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Clinical Study

Bone Mineral Density in Spinal Cord Injury: An Evaluation of the Distal Femur

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Osteoporosis (OP) in spinal cord injury (SCI) patients is a secondary process in which numerous factors are involved. Diagnosing OP and the threshold for fractures in this population, based on bone mineral density (BMD) measured by double energy X-ray absorptiometry (DXA), is still a challenge. The aim of this study was to evaluate bone mineral loss by DXA, its relationship with body composition and fracture incidence, in complete paraplegics patients, compared with aged-matched controls; we include a nonstandard bone site, the distal femur, and describe the technical and practical aspects of this procedure. Twenty-five SCI patients were included in the study and 17 subjects as control group. No prior or recent fractures were observed in X-ray analysis. The BMD of all femoral sites was significantly lower in patients than in controls (femoral neck, total femur, and distal femur); no difference was observed between BMD of the lumbar spine of patients and controls. We found inverse relationship between time of SCI and bone mineral mass only for distal femur BMD. We conclude that the distal femur is a more sensitive bone site for assessing bone loss by DXA, in SCI patients, than the proximal femoral sites.

1. Introduction

Osteoporosis (OP) is characterized by low bone mass (LBM), microarchitecture deterioration with bone fragility, and increased risk for fractures [1]. Its pathophysiology involves a remodeling process with imbalance between bone reabsorption and formation. In SCI patients this process is even more complex as mechanical, neurovascular, and hormonal factors are involved [2–4]. Bone loss in these patients is higher in the first six months after the SCI and stabilizes between 12 and 16 months, with about 30% loss of bone mass [5]. Although fractures occur, they are often subdiagnosed due to sensibility decrease below the SCI level. The average time for fracture occurrence is nine years [6–8].

Diagnosing OP and the threshold for fractures in this population based on bone mineral density (BMD) measured by dual energy X-ray absorptiometry (DXA) is still a challenge. Nowadays, we still use diagnosis criteria, protocols, and data obtained from different populations, without knowing if SCI patients have the same evolution for bone loss.

Other neurological conditions, such as cerebral palsy, with similar motor incapacity as SCI, have been studied to find a way to predict bone loss and fracture risk. Some factors were associated with bone mass loss, such as decreased weight bearing and muscle mass below lesion, calcium and phosphorus metabolism alterations, and use of anticonvulsants. The authors tried to identify which bone site would be most predictive of fractures in these patients [9–11].

In SCI patients, although we do not have specific criteria, DXA is still the method of choice for bone mass assessment [12–14]. BMD by DXA is based on the absorption of two X-ray low-energy beam by tissues; the difference of energy absorption by lean mass, fat mass, and bone mass allows the identification of each body compartment.

For bone mass analysis, the energy absorption by bone is directly proportional to BMD, and once there is an exponential relationship between the lowest BMD and the increased risk for fracture by insufficiency, we can evaluate this risk. OP definition by the WHO criteria, using DXA, is based on T-score: the number of standard deviations (SDs) from the mean of young adults. A T-score value equal or below −2.5

SD is diagnostic of OP, even in the absence of fractures; values of T-score between −1.1 and −2.4, are defined as osteopenia and above or equal to −1.0 correspond to normal. The Z-score, number of SD from the average BMD observed at a same age population, is the parameter recommended by The International Society for Clinical Densitometry (ISCD), on its Official Position of 2005, to assess young individuals, premenopausal women and men younger than 50 years. In these cases we must follow the classification "below the estimate for the age" for Z-scores ≤ −2.0 and "within the estimate for the age" for Z-scores > 2.0.

BMD in SCI patients can be influenced by a number of factors such as vertebral fractures, lumbar spine degenerative disease, aortic calcification, and lumbar spine instrumentation/internal fixation. Femur segment analysis may also be affected by prior fractures and healing, heterotopic ossification presence, and lower limb deformities**,** avoiding proper positioning for analysis.

BMD by DXA in SCI patients evaluates bone loss through specific segments already defined initially for postmenopausal women, including lumbar spine (L1–L4) and femur (total and neck femur) and, in some cases, radius. Other segments such as distal femur, proximal tibia, or sometimes both, mentioned as knee, can also be analyzed, but there is no regular protocol for this procedure.

