Use of Bone Biochemical Markers With Dual-Energy X-Ray Absorptiometry for Early Determination of Bone Loss in Persons With Spinal Cord Injury

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Our cross-sectional study aimed at the early determination of changes in bone metabolism in terms of bone mineral density (BMD) and bone turnover in persons with complete spinal cord injury (SCI) during the acute phase of paraplegia. Combined dual-energy x-ray absorptiometry (DXA) and specific biochemical markers of bone turnover were used to determine bone metabolism. Seven persons with SCI (age, 31.3 ± 9.5 years) who had sustained injury an average of 3 months earlier (103 ± 10.8 days) were compared with 10 able-bodied controls (27.5 ± 4.3 years). Four paraplegics and 3 quadriplegics composed the SCI group. BMD was measured by DXA, while bone turnover was evaluated by serum osteocalcin (OC), bone alkaline phosphatase (B-ALP), and serum and urinary type I collagen C-telopeptide (CTXs and CTXu). Regional BMD (proximal femur, lumbar spine, radius, lower limb) was similar in the 2 groups except in the upper limb ($P < .05$). CTXs and CTXu were significantly higher in SCI ($P < .01$ and $P < .001$, respectively), whereas among the bone formation markers used, only serum OC was affected by immobilization ($P < .05$). The SCI group developed hypercalciuria (0.76 ± 0.37 *v* 0.35 ± 0.14), whereas calcemia was normal (2.42 ± 0.09 *v* 2.31 ± 0.10). Intact parathyroid hormone (iPTH) and 1.25 $(OH)_2$ vitamin D levels were suppressed in persons with SCI ($P < .001$) by 80.6% and 66%, respectively. In conclusion, it was not possible to detect any variation in BMD from the DXA technique at this early stage of demineralization, but the sensitivity and early response of the biochemical markers strongly suggested their usefulness for the early identification of persons with SCI at risk of severe osteoporosis.

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BOTH CANCELLOUS AND cortical bone mass decline in men over the normal course of aging by approximately 30%, which results in "elderly osteoporosis". This disease has been characterized by low bone mass associated with microarchitectural deterioration of bone tissue, leading to increased bone fragility and fracture risk.[1] On the other hand, under certain conditions, such as short periods of weightlessness or immobilization, the lack of mechanical loading induces the rapid bone loss that characterizes "immobilization osteoporosis". In persons with spinal cord injury (SCI), loss of bone mass has been found to occur mainly in the lower limbs and in areas richly provided with trabecular bone, such as the pelvis.[2-11] During the first 4 months postinjury, the bone mineral content (BMC) of the distal femur is rapidly depleted,[5] whereas the lumbar spine is not affected.[3,7,8,10] The calcium loss in the bone matrix modifies bone architecture and is at the origin of pathologic fractures after minor trauma.[12]

Bone mineral density (BMD), which reflects bone solidity, can be accurately evaluated in paraplegics[2-11] using the dual-energy x-ray absorptiometry (DXA) technique. This technique, however, cannot be used for the early identification of those persons with SCI who are developing a fast demineralization process and thus present a high risk of acute osteoporosis. Various investigators have reported that bone biochemical markers could constitute reliable indicators leading to early characterization of bone turnover.[13,14]

Until now, only a few studies have simultaneously examined BMD and the responses of biochemical markers of bone turnover in persons with SCI.[9,15] Moreover, these studies did not evaluate specific biochemical markers of bone turnover, such as serum and urinary C-telopeptide (CTX) or bone alkaline phosphatase (B-ALP). Yet because of their specificity and sensitivity, these markers might provide useful and complementary information.

Our cross-sectional study aimed at the early determination of changes in bone metabolism in terms of BMD and bone turnover in persons with complete SCI during the acute phase of paraplegia. Combined DXA and specific biochemical markers of bone turnover were used to determine bone metabolism. In addition, we analyzed the hormonal calciotropic factors that influence bone metabolism. Our work may constitute a starting point for future studies aiming at the early estimation of the risk of severe osteoporosis in persons with SCI.

