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Demineralization in tetraplegic and paraplegic man over time

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The aim of the present study was to compare bone mineral density (BMD in g/cm^2) in the lumbar spine and three hip regions of male spinal cord injured subjects at various times post injury to age-matched able-bodied controls and to correlate their BMDs to their age and level of their spinal cord lesion. Patients and controls were stratified into three 20 year age groups (20–39, 40–59, and 60$^+$ years of age). BMD measurements were obtained using dual energy X-ray absorptiometry (DEXA, Lunar Model DPX). BMD levels taken within the first year of injury were not significantly lower than the age-matched able-bodies controls. The 20–39 year old patients injured longer than 1 year had significantly lower ($P \leqslant 0.01$) BMDs in their femoral region than both their age matched controls and the 20–39 year old acutely injured (injured for less than 1 year) patients. Although femoral BMDs of both paraplegic and quadriplegic patients 40–59 and 60$^+$ years of age decreased over time, none showed significant bone loss in this region until 10 years after their injury. These results indicate that spinal cord injury associated bone loss occurs most dramatically in the femoral region of young men. These results also indicate that initial bone mass loss does not occur prior to 1 year post-injury to the extent that it is detectable by densitometry, or at least it did not occur in our patients.

Keywords: spinal cord injury; spinal cord injury associated bone mass loss; bone mineral density, (BMD); dual energy X-ray absorptiometry (DEXA); paraplegia; tetraplegia

Introduction

Spinal cord injury is well known to cause multiple system dysfunctions, among which is marked atrophy of the appendicular skeleton. The natural history of the development of the atrophy and its temporal pattern is not well understood. Measurement of bone mineral content (BMC) or bone mineral density (BMD) after spinal cord injury in an attempt to quantify bone loss has been reported in only a few publications. Early studies primarily measured BMC at the distal radius[1,2] or at the iliac crest.[3,4] Later studies included either BMC or BMD measurements of the lower extremeties.[5–12] These studies were performed on small patient populations and did not take into account the length of time of injury nor the age of the patient. The purpose of the present preliminary study was four-fold: (1) to assess if changes in bone mass using substantial numbers of patients were consistent with previous reports using small patient populations; (2) to determine if these changes were age related; (3) to determine when did these changes begin to appear, and (4) to determine if there were any differences between individuals with tetraplegia or paraplegia in the pattern of bone mass loss.

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Materials and methods

Laboratory studies including complete blood count (CBC) with differential, erythrocyte sedimentation rate (ESR), electrolytes, liver and renal function studies, standard X-rays, and BMD measurements were performed on 355 young active duty military, mid-age and older male veterans (92 able-bodied individuals and 263 male patients with spinal cord injuries who had been admitted to the spinal cord injury unit at the Veterans Affairs Medical Center from 1994 to 1996). This initial spinal cord injured patient population included new patients with acute injuries as well as patients who were readmitted for various medical reasons. The subjects selected to participate had all laboratory studies within normal limits and had no clinical or laboratory evidence of heterotopic bone formation. None of the controls or patients had metabolic diseases or other conditions known to influence their calcium metabolism or BMD, and, none of the participants had received treatment influencing these parameters. Patients with internal fixation devices were excluded.

Of the initial 475 men, 355 were selected to participate: 92 of the able-bodied individuals (mean age = 51.1 ± 1.7 years, range 24–76 years) and 263 of the spinal cord-injured patients (mean age = 48.8 ± 1.3 years, range 20–78 years). Since changes in the

appendicular and axial skeleton with aging has been shown to occur in 20 year intervals,[13–15] participants were stratified into three 20 year age groups (20–39, 40–59, and 60^{+} years). Patients within each age group were further stratified according to the time since their injury occurred (less than 1 year, 1–5 years, 6–9 years, 10–19 years, 20–29 years, 30–39 years, 40–49 years, and 50–59 years) and level of injury (Table 1).

Bone mineral density measurements (g/cm^2) of the lumbar spine (L1–L4) and three regions of the proximal femur (the femoral neck, Ward's triangle, and the trochanter) were obtained using dual energy

Table 1 Summary of the stratification of able-bodied and spinal cord injured males according to age, completeness of injury, and time since injury