Bone mineral loss in SCI patients could also be evaluated by peripheral quantitative computed tomography (pCQT) and with calcaneus quantitative ultrasound (US), but these methods also have limitations. The pCQT is a high-cost method and not available everywhere. Calcaneus US seems to be sensitive to bone loss at an early SCI stage**,** [14], but there are few studies supporting its use.

Although DXA is still the best method to analyze bone mass in SCI patients, there are many aspects to be studied to define the best protocol and practical aspects at this specific population. The aim of this study was to evaluate bone mineral loss using DXA and fracture incidence, in traumatic complete paraplegics, in comparison with a control group, including a nonstandard site, the distal femur, and describe technical and practical aspects of this method, based on preexisting literature.

2. Subjects and Methods

This cross-sectional observational study was carried out at the school Hospital of Federal University of São Paulo (UNIFESP) and at the AACD Rehabilitation Center, São Paulo, Brazil. The protocol was approved by the hospitals' (UNIFESP and AACD) ethics committees based on Human Subjects Institutional Review Board, and all subjects provided written informed consent.

Inclusion criteria were traumatic SCI male patients aged between 18 and 50 years, nonwalking (ASIA A and B) and with more than 6 months of neurologic lesion. Exclusion criteria for SCI subjects were use of any kind of medication that could interfere with bone metabolism, like corticosteroids, calcitonin, or bisphosphonates, any history of bone metabolic diseases, cancer, thyroid disorder, kidney, or liver diseases, spasticity above grade 3 in Ashworth modified scale [15] and those who had spine instrumentation in more than 2 vertebras or heterotopic ossifications in the left hip.

Thirty-two males with SCI (ASIA A and B) level T2–T12 were recruited to the study, but 7 subjects were lost because of technical problems (internal lumbar spine fixation and heterotopic ossification in both hips), and 25 subjects were included for data conclusion. Additional seventeen age-matched able-bodied subjects were recruited and served as control group. All SCI subjects were examined and classified prior to all exams by the same physical medicine and rehabilitation physician (APG), using ASIA classification [16]. Spasticity was classified according to the Ashworth modified scale [15].

SCI subjects also answered a questionnaire regarding time of injury (SCI duration) and antecedent of fractures. All were submitted to a lumbar spine and inferior limbs radiographies to evaluate fracture evidences or deformities. Subjects were also investigated if they were submitted to standing, considered as positive result if a subject stood for at least 3 times a week for a minimum of 30 minutes with an orthosis or stand-in-table.

The mean time of SCI was 68.4 ± 65.4 months and median 36 months. There was no statistical difference between SCI subjects and controls regarding age (30.8 ± 6.6 and 31.9 ± 5.6 years, resp., $P = 0.87$) and height (177.5 ± 0.7 and 176.9 ± 0.6 cm, resp., $P = 0.75$). The BMI for the control group was 26.6 ± 3.6 kg/m^2 and for the SCI subjects 23.6 ± 3.2 kg/m^2 ($P = 0.005$). SCI levels varied from T2 to T12.

2.1. Dual X-Ray Absorptiometry (DXA). Subjects (patients and controls) were submitted to DXA exams (Discovery A, Hologic, Bedford, MA), which provide the areal BMD (g/cm^2), Z-score and T-score, using NHANES III database [17]. *In vitro* quality control (long-term precision) was done daily using a reference phantom, for lumbar spine and total body, according to the manufacturer. *In vivo* short-term precision was calculated by repeated scanning of hospital patients, according to the convention of the International Society for Clinical Densitometry [18].

The bone sites scanned were femoral neck (FN), total femur (TF), lumbar spine (LS), and total body (including body composition and analysis of the distal femur). The Quality Control Program showed coefficients of variation (CV%) of 0.8% for LS and TF and 1.2% for FN. DF in the AP position was analyzed using the image from the total body scan, and CV was 2.2%. For CV calculation, we used 15 subjects as controls with 3 measures for each one including area (cm^2), BMC (g), and BMD (g/cm^2).

2.2. Lumbar Spine (LS). The evaluation included the four lumbar vertebral bodies (L1–L4). In case of some technical limitations for all 4 vertebrae analysis, like scoliosis, spine instrumentation or lumbar osteodegenerative process, at least two vertebrae were included. Patients were evaluated in dorsal decubitus and, legs were supported using a cushion to maintain 90 degrees of flexion for hip and knees.