MATERIALS AND METHODS

Subjects

The difficulties related to moving persons with recent SCI from a rehabilitation center to a specialized service (Nuclear Medicine) were such that only 7 Caucasian male subjects participated in this study. Seven acute spinal cord-injured subjects (20 to 41 years) who had sustained injury an average of 3 months (103 ± 10.8 days) earlier were recruited from the spinal injuries clinic, Propara (Montpellier, France). All patients had traumatic and complete lesions of the spinal cord; 4 were paraplegic (D4 to D10) and 3 were quadriplegic (C4 to C8). Treatment of the spinal fracture was performed by osteosynthesis. Five persons had been injured in road accidents, 1 in a fall, and 1 in a sports accident. Three months after injury, all of the paraplegic individuals were using manual or electrical wheelchairs. The control group comprised 10 individuals who were age-matched (22 to 35 years), with a

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level of physical activity that had not exceeded 2 hours per week for the last 2 years. Subjects had no history of metabolic bone disease and were not taking any medication known to affect bone or calcium metabolism. Furthermore, the paraplegic individuals had no history of pathologic fractures or heterotopic ossification. Other exclusion criteria were smoking, excessive alcohol intake, eating disorders, diabetes mellitus, hyperparathyroidism, thyroid dysfunction, liver disease, and renal disorders.

The protocol was reviewed and approved by the Regional Research Ethics Committee (Languedoc-Roussillon, France), and each subject gave informed consent before entering the study.

Bone Densitometry and Body Composition

DXA (Hologic QDR-4500A; Hologic, Waltham, MA) was used to measure the BMC (g), bone area (cm^2), and BMD (g/cm^2) of the whole body (TBMD), the anteroposterior lumbar spine (L2 to L4), the proximal part of the left femur at specific sites of the femoral neck, the trochanteric and intertrochanteric areas, and Ward's triangle. The dominant arm was also evaluated. The BMD of the skull, pelvis, ribs, legs, and arms, and the soft tissue body composition, ie, fat mass (FM, kg), percent body fat mass (FM, %) and lean tissue mass (LTM, kg), were derived from the whole body scan. All scanning and analyses were performed by the same operator to ensure consistency, and they followed standard quality control procedures. Quality control for DXA was checked daily by scanning a lumbar spine phantom consisting of calcium hydroxyapatite embedded in a cube of thermoplastic resin (DPA/QDR-1; Hologic x-caliber anthropometrical spine phantom). For BMD, the coefficient of variation was 1% at the lumbar spine, less than 1% at the femoral neck, less than 1% at the forearm, less than 0.5% for the whole body, and less than 1% for the LTM and FM.

Laboratory Assays of Bone Metabolism

Blood and urine samples. The subjects were instructed to collect their urine for 24 hours beginning at 8 AM. The consumption of coffee, tea, tobacco, and alcohol and the practice of strenuous exercise were avoided for 48 hours before the day of investigation. Blood samples (20 mL) were taken between 8 to 9 AM, then centrifuged at 3,000 rpm for 10 minutes at 4°C. Serum and urine samples were stored at -80°C until analysis. All samples were processed in duplicate and, to eliminate interassay variation, all of the serum or urine samples were analyzed in a single session.

Phosphocalcic balance and creatinine. Urine and serum concentrations of calcium, phosphorus, and urine creatinine (Cr) were measured by routine laboratory methods. Ionized serum calcium was measured by an ion-selective electrode (BGE Electrolytes Instrumentation Laboratory, Lexington, MA). All urinary parameters were expressed as the ratio of urinary creatinine concentration, determined by routine colorimetric methods.

Biochemical Markers of Bone Turnover

Bone formation markers. Serum intact osteocalcin (OC) was measured with a human immunoradiometric assay (IRMA), which uses 2 monoclonal antibodies recognizing the 5-13 and 43-49 sequence of the molecule, respectively, and purified intact human bone OC as standard (Elsa-OST-NAT, CIS Biointernational, Gif/Yvette, France). The intra- and interassay coefficients of variation (CV) are below 5%, and the sensitivity is 0.3 $ng \cdot mL^{-1}$. The reference range for serum OC in our laboratory is 5 to 20 $ng \cdot mL^{-1}$.

