on the changes of BMD in SCI subjects.

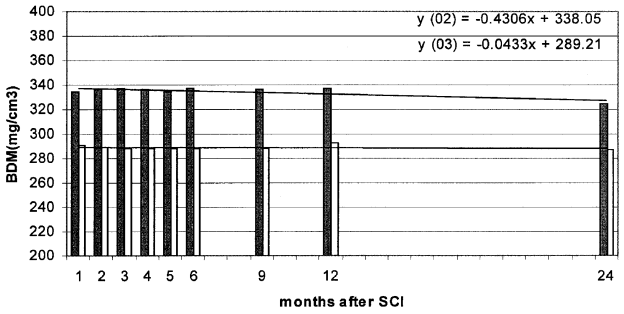

Figure 3 Tibia trabecular bone in two patients, who performed regular standing activity over 24 months. The BMD loss was 3% in patient No. 01 and 1.5% in patient No. 03

Conclusions

Highly precise and accurate methods for measuring the dissociation of trabecular and cortical bone loss has never been applied in spinal cord injured patients. In our study, a dissociated loss of trabecular and cortical BMD has been shown in subjects with SCI. Every individual with SCI may also experience a quantitatively different evolution of bone loss. Exact measurements of BMD are recommended to assess the possible risk of pathologic fractures in SCI subjects.

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