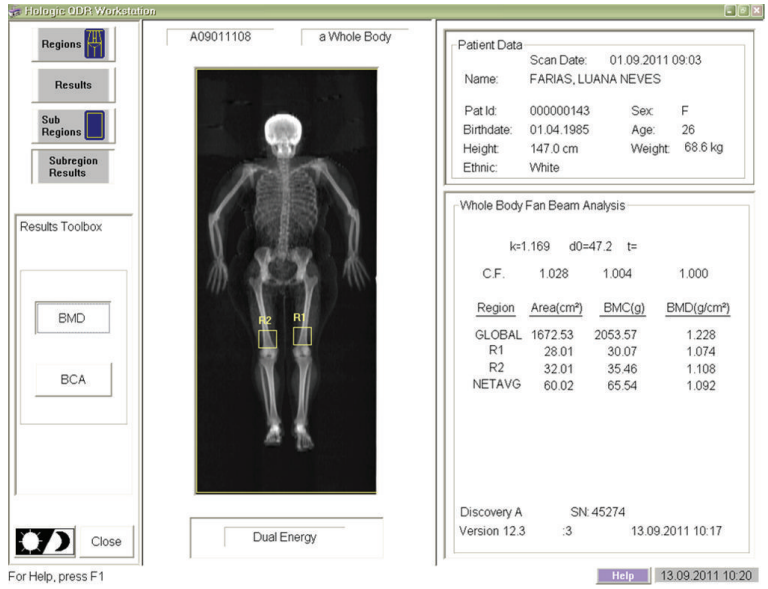

Figure 1: DF analysis by DXA. The square represents the studied site.

Table 1: BMD values between groups, at left femoral sites.

BMD	Group	Mean	SD	Minimum	Maximum	*N*	*P*
DF left	Control	1.25	0.19	1.01	1.66	17	<0.001
	Patient	0.88	0.17	0.61	1.28	25	
TF left	Control	1.06	0.15	0.80	1.43	17	<0.001
	Patient	0.77	0.13	0.48	0.98	25	
FN left	Control	0.96	0.14	0.69	1.27	17	<0.001
	Patient	0.73	0.12	0.54	0.96	25	

FN: femoral neck, DF: distal femur, TF: total femur.

2.3. Proximal Femur. Femoral analysis included NF and TF, an area that included the neck, the greater trochanter, and proximal diaphysis. The patient was positioned with lower limbs in extension using a special cushion, and, if necessary, lower limbs were fixed by someone to help maintain thighs in internal rotation.

2.4. Distal Femur (FD). In this analysis the patient was kept in dorsal decubitus with lower limbs in extension. The extension was obtained using proper equipment.

A special ROI was created, based on a prior study [19]. The images were acquired using the full body program. We used the closest image, which allows the creation of non-standard area of interest (ROI). The ROI had 1.0 cm^2; the condyles were used as boundaries excluding the patella. The area included both cortical and trabecular bones, without distinction between compartments (Figure 1).

2.5. Body Composition. We obtained the parameters of body composition based on total body data acquisition: percentage of total fat mass (%), percentages of lean mass of lower limbs (%), and superior limbs with trunk (%). The percentages of each segment were calculated from the percentage of total lean mass.

2.6. Statistical Analysis. Data is described as numerical summaries (mean ± standard deviation) for continuous variables and frequencies for all categorical variables. Comparisons between right and left femurs were examined by Student's paired *t*-test. Nonpaired *t*-test was used to evaluate group differences for age, height, BMI and BMD, and body composition. Correlations were done using Pearson or Spearman as needed data were tested for normality. Statistical analysis were performed using SPSS version 18.0 software (SPSS Inc., Chicago, IL, USA) and STATA version 10 (STATA Corp, College Station, TX, USA). Differences were considered significant if $P < 0.05$.

3. Results

No previous or recent fractures were found.

3.1. DXA

3.1.1. Lumbar Spine. The mean value for LS BMD for the control group was 1.10 ± 0.19 g/cm^2 and for the patients 0.87 ± 0.16 g/cm^2. Z-score for the control group showed that none of the subjects had low bone mass, differing from patients that had 2 subjects with Z-score under −2.0, but

Table 2: Correlation between time of injury and BMD sites in SCI group.

BMD	Correlation (r)	N	P
DF L	−0.38	25	0.05
LS	0.08	25	0.73
TF L	−0.25	25	0.19
FN L	−0.18	25	0.35

FN: femoral neck, DF: distal femur, TF: total femur, LS: lumbar spine.

there was no statistical difference between groups ($P = 0.51$). There was also no statistical difference between groups when each vertebrae was analyzed: L1, $P = 0.48$, L2 $P = 0.76$, L3 $P = 0.64$, and L4, $P = 0.49$.