Serum B-ALP was measured with an IRMA technique using 2 monoclonal antibodies directed against the human bone isoenzyme and B-ALP purified from human SAOS-2 osteosarcoma cells as a standard (Tandem-R Ostase; Hybritec, San Diego, CA). The cross-reactivity of B-ALP with the circulating liver isoenzyme is 16%. The sensitivity of the assay is 0.2 $ng \cdot mL^{-1}$, and the intra- and interassay CVs are less than 7% and 9%, respectively. The reference range for serum B-ALP in our laboratory is 4 to 15 $ng \cdot mL^{-1}$.

Bone resorption markers. Urinary and serum type I-C telopeptide breakdown products (CTXu and CTXs) were measured by enzyme-linked immunosorbent assay (ELISA) (CrossLaps ELISA; OSTEOMETER A/S, Rodovre, Denmark) based on an immunobilized synthetic peptide with an amino acid sequence specific for a part of the C-telopeptide of the α 1-chain of type I collagen (Glu-Lys-Ala-His-Asp-Gly-Gly-Arg; CrossLaps antigen). This assay does not cross-react with urinary free cross-links. The intra- and interassay CVs are less than 5.7% and 9.4%, respectively, and the detection limit is 0.5 $\mu g \cdot L^{-1}$. All urinary data obtained from 24 urine samples were corrected by the urinary Cr concentration measured by standard colorimetric method. The reference range for urinary CTX is 71 to 279 $ng \cdot mmol^{-1}$ Cr in our laboratory, whereas reference range for serum CTX is less than 5,500 $pmol \cdot L^{-1}$ (manufacturer's specification).

Intact parathyroid hormone molecule and 1.25 $(OH)_2$ vitamin D. Intact parathyroid hormone (iPTH) (1-84) was measured in serum from an immunoradiometric assay, using 2 different polyclonal antibodies. The first antibody, specific for PTH 39-84, was bound to polystyrene beads; the second antibody, specific for PTH 1-34, was labeled with iodure-125 (N-tact PTH SP, Diasorin, MN). The sensitivity of the test is 0.7 $pg \cdot mL^{-1}$ with no cross-reaction with human PTH fragments. The reference range for iPTH in our laboratory is 10 to 55 $pg \cdot mL^{-1}$.

1.25 $(OH)_2$ vitamin D of delipidate serum was purified by immunoextraction with a solid phase monoclonal 1.25 $(OH)_2$ vitamin D antibody. The level of 1.25 $(OH)_2$ vitamin D was then evaluated by a radioimmunoassay using a polyclonal 1.25 vitamin D antibody and I^{125}-1.25 vitamin D (1.25 dihydroxyvitamin D radioimmunoassay kit, Nichols Institute Diagnostics, Paris, France). Cross-reactivity of the radioimmunoassay with 1.25 OH D_2 and 1.25 OH D_3 is, respectively, 100% and 83%, without cross-reactivity with 25 OH D_3 and 24.25 OH D_3. The sensitivity of the assay is 2.1 $pg \cdot mL^{-1}$. The reference range for 1.25 $(OH)_2$ vitamin D in our laboratory is 20 to 66 $pg \cdot mL^{-1}$.

Statistical Analysis

The results are expressed as means and standard deviations. For continuous variables (age, weight, etc), the distribution was tested by the Shapiro-Wilk statistical method. The comparisons of means between the SCI and control groups were performed using a nonparametric Mann-Whitney Wilcoxon test. A level of $P < .05$ was accepted as significant. SAS software, version 6.12 (SAS Institute, Cary, NC), was used for statistical analysis.

RESULTS

Physical Characteristics and Body Composition

The descriptive characteristics of the subjects are summarized in Table 1. There was no statistical difference between the SCI and control groups with regard to age, height, and weight. No statistical difference was observed between the 2 groups for body mass index (BMI), but the persons with SCI had significantly higher whole body fat mass and lower LTM than the controls ($P < .05$, Table 1).

