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Bone Mineral Density After Spinal Cord Injury: A Reliable Method for Knee Measurement

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Abstract

Objectives—To test the interrater reliability of a standardized method to analyze knee bone mineral density (BMD) using dual-energy x-ray absorptiometry (DXA); to compare spine, hip, and knee BMD of people with spinal cord injury (SCI) with able-bodied controls; and to determine the relation between hip BMD and knee BMD in SCI and able-bodied subjects.

Design—Criterion standard and masked comparison.

Setting—Primary care university hospital.

Participants—A convenience sample of 11 subjects with complete SCI was age and sex matched with 11 able-bodied control subjects.

Interventions—Not applicable.

Main Outcome Measures—Four raters analyzed regions of interest according to operational definitions recently developed to standardize the analysis of BMD of the knee. Subjects with chronic SCI and matched controls underwent conventional DXA scans of the spine and hips and “less conventional” scans of the distal femurs and proximal tibias. The relation between hip and knee BMD was analyzed.

Results—The knee measurements were highly reliable (femur intraclass correlation coefficient model 2,1 [ICC_{2,1}]=.98; tibia ICC_{2,1}=.89). Subjects with SCI had lower BMD values than controls at all hip and knee sites ($P<.05$). Lumbar spine BMD did not differ between groups. Hip BMD was moderately predictive of distal femur BMD ($R^2=.67$), but less correlated with the proximal tibia ($R^2=.38$).

Conclusions—Knee BMD can be reliably analyzed using DXA with this protocol. Subjects with SCI have diminished knee and hip BMD. Low hip BMD is associated with low distal femur BMD.

Keywords

Fractures; Osteoporosis; Paralysis; Rehabilitation; X-ray absorptiometry; dual energy

Osteoporosis is a severe and debilitating secondary complication of complete spinal cord injury (SCI). Bone mineral density (BMD) of the paralyzed extremities declines precipitously in the first 2 years after SCI, eventually reaching a level below fracture threshold.¹⁻⁴ Between 1% and 6% of people with SCI will sustain fractures in their paralyzed extremities.⁵⁻⁷ Fractures are often caused by trivial insults to the limbs^{5,7,8} that people with SCI frequently encounter during everyday mobility.

The main instrument used to measure BMD is dual-energy x-ray absorptiometry (DXA). In postmenopausal women, DXA-based BMD T scores are used to diagnose osteoporosis and the technique is valuable for monitoring longitudinal changes in bone density. The progression of osteoporosis after SCI has been described for the hip and lumbar spine. In general, hip BMD declines rapidly for the first several months, then declines more slowly until reaching equilibrium at 12 to 16 months postinjury.^{1,2,4} Lumbar spine BMD generally does not decline and may even increase after SCI.^{4,9}

By far the most common sites for fracture after SCI are the distal femur and the proximal tibia.^{5,7,10} In general, those with SCI have 2 times the risk of developing a fracture than those without an SCI. Because femur and tibia BMD are not commonly used to diagnose osteoporosis in the able-bodied population, specified protocols to measure these regions are not available. Previous studies of femur and tibia BMD after SCI have used an array of protocols, usually without addressing the reliability of the methods used. Many lack important methodologic details, such as the type of DXA scan algorithm used (forearm or spine), how the region of interest (ROI) was determined,¹⁰⁻¹² and whether these procedures are reproducible.^{11,12} One previous study¹³ adequately described the methodologic details; however, the researchers did not establish the reliability of their procedure.

Because a definitive technique to measure knee BMD with DXA does not exist, it remains unclear whether knee BMD declines in a manner similar to other sites, or whether the development of osteoporosis at the knee follows a different time course. Moreover, DXA z scores for knee BMD after SCI do not exist.¹⁰ Therefore, clinical estimation of fracture risk at these sites is not possible. Rehabilitation specialists routinely make clinical decisions regarding loading of the knee during standing,¹⁴ electric stimulation,^{15,16} suspended treadmill training,¹⁷ and various rehabilitative transfer techniques. Because of the prevalence of post-SCI fractures about the knee, a reliable method to determine knee BMD is important for rehabilitation specialists working with people with SCI.

We operationally defined a protocol to analyze the proximal tibia and distal femur with DXA and determine the interrater reliability of the method. We then compared the hip, spine, and knee BMD in people with SCI with that of able-bodied controls. Finally, we examined the relation between hip and knee BMD measurements after SCI.