3.1.2. Femur. Analysis from right and left femur showed no statistical difference for all femur sites (TF-$P = 0.91$, NF $P = 0.87$, and DF $P = 0.76$), and because of this only the left femur was used for group comparisons.

A statistical correlation between DF and FN BMD was found, and this correlation was higher for the control group (control group $r = 0.73$; $P < 0.001$ and patients $r = 0.50$; $P = 0.007$).

All femoral left sites had statistical difference for BMD when groups were compared ($P < 0.001$) (Table 1).

None of the controls had low bone mass (Z-score < −2.0) at TF, while 7 patients (28%) showed Z-score < −2.0. Regarding FN, none of the control groups had Z-score < −2.0, and 5 (20%) patients showed low bone mass.

No statistical difference was found for proximal femur BMD between SCI subjects that stood ($n = 22$) and subjects that did not stand ($n = 3$); the lack of correlation between orthostatism and BMD may be because 88% of the patients were in the standing group.

Only BMD at DF L showed a significant inverse relationship with time of SCI (Table 2).

3.2. Body Composition. The proportion of total fat was not different in patients and controls, but we found significant differences between groups for the percentages of lean mass even for inferior limbs and superior limbs and trunk but in different ways: patients have increased muscle mass in arms and trunk while they had lower muscle mass in the lower limbs compared to controls (Table 3).

No correlation between total mass and BMD was found for none of the sites; there was a positive correlation between DF BMD and % of inferior limbs lean mass (Table 4).

4. Discussion

In order to better understand the bone loss process after spine injury, we measured bone mass and body composition by DXA in a homogenous population of paraplegic traumatic patients and compared them to control group paired by age. The majority of related literature is based on data obtained from heterogeneous populations, with different kind of SCI patients (complete and incomplete, both genders, very different levels of injury) [5, 8, 12, 20].

Although there are technical limitations to acquire and interpret data from DXA exams of SCI patients, it is still the best exam to analyze bone mass in these individuals, even if most rehabilitation physicians do not order it. In a study with 126 American SCI specialists physicians, only 54% asked for the exam to evaluate OP in their clinics [21]. The reason for that is probably the lack of data to assure the exam's importance to predict fractures in SCI patients.

The analysis for the general population to predict risk fracture includes LS (L1–L4), proximal femur (FN and TF) as determined by the Standards of the ISCD Consensus [18]. SCI patients have no specific protocols showing the best sites to evaluate bone mass loss, and we still do not know if the same segments used for the general population are the most effective to predict fractures, once DF and proximal tibia have the highest incidence of fractures [22–24].

There were no fractures in our patients, differing from other studies [6–8]. This fact might be related with our mean time of injury, below the 9 years described in literature as the mean for the first fracture [7].

A cross-sectional study with 100 complete paraplegic patients showed that FN BMD decreased with time but the distal tibial diaphysis was better to demonstrate bone loss in those with longer time of injury [8]. Although we have not studied the distal tibia, the distal femur has the same type of bone (cortical), so we assume the possibility that both sites are helpful to predict a fracture.

DF is an interesting segment to be analyzed, according to our results. It was the only femoral site that showed correlation with time of injury; furthermore it presented good correlation with the sites used for general population (FN and TF). The loss of correlation between distal and proximal femur BMD observed in patients seems to indicate that the distal femur is more sensitive to bone loss in those individuals. DF also showed a good correlation with lean mass of the inferior limbs in SCI group while the proximal sites did not; in controls the correlation between BMD and lean mass is positive for all femoral sites. These observations reinforce the importance of distal femur for SCI patients. Clasey and col found an inverse correlation between log of time of injury and BMD of inferior limbs although the population studied was heterogeneous (tetra- and paraplegic, men and women) [25].

Morse and col evaluated the knee region, described as proximal tibia and distal femur, in 20 chronic SCI patients, using a different technique, in a Lunar Prodigy Advance densitometer: the proximal edge of the ROI was at 20% of the femur length (measured from lateral condyle), the patella was excluded, and distal edge was set at a line between patella and femur. The CV% obtained was 3.01%, whereas ours was 2.2%, both still higher than TF and FN CV%. The creation of standardized rules and dedicated software to DF analysis will provide the answers about the predictive ability of DF bone site. We observed in our study that reproducing DF analysis using total body image was easily reproducible.