BMD

Table 2 shows no statistically significant difference in lumbar spine (L2 to L4) BMD between persons with SCI and controls. Similarly, there was no difference in total and regional proximal femur, distal radius, and other regions measured with total body scan (skull, lower limb, pelvis). Only BMD in the

Table 1. Physical and Body Composition in Control Subjects and Persons With SCI, 3 Months After Injury

Parameter	SCI Group (n = 7)		Control Group (n = 10)		*P* Value
	Mean ± SD	Range	Mean ± SD	Range	
Age (yr)	31.3 ± 9.5	20-41	27.5 ± 4.3	22-35	NS
Weight (kg)	67.5 ± 6.1	56.9-73.34	69.4 ± 8.1	61.4-89.5	NS
Height (m)	1.77 ± 0.07	1.64-1.85	1.75 ± 0.03	1.70-1.80	NS
BMI ($kg \cdot m^{-2}$)	21.5 ± 2.3	18.5-25.7	22.7 ± 2	20.2-27.6	NS
Body fat mass (%)	23.9 ± 5.7	17-31.2	18.2 ± 4.3	13.6-22.7	.028
Body lean mass (kg)	45.2 ± 5.5	33.9-51.2	50.5 ± 4.2	44.7-59.1	.045

Abbreviations: NS, not significant; SCI, spinal cord injury; BMI, body mass index.

upper limb was found to be slightly higher in the SCI individuals ($P < .05$).

Bone Biochemical Markers

The concentrations of biochemical markers are presented in Table 3. Bone resorption markers indicated a striking increase. The levels of urinary CTX (CTXu) and serum CTX (CTXs) were substantially increased in the SCI group (5-fold and 2.5-fold, respectively) as compared with the control group and the reference range. The 2 markers of bone formation, OC and B-ALP, were differently affected by immobilization. OC was significantly higher (1.6-fold) in the SCI group than in the control group. Among the persons with SCI, 1 had an OC concentration value (11.6 $ng \cdot mL^{-1}$) below the upper limit of the reference range (20 $ng \cdot mL^{-1}$). B-ALP was not statistically different between the 2 groups and, except for 1 SCI individual (20.8 $ng \cdot mL^{-1}$), all the B-ALP concentrations were within the reference range (4 to 15 $ng \cdot mL^{-1}$).

Calcium Homeostasis

Parameters of calcium homeostasis are shown in Table 4. Serum phosphate concentrations were significantly higher in persons with SCI than in the controls and the mean value (1.45 $mmol \cdot L^{-1}$) corresponded to the upper limit of the normal range. Although total serum calcium was moderately increased in the SCI group (5%), no significant difference was noted in controls, and all values were in the normal range. Ionized calcium increased slightly, but significantly ($P < .05$) in the SCI group. The calciotropic hormones were suppressed by 80.6% and 66% for iPTH and $1.25(OH)_2$ vitamin D, respectively, in the SCI group and were below the reference range. Urinary 24-hour calcium excretion after urinary creatinine correction was markedly elevated in persons with SCI, exceeding 8 mmol/day in 2 of them. Urinary phosphate excretion after urinary creatinine correction was unchanged, but the dispersion of the values was greater than in the control group.

DISCUSSION

This study attempted to determine the respective contributions of DXA and biochemical markers of bone turnover for the characterization of bone metabolism soon after injury in SCI individuals.

BMD Measurements

Three months after SCI, no BMD difference in the lumbar spine, proximal femur, or radius was found between persons with SCI and controls. Different investigators have found that BMD in the lumbar spine is conserved[2,7,8] or slightly increased[3] or decreased,[15] whatever the time following injury. The maintenance of normal lumbar spine BMD may result from continuous body weight-bearing during wheelchair use. Tsuzuku et al[16] demonstrated BMD variation with the injury level, in relationship with compressive stress on the lumbar spine generated by gravitational or muscular forces. Studies of the evolution of BMD in the forearm have shown conflicting results. Garland et al[5] observed an initial decrease in BMD in the upper extremities followed by partial recovery, while Biering-Sorensen et al[2] and Wilmet et al[11] found no BMD variation at this site. In our study, no difference was observed between the SCI and control groups for the lower limbs and in the region of the