METHODS

Eleven subjects with SCI (10 men, 1 woman) and 11 age- and sex-matched able-bodied controls underwent DXA evaluation of the spine, hips, distal femurs, and proximal tibias. All subjects signed an informed consent document approved by the human subjects institutional review board of our facility. All subjects with SCI were American Spinal Injury Association grade A (complete motor and sensory SCI).¹⁸ Exclusion criteria for subjects with SCI were poor medical health, decubitus ulcers, fracture in the lower extremities, endocrine disorders, severe spasms that might induce scan artifacts, or antiosteoporosis medications. Exclusion criteria for able-bodied subjects were fracture in the lower extremities, endocrine disorder, or antiosteoporosis medications.

DXA (QDR 2000)^a measurements of bilateral hips and knees were taken with the subject supine. DXA is the primary method used to monitor spine and hip osteoporosis because of its precision and low dose of radiation exposure. A physical therapist palpated the greater trochanter and the lateral condyle of the femur and then measured femur length with a tape measure. A radiology technician secured the subject's limbs into appropriate alignment and rotation and performed the scans. For the lumbar spine scan, the technician positioned the subject in 90° of hip flexion and 90° of knee flexion (with the feet and lower legs supported by a square bolster with straps). Two analytic software algorithms (version 7.20^a) automatically detected ROIs in the hip and lumbar spine, as is routinely done in clinical examination and diagnosis of osteoporosis. After consultation with Hologic,^a we elected to use the spine algorithm during knee analysis consistent with previous reports.² The scan width using the lumbar spine protocol was also able to accommodate the width of larger limbs. Four raters underwent 8 hours of training in manually setting femur and tibia ROIs. All raters were masked to analyses performed by other raters and to the SCI status of the subjects. The protocol for ROI detection of the distal femur and proximal tibia appears in appendix 1.

The between-rater reliability of the protocol was determined by establishing the association among the raters using a Pearson product moment correlation. The coefficient of determination (R^2) was calculated using a linear regression model. The degree of agreement among the raters was determined by the intraclass correlation coefficient, model 2,1 ($ICC_{2,1}$).¹⁹ Statistical analysis included a 2-way analysis of variance to compare the BMD at each region of the hip (trochanter, intertrochanteric, neck, Ward's triangle, total), lumbar spine (L1, L2, L3, L4, total), and knee between the SCI and control groups; significance was set at P less than or equal to .05. Pearson product moment correlations were also calculated to estimate the strength of the relation between the hip BMD and the knee (distal femur, proximal tibia) BMD. Given the large estimated differences between the control and able-bodied groups and the established variability, we were adequately powered (>80%) to detect the difference between the 2 groups with 11 subjects.

RESULTS

There was no difference in age, height, or weight between the SCI and able-bodied groups ($P>.05$). Subject injury level and demographic data appear in table 1.

Reliability and Reproducibility

There were strong associations among all 4 raters' BMD measurements at the distal femur (all Pearson product moment correlations $>.97$) (table 2). The overall $ICC_{2,1}$ for the femur was .98. Individual ICCs among raters were high ($>.975$; see table 2). Similar strong associations occurred among all raters' BMD measurements at the proximal tibia (all Pearson product moment correlations $>.87$) (table 3). The overall $ICC_{2,1}$ for the tibia was .89, and ICCs among raters exceeded .870 (see tables 2, 3).

SCI Versus Control

There was no difference between right and left hip BMD for both SCI and control groups ($P>.05$); therefore, the group mean data were collapsed across sides. BMD at all hip regions was lower in the SCI group than in the control group ($P<.05$; fig 1A). No difference in spine BMD existed between the SCI and the control group at any lumbar spine region ($P>.05$; fig 1B). Distal femur BMD was lower for the SCI group than for controls in both the right and left leg comparisons across all 4 raters ($P<.05$; fig 2A). Proximal tibia BMD was lower for

^aSupplier Hologic Inc, 35 Crosby Dr, Bedford, MA 01730.

the SCI group than for controls for both right and left leg comparisons across all raters ($P < .05$; fig 2B).

Predictive Ability of the Knee Measurement

The total BMD at the hip was moderately predictive of the BMD at the distal femur ($R^2 = .67$) (fig 3A). The total BMD at the hip was less predictive of the BMD at the proximal tibia ($R^2 = .38$) (fig 3B).