Biering-Sørensen et al. in systematic review suggested that knee BMD analysis for SCI injury is a good parameter to

Table 3: Body composition (percentage of total fat mass and lean mass): comparison between SCI group and controls.

Variable	Group	Mean	SD	Minimum	Maximum	N	P
% total fat	Patient	26.15	5.88	23.91	28.38	25	0.19
	Control	23.73	6.86	20.42	27.03	17	
% lean mass SS	Patient	51.06	4.67	49.28	52.83	25	0.03
	Control	48.15	4.23	46.12	50.20	17	
% lean mass IS	Patient	20.26	3.27	19.01	21.51	25	0.02
	Control	26.98	14.1	20.17	33.78	17	

SS: % lean mass superior segment (arms + trunk); IS: % lean mass inferior segment (limbs).

Table 4: Correlation between BMD and total mass (g) and % lean inferior limbs.

Variable		BMD DF	BMD TF	BMD FN	BMD LS
Control					
Total mass (g)	r	−0.21	0.19	0.46	0.33
	P	0.40	0.43	0.06	0.17
% lean mass IILB*	r	0.47	0.60	0.91	—
	P	0.05	0.07	0.00	—
Patient					
Total mass (g)	r	−0.23	−0.14	−0.04	0.20
	P	0.22	0.46	0.80	0.31
% lean mass IILB*	r	0.41	0.15	0.54	—
	P	0.02	0.44	0.22	—

* lean mass IILB: % lean mass inferior limbs.

evaluate fracture risk [26]. Other authors reached the same conclusion about the utility of the distal femur [20, 27] although using different techniques. The most adequate ROI for this region still needs to be evaluated.

Our study showed low bone mass at all patient femoral sites when compared with the control group, and this is in agreement with others [28, 29]. Other neurologic pathologies like cerebral palsy (CP) have been studied and also showed low bone mass. A transversal study with 619 patients with CP observed high correlation between femur fracture and DF Z-score: 35–42% of the patients with Z-score below −5 had fractures, against 13–15% with Z-score above −1, showing that each SD above the mean increases 6–15% the risk for femur fracture [30].

Regarding the lumbar spine, we observed the same results seen in the literature [31], with no statistical difference between patients and controls regarding the BMD. Other authors showed LS BMD values above the mean for the normal population [20, 32–34]. This gain might be explained by the shear force and the existent forces at lumbar region while sited on a wheelchair. There is also the neurogenic degeneration hypothesis, a cause for increased bone formation at LS. We observed in our study a correlation between LS BMD and bone mass index but not with time of injury, as also shown by other authors [7, 34].

Baumann and col [31] in their study using qCT (quantitative computerized tomography) showed LS bone loss in SCI patients even for those with normal BMD by DXA [35]. The acquisition of the DXA image in an anteroposterior position makes the analysis of the trabecular compartment of the vertebrae impossible more sensitive to bone loss, and this position is affected by the presence of osteodegenerative processes, compromising the accuracy of this site. Another important observation is that vertebral fractures in this population are not observed [8, 31, 35, 36]. We conclude that it is more important to prioritize the analysis of the inferior limbs, including DF, saving time during the exam, avoiding technical problems (many LS had internal fixations) and evaluating the sites with higher fracture risk.

Regarding body composition analysis, we found no significant differences in percentage of fat mass between groups, diverging from Jones and col study, which showed that even if the BMI was similar for control and patients, the body composition measured by DXA showed statistical difference for fat mass [37], but as this study had only five patients, it is difficult to compare to our results. On the other hand, we found a significant difference in lean mass between groups, both for the superior and lower limbs. In SCI patients, the distribution of lean mass is different between the superior and inferior compartments of the body, with a positive correlation between DF BMD and % of inferior limbs lean mass.

As this is a transversal study and the period of spine cord injury was short, we could not make correlations between bone mass and fractures.

We conclude that, in a paraplegic population, the analysis of BMD by DXA is capable of demonstrating bone loss at all femoral sites, but only the DF had correlation with time of injury; LS showed no significant bone loss. The study reinforces the idea that LS can be excluded from bone mass analysis in SCI patients and that the DF site must be included in this evaluation. The technical description of the ROI

for distal femur analysis helps to reproduce and collect more data on bone mass diagnosis, for future development of osteoporosis treatment and fracture prevention in SCI patients.

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