Table 2. BMD ($g \cdot cm^{-2}$) in Different Sites in Control Subjects and Persons With SCI, 3 Months After Injury

Measurement Site	SCI Group (n = 7)		Control Group (n = 10)		*P* Value
	Mean ± SD	Range	Mean ± SD	Range	
Total proximal femur	0.987 ± 0.222	0.726-1.286	1.006 ± 0.058	0.897-1.068	NS
Femoral neck	0.991 ± 0.189	0.774-1.241	0.880 ± 0.059	0.816-0.971	NS
Trochanter	0.774 ± 0.173	0.605-1.056	0.769 ± 0.073	0.859-0.878	NS
Intertrochanter	1.190 ± 0.214	0.967-1.503	1.195 ± 0.074	1.075-1.298	NS
Ward's triangle	0.886 ± 0.193	0.668-1.136	0.776 ± 0.096	0.634-0.904	NS
Lumbar spine (L2-L4)	1.016 ± 0.093	0.870-1.135	1.016 ± 0.056	0.895-1.016	NS
Distal radius	0.656 ± 0.056	0.576-0.747	0.619 ± 0.043	0.548-0.676	NS
Skull	2.070 ± 0.274	1.602-2.285	2.080 ± 0.247	1.713-2.441	NS
Upper limbs	0.894 ± 0.068	0.830-1.023	0.829 ± 0.027	0.800-0.885	.013
Lower limbs	1.310 ± 0.184	1.126-1.600	1.273 ± 0.057	1.187-1.336	NS
Pelvis	1.229 ± 0.166	1.034-1.507	1.210 ± 0.108	1.060-1.378	NS

Table 3. Serum and Urinary Biochemical Markers of Bone Turnover in Control Subjects and Persons With SCI, 3 Months After Injury

Bone Marker	SCI Group (n = 7)		Control Group (n = 10)		*P* Value	Normal Range
	Mean ± SD	Range	Mean ± SD	Range		
Bone formation						
Serum OC ($ng \cdot mL^{-1}$)	24 ± 8	11.6-36.7	14.6 ± 4.8	7.4-23.1	.022	5-20
Serum B-ALP ($ng \cdot mL^{-1}$)	13.8 ± 5.5	7-20.7	14.7 ± 4.3	9.2-20.9	NS	4-15
Bone resorption						
Serum CTX ($pmol \cdot L^{-1}$)	13,340 ± 4,921	6,838-21,000	5,396 ± 1,752	3,323-9,050	.002	<5,500
Urinary CTX ($\mu g \cdot mmol^{-1}$ Cr)	894 ± 371	415-1,407	174.6 ± 54.3	105-278	.001	71-279

Abbreviations: NS, not significant; SCI, spinal cord injury; OC, osteocalcin; B-ALP, bone alkaline phosphatase; CTX, serum and urinary type I collagen C-telopeptide.

Urinary bone resorption marker level was obtained from 24-hour fasting urine samples, after urinary creatinine (Cr) correction.

proximal femur. This observation is in agreement with the results of Roberts et al,[9] who reported no BMD variation in the femoral neck between 8 and 24 weeks after injury. These results suggest that using DXA only cannot show evidence of demineralization 3 months after lesion.

However, early osteoporosis in sublesional areas, and principally in the lower extremities, has been demonstrated by various investigators using the DXA technique. Garland et al[5] found that bone mass alteration was detectable as early as the first 3 to 4 months after SCI, while the bone loss rate reached 22% at the distal femur and the proximal tibia. Wilmet et al[11] observed during the first year a rapid decrease in bone mineral content (4%/month) in areas richly composed of trabecular bone, such as the pelvis, and a slower decrease (2%/month) in areas containing mainly compact bone. This decrease gradually slowed until 16 to 24 months postinjury, when a new equilibrium seemed to be established at a BMC level corresponding on average to about 50% to 70% of normal values, depending on the bone sites considered.[3,5,17] Bauman,[18] however, reported a relationship between the duration after injury and the degree of leg bone loss, which suggests that bone loss continues to decline during the postlesional chronic phase.