DISCUSSION

The major findings of this study support that knee BMD can be reliably analyzed using DXA, subjects with SCI have diminished knee and hip BMD despite maintaining the spine BMD, and low hip BMD is associated with low distal femur BMD. The method developed to evaluate distal femur and proximal tibia BMD had excellent reliability among raters. Pearson correlation coefficients and ICCs support a high association as well as high agreement between repeated analyses (see tables 2, 3).¹⁹ It is important to point out that the purpose of this study was to explore the sources of error attributed to analyzing the scans between raters. Because of the high between-rater reliability, we chose to not focus on the within-rater reliability in this study ($ICC_{1,k} = .99$). It is generally recognized that high internal consistency among various raters is associated with high within-rater repeatability. We also minimized a major source of error in this protocol by operationally defining a procedure to determine the anatomic ROIs (see appendix 1) and by testing the degree to which 4 raters could uniformly implement this protocol. However, during longitudinal assessments, other sources of error would need to be considered. Repositioning the subjects' limbs from day to day²⁰⁻²³ and significant changes in soft tissue (disuse atrophy of muscle) may contribute to error during longitudinal studies using DXA scans. Accordingly, an intervention that has a small effect ($\approx 10\%$) may be very difficult to reliably measure at the distal femur and proximal tibia, once all sources of error using DXA are taken into account. In 2 studies that obtained a small-effect size, 1 contained detailed¹³ methods and the other was less detailed.¹¹ It is imperative that the methods used to establish BMD at nonstandard sites be clearly delineated if the effectiveness of antiosteoporosis interventions is to be fully understood.

Systematic differences existed between the subjects with and without SCI. For the hip, distal femur, and proximal tibia, BMD was lower in people with SCI, a finding that generally agrees with different measurement methods from previous reports.^{3,11,12,24} No difference existed between the BMD of the 2 groups at the lumbar spine. One explanation for this dissociation between the lumbar spine and the hip is that during wheelchair use after SCI, the lower extremities receive very little loading. Conversely, the lumbar spine may experience a substantial stimulus for maintenance of bone density in that region. Although this is a plausible explanation, no report has adequately defined the biomechanic stresses encountered by the paralyzed trunk during wheelchair use after spinal cord injury. Moreover, a recent report using peripheral quantitative computed tomography suggests that BMD values of the lumbar spine as determined by DXA may be artificially elevated by inclusion of the posterior vertebral elements, heterotopic ossification, or vascular calcification.²⁵ Despite this possibility, the incidence of lumbar spine fractures is very low in people with chronic SCI, suggesting that the spine bone density does not approach fracture threshold.

The hip BMD correlated moderately to the distal femur BMD, but correlated less to the proximal tibia BMD. A contributing factor may be that the tibia and femur appear to lose BMD at different rates after SCI. Garland et al,² using a DXA scan, found that the distal femur lost bone more rapidly than the proximal tibia for the first year after SCI. After 1 year,

the femur rate of decline matched able-bodied rates, but the tibia continued to lose bone mineral at an accelerated rate. By 10 years postinjury, the femur and tibia had lost equal quantities of bone. However, several issues must be addressed when considering this interpretation. In the able-bodied group of the present study, absolute BMD (in g/cm^2) was lower in the proximal tibia than in the distal femur (see figs 2A, 2B). Therefore, a similar relative difference in BMD ($>10\%$) for the proximal tibia and distal femur would reflect a smaller absolute difference in BMD for the tibia. Tibia measurements using DXA may thus be less sensitive to change because of reduced resolution at this site. In the present group of subjects with chronic SCI, the relative difference in BMD for femur and tibia appeared similar ($\approx 30\%$ reduced from able-bodied; see figs 2A, 2B). The low range of BMD values for the tibia, relative to its variation, suggests that the signal-to-noise ratio for the tibia is lower than the distal femur, which, in turn, is lower than the hip. Consequently, small changes in BMD at nonstandard scan sites must be scrutinized carefully in longitudinal studies, such as those that investigate the effectiveness of short-duration exercise interventions.¹¹ The present study, however, verified that the effects of long-term paralysis are clearly measurable in the distal femur and proximal tibia using DXA and the protocol presented in appendix 1.

People with SCI routinely expose their limbs to forces with the potential to cause a fracture (transfers, dressing, passive or active standing, treadmill training, and other contemporary rehabilitation interventions). Despite the skeletal deterioration that occurs after SCI,^{3,26} persons with SCI must continue these necessary activities. Similarly, rehabilitation specialists instruct people with SCI in necessary functional activities without a dependable estimate of BMD for the primary sites of fracture; the distal femur and proximal tibia. The protocol presented here provides an operationally defined method to obtain reliable estimates of knee BMD. With improved understanding of knee BMD, rehabilitation specialists and scientists may be able to establish efficacious treatments for the maintenance of skeletal integrity following SCI.

CONCLUSIONS

The BMD of the distal femur and proximal tibia can be reliably assessed using the protocol operationally defined in this report. People with SCI have reduced BMD in the hips, distal femurs, and proximal tibias, compared with age- and sex-matched controls. The hip BMD is associated with the distal femur BMD and marginally associated with the proximal tibia BMD. DXA-based studies that strive to assess the efficacy of an intervention in people with SCI should consider the sources of error that may obscure the integrity of the BMD measurements.

