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

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OBJECTIVE. 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.

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

RESULTS: The knee measurements were highly reliable (femur intraclass correlation coefficient model 2,1 [ICC_{2,1}=0.98; tibia ICC_{2,1}=0.89]. 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=0.67), but less correlated with the proximal tibia (R^2=0.38).

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.

KEY WORDS: Fractures; Osteoporosis; Paralysis; Rehabilitation; X-ray absorptiometry, dual energy.

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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). 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 antosteoporosis medications. Exclusion criteria for able-bodied subjects were fracture in the lower extremities, endocrine disorder, or antosteoporosis medications.

DXA (QDR 2000) 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 7.20a) automatically detected ROIs in the hip and lumbar spine, as is routinely done in clinical examination and diagnosis of osteoporosis. After consultation with Hologic, we elected to use the spine algorithm during knee analysis consistent with previous reports. 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$_{2,1}$). 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.

### Table 1: Subject Demographics

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</table>

**Mean ± SD**

- Control: 35.9 ± 12.7, 181.5 ± 6.9, 80.2 ± 10.5 (women: 37.0 ± 13.2, 179.9 ± 6.7, 79.3 ± 10.0; men: 35.2 ± 11.7, 184.3 ± 7.8, 82.1 ± 10.3)
- SCI: 41.1 ± 12.8, 175.7 ± 10.2, 77.3 ± 18.7 (women: 41.3 ± 12.9, 178.8 ± 10.4, 78.7 ± 18.9; men: 40.8 ± 12.7, 173.5 ± 10.2, 75.9 ± 19.2)

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

### Table 2: Correlations Between Raters for BMD Measurements at the Distal Femur

<table>
<thead>
<tr>
<th>Coefficients</th>
<th>Rater 1</th>
<th>Rater 2</th>
<th>Rater 3</th>
<th>Rater 4</th>
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<td>Pearson correlation coefficients</td>
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</table>

**NOTE:** ICC$_{2,1}$ for all raters versus all other raters was equal to .98. *$P<.05$.**
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 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). 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$_{2,1} = .99$). 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 day 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 detailed methods and the other was less detailed. It is imperative that the methods used to establish BMD at nonstandard sites be clearly delineated if the effectiveness of antosteoporosis 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. 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. 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, 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/cm²) 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 (~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. 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.

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.

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, 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.

Acknowledgments: We thank Deanna Frei, RTR, CT, and Marta Tullis, RN.

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.

References