Several assumptions could be put forward to explain our divergent findings. First, the bone sites we selected for our study were different from the ones chosen by other investigators. Second, since we did not know the basal values of BMD in our patients just after injury, these data were estimated from measurements in our control subjects. Consequently, this might have introduced bias in estimating the real bone loss. Third, as the majority of our patients with SCI were athletes and manual workers, the basal value of bone mass before injury was probably higher than in the sedentary individuals who formed our reference group.[19] This hypothesis was supported by the higher value of BMD found in our SCI group in the upper limb, an area that is generally less affected by immobilization osteoporosis.[3-5]

In addition, other investigators have suggested that BMD could be falsely increased in the proximal femur by heterothopic ossification (HO).[20] In our study, we systematically searched for HO, and none of our patients had developed it at 3 months.

Although it has been reported that bone mineral loss in the upper extremities of persons with tetraplegia is higher than that observed in persons with paraplegia,[3-5,15,21] we could not find any significant difference according to the level of lesion due to the small size of our SCI sample.

Use of Biochemical Markers

The dramatic and rapid increase in CTXs and CTXu bone resorption markers after 3 months of immobilization demonstrates a substantial demineralization process. This is in accordance with previous research using other markers.[9,22] Roberts et al[9] showed that the increase in resorption markers, such as deoxypyridinoline and urinary N-telopeptide of type I collagen (NTX), began the first week after injury and peaked around 10

Table 4. Serum and Urinary Parameters of Calcium Homeostasis in Control Subjects and Persons With SCI, 3 Months After Injury

Parameter	SCI Group (n = 7)		Control Group (n = 10)		*P* Value	Normal Range
	Mean ± SD	Range	Mean ± SD	Range		
Serum						
Ca ($mmol \cdot L^{-1}$)	2.42 ± 0.09	2.29-2.55	2.31 ± 0.10	2.21-2.52	NS	2.10-2.55
iCa ($mmol \cdot L^{-1}$)	1.27 ± 0.05	1.21-1.37	1.22 ± 0.03	1.16-1.31	.056	1.10-1.25
P ($mmol \cdot L^{-1}$)	1.45 ± 0.24	1.17-1.85	1.05 ± 0.17	0.81-1.26	.003	0.81-1.45
iPTH ($pg \cdot mL^{-1}$)	5.14 ± 1.2	4-7	26.50 ± 13.01	11-50	.0007	10-55
$1.25(OH)_2$ D3 ($pg \cdot mL^{-1}$)	13.57 ± 7.8	5-28	40 ± 10.65	26-57	.001	20-66
Urine						
Ca ($mmol \cdot mmol^{-1}$ Cr)	0.76 ± 0.37	0.2-1.65	0.35 ± 0.14	0.22-0.69	.054	-
P ($mmol \cdot mmol^{-1}$ Cr)	1.81 ± 1.23	0.5-4.2	1.84 ± 0.34	1.44-2.55	NS	-

Abbreviations: NS, not significant; SCI, spinal cord injury; Ca, calcium; iCa, ionized calcium; P, phosphate; iPTH, intact parathormone; $1.25(OH)_2D$, $1.25(OH)_2$ vitamin D; Cr, creatinine.

Concentration values of urinary parameters were obtained from 24-hour fasting urine samples after urinary creatinine correction.

to 16 weeks. These markers did not return to normal values at 6 months. Pietschmann et al[22] showed that hydroxyproline, an old marker of bone resorption, was always higher in SCI than in controls 1 month after injury. The extremely high values of bone resorption markers in our study, in comparison with those reported in short[23,24] and long duration[23,25] bed rest investigations, support the assumption that immobilization is not the only factor affecting bone metabolism. Neuromuscular deprivation or hormonal factors yet to be determined may play an important role in the acute bone resorption in persons with SCI.