APPENDIX 1: DISTAL FEMUR AND PROXIMAL TIBIA MEASUREMENT PROTOCOL

1. **Obtain Femur Length:** Palpate landmarks and measure from proximal rim of trochanter to terminus of lateral condyle.
2. **Set ROI 1:** Scrutinize the image for movement artifact if subject experienced spasms. Discard images that show movement artifact. Place the distal edge at 13% of femur length and the proximal edge at 20% of femur length, measured from the terminus of the lateral femoral condyle. If the terminus is not visible in the scan, use the most distal portion of the image. Set the ROI width outside the bone area but inside the global area.
3. **Set ROI 2:** Place the proximal edge at the uppermost point of contact between the fibular head and the tibia. The total height of ROI 2 should match the total height of

ROI 1: position the bottom edge of ROI 2 accordingly. If insufficient tibia length is visible in the scan, place the distal ROI edge at the most distal portion of the image possible.

4. **Set Global Area:** Set global window vertical edges to 1 pixel above and 1 pixel below the ROIs. Set global width just narrow enough to exclude all air-space pixels. If this is not possible because of large ROI widths, up to 6 pixels of air space may be included medially and/or laterally.
5. **Initialize BMD Software Analysis.**
6. **Image Correction:** Manually shade bone pixels that were erroneously excluded by the analysis algorithms. Place the line of demarcation on the edge of the whitest pixels. Erase soft tissue erroneously identified as bone. Erase fibula bone pixels.

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Fig 1. Mean and standard deviation of BMD of subjects with and without SCI. (A) BMD at every hip region was significantly reduced for SCI group ($P < .05$). (B) BMD at the lumbar spine did not differ at any level between SCI and able-bodied group ($P > .05$).

Fig 2.
 (A) BMD at the distal femur and (B) BMD at the proximal tibia were significantly less ($P < .05$) for the SCI group, as determined by 4 masked raters using a newly developed protocol (see appendix 1).

Fig 3. Correlations between (A) hip and distal femur BMD and (B) hip and proximal tibia BMD, as assessed by 4 masked raters.

Table 1

Subject Demographics

Subject	Age (y)	Height (cm)	Weight (kg)	Injury Level	Years Post SCI	Sex
1	31	177.8	75			M
2	54	182.9	97.7			M
3	34	177.8	80.9			M
4	36	190.5	79.5			M
5	43	177.8	72.7			M
6	36	188	81.8			M
7	28	167.6	61.2			F
8	62	188	93.2			M
9	26	188	90.9			M
10	23	175.3	75			M
11	22	182.9	74.1			M
12	28	182.9	67.3	C6	11	M
13	28	188	96.4	C6	11	M
14	36	177.8	54.5	T1	12	M
15	67	185.4	84.1	T5	11	M
16	54	170.2	102.3	T6	9	M
17	28	154.9	47.7	T7	10	F
18	37	172.7	102.3	T8	2	M
19	49	162.6	75	T11	2	M
20	39	177.8	72.7	T12	4	M
21	52	175.3	86.4	T12	35	M
22	34	185.4	61.4	T12	5	M
Mean ± SD						
Control	35.9±12.7	181.5±6.9	80.2±10.5			
SCI	41.1±12.8	175.7±10.2	77.3±18.7		10.2±9.1	

Abbreviations: F, female; M, male; SD, standard deviation.

Table 2

Correlations Between Raters for BMD Measurements at the Distal Femur

Coefficients	Rater 1	Rater 2	Rater 3	Rater 4
Pearson correlation coefficients (N=44 scans)				
Rater 1	1			
Rater 2	.977 [*]	1		
Rater 3	.985 [*]	.970 [*]	1	
Rater 4	.984 [*]	.974 [*]	.989 [*]	1
ICC _{2,1} (N=44 scans)				
Rater 1	1			
Rater 2	.998 [*]	1		
Rater 3	.983 [*]	.975 [*]	1	
Rater 4	.982 [*]	.978 [*]	.983 [*]	1

NOTE. ICC_{2,1} for all raters versus all other raters was equal to .98.^{*} $P < .05$.

Table 3

Correlations Between Raters for BMD Measurements at the Proximal Tibia

Correlations	Rater 1	Rater 2	Rater 3	Rater 4
Pearson correlation coefficients (N=44 scans)				
Rater 1	1			
Rater 2	.905 [*]	1		
Rater 3	.915 [*]	.872 [*]	1	
Rater 4	.937 [*]	.893 [*]	.956 [*]	1
ICC _{2,1} (N=44 scans)				
Rater 1	1			
Rater 2	.876 [*]	1		
Rater 3	.920 [*]	.870 [*]	1	
Rater 4	.915 [*]	.888 [*]	.910 [*]	1

NOTE. ICC_{2,1} for all raters versus all other raters was equal to .89.^{*} $P < .05$.