Conversely to the resorption markers, the bone formation markers showed different variation rates. OC was found to be significantly higher in SCI ($P < .05$) than in controls, while B-ALP remained unchanged. OC increase during immobilization has already been reported. Pietschmann et al,[22] in a cross-sectional study, found OC serum levels significantly higher in SCI than in normal subjects 61.5 weeks after injury. In a longitudinal study, the same investigators found normal OC serum values 1 month after injury that then continuously increased until the end of the study, 6 months later.[22] This increase in OC serum could be partly explained by the low level of $1.25(OH)_2$ vitamin D concentration, as it has been shown that OC is directly stimulated by $1.25(OH)_2$ vitamin D in osteoblasts and osteosarcoma cells.[26] The changes observed in OC concentration cannot be related to a modification in glomerular filtration, since no variation in urinary creatinine concentration was demonstrated during immobilization. Until now, only total alkaline phosphatase (tALP) has been analyzed, although this biochemical marker is less specific than B-ALP. Demirel et al[4] noted a moderately positive correlation between the time elapsed since the occurrence of lesion and tALP serum concentration, but this has not been confirmed by other investigators.[2,9]

The increased OC levels found in our study might indicate a bone repair process. However, the value of B-ALP was not modified, which is not in accordance with this hypothesis. In fact, OC and B-ALP could reflect different aspects of bone formation.[27] Lueken et al[24] reported similar observations in valid subjects during 7 days of bed rest. The chemoattractant effect of OC on osteoclasts[28] would allow the osteoblasts to regulate bone resorption.[24]

Moreover, because of the small size of our SCI sample, we were unable to analyze the demineralization process according to lesional level. However, no difference between paraplegic and tetraplegic populations was discerned in previous studies.[9,22]

Calciotropic Hormones

Urinary calcium excretion, serum phosphorus, and ionized calcium were significantly higher in subjects with SCI, whereas serum calcium was normal. Various investigators have reported similar results in adult men, 3 or 4 months after injury.[9,29,30] Generally, hypercalciuria is a common metabolic complication following the acute phase of paraplegia,[29,30] whereas hypercalcemia has only been found in children and adolescents with SCI[31]. These findings may reflect the release of the mineral phase of bone tissue into the blood circulation with decreasing calcium absorption.[30] In our study, the parathyroid-1.25-dihydroxyvitamin D axis was suppressed. The decrease in serum iPTH in the early period after injury was due to the increase in serum calcium, which presumably constitutes a protective mechanism of bone tissue.[30] Various investigators have also reported an initial decrease in serum iPTH level in persons with SCI from 1 to 4 months after spinal cord section, which tended to increase thereafter.[9,22,30] The serum concentration of $1.25(OH)_2$ vitamin D, the active hormonal form of vitamin D, was also significantly reduced ($P < .001$) in our SCI group. This alteration seems to be independent of the modification of 25-hydroxyvitamin D, which was within the reference range, indicating the presence of normal vitamin D stores.[30,32] In fact, the reduction in iPTH concentration, which promotes 1 α-hydroxylation of vitamin D in the kidney, seems to be the most important factor influencing the decrease in $1.25(OH)_2$ vitamin D concentration. The deficiency of $1.25(OH)_2$ vitamin D could also be related to sunlight deprivation and to the subject's lesional level.[32]

Conclusion

BMD measurement in our SCI group 3 months after injury did not demonstrate any difference with our valid reference group. Early measurement is nevertheless necessary to determine the basal bone mineral status because a low BMD value may indicate a predisposition to acute osteoporosis. Using biochemical markers, we found a striking increase in the bone resorption process with a modest increase in bone formation activity. The sensitivity and rapid response of biochemical markers at the early stage of SCI strongly suggests their potential effectiveness as indicators of individuals at high risk of developing later severe osteoporosis.

From the complementary information provided by associating DXA and biochemical marker methods, we can obtain more complete and reliable information on an individual's bone metabolism soon after SCI. Combining both techniques may be an effective means of early characterization of osteoporosis risk. The use of biochemical markers, in particular, may be of high clinical value, as the techniques are easily applicable, and they have strong potential for monitoring persons with SCI for subsequent adjustment of appropriate preventive treatments.

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