	Overall age of controls	*Overall age of patients*	*Average time since injury (year)*	*Stratification by age of injury (year)* 0–1	1–5	6–9	10–19	20–29	30–39	40–49	50–59
20–39 year olds											
• mean age	31.6	30.4	5.2								
• st. error	1.0	0.8	0.8								
• range	24–39	20–39	0.08–18								
• number	18	65									
• paraplegic persons											
mean age		28.9	4.6	23.6	28.6		36.5				
st. error		1.1	1.1	1.0	1.6		0.6				
range		20–39	0.08–18	20–29	21–38		34–39				
number			33	11	14	0	8				
• tetraplegic persons											
mean age		31.9	6.0	29.2	30.0	31.5	36.3				
st. error		1.0	1.1	1.6	2.6	1.6	0.6				
range		20–39	0.08–17	21–39	22–37	29–36	32–39				
number			32	11	7	4	10				
40–59 year olds											
• mean age	49.9	47.7	16.5								
• st. error	0.8	0.5	1.0								
• range	40–59	40–58	0.08–34								
• number	44	108									
• paraplegic persons											
mean age		47.1	16.5	46.6	53.0	47.8	44.1	47.4	50.3		
st. error		0.6	1.5	2.1	4.0	0.7	1.4	0.9	1.5		
range		40–58	0.08–31	40–58	49–57	46–50	40–54	40–58	48–53		
number			49	8	2	5	9	22	3		
• tetraplegic persons											
mean age		48.3	16.5	43.7	47.9	51.6	47.3	47.8	54.2		
st. error		0.6	1.4	1.6	2.2	2.0	1.3	0.9	0.9		
range		40–58	0.08–34	40–49	40–56	46–58	40–54	43–56	51–56		
number			59	6	7	5	13	22	6		
60+year olds											
• mean age	68.7	67.4	21.3								
• st. error	0.9	0.6	1.9								
• range	60–79	60–82	0.08–53								
• number	30	89									
• paraplegic persons											
mean age		67.6	24.6	72.3	64.8	65.0	68.8	63.9	63.3	67.4	74.7
st. error		0.8	2.5	1.3	1.1	2.7	2.8	1.2	1.3	1.5	1.6
range		60–78	0.08–53	68–78	62–69	60–73	61–77	60–70	61–67	62–77	67–78
number			54	6	6	5	6	9	4	11	7
• tetarplegic persons											
mean age		67.0	16.2	66.3	65.7	69.3	69.2	64.0	68.3	66.6	75
st. error		0.9	2.8	1.3	1.3	4.2	3.0	3.5	3.4	2.4	
range		60-82	0.08–49	63–71	63–72	61–74	60–82	60–71	61–75	62–74	
number			36	8	6	3	6	3	4	5	1
Total	92	263	263	50	42	22	52	56	17	16	8

X-ray absorptiometry (DEXA) (LUNAR Model DPX; LUNAR CORP., Madison, WI). Spine BMD was assessed both at individual levels and as average density of L2–L4. Overall BMD of the lumbar spine was determined as the total BMD in the 2nd, 3rd, and 4th vertebrae.

BMD measurements of both controls and patients were calculated as a percentage of the standardized parameters for healthy nonselected age-matched men provided by the densitometry manufacturer. BMD measurements of patients were then compared to their age-matched controls. Mean and standard error of the mean were calculated for each age group. Statistical analysis was conducted using analysis of variance (ANOVA) followed by a post-hoc analysis using Tukey's honest significant difference (HSD) test.

Results

Figure 1 shows the results of the BMDs for both the lumbar and femoral regions in the 20–39 year old patients compared to the 20–39 year old able-bodied controls and to each other. Both the paraplegic and tetraplegic patients injured for less than 1 year had BMDs approximately the same as their able-bodied controls for all the regions studied. Although the tetraplegic patients had BMDs less than their comparable paraplegic counterparts none of the differences were significant. There was a steady increase in BMD in the lumbar region of the paraplegic patients which reached significant levels at 10–19 years after injury when compared to the controls ($P=0.038$) and paraplegic patients injured less than one year ($P=0.005$) whereas the tetraplegic patients injured for 1–5 years showed a slight decrease of the BMD in this area which increased to above control levels after 5 years of injury (Figure 1a). There was a steady decrease in the BMDs in the three femoral regions in both the paraplegic and tetraplegic patients (Figure 1b–d). Both paraplegic and tetraplegic patients injured for more than 1 year had the hip region BMDs significantly lower than the controls ($P<0.05$) and their respective newly injured (injured less than 1 year) counterparts ($P<0.014$ and $P<0.04$, respectively).

Figure 2 shows the results obtained when BMD measurements were made on the patients and able-bodied controls 40–59 years of age. Neither paraplegic nor tetraplegic patients injured for less than 1 year had BMDs in any of the regions studied significantly different from the controls. Although, with time, the BMDs in the lumbar region increased in both paraplegic and tetraplegic patients, none were significantly different from either the controls or their respective counterparts injured for less than 1 year (Figure 2a). The femoral regions showed a decrease in BMD over time in both paraplegic and tetraplegic patients (Figure 2b–d). This decrease reached significant levels in all three regions studied in tetraplegic patients injured for 10–19 years when compared to able bodied controls ($P<0.04$) and tetraplegic injured for less than one year ($P<0.04$) and then increased slightly thereafter. Paraplegic patients showed a significant decrease in BMD only after 19 years of injury and then only in the femoral neck region when compared to the controls ($P<0.02$) and paraplegic males injured for less than 1 year ($P=0.017$).

Figure 3 shows the results of the BMDs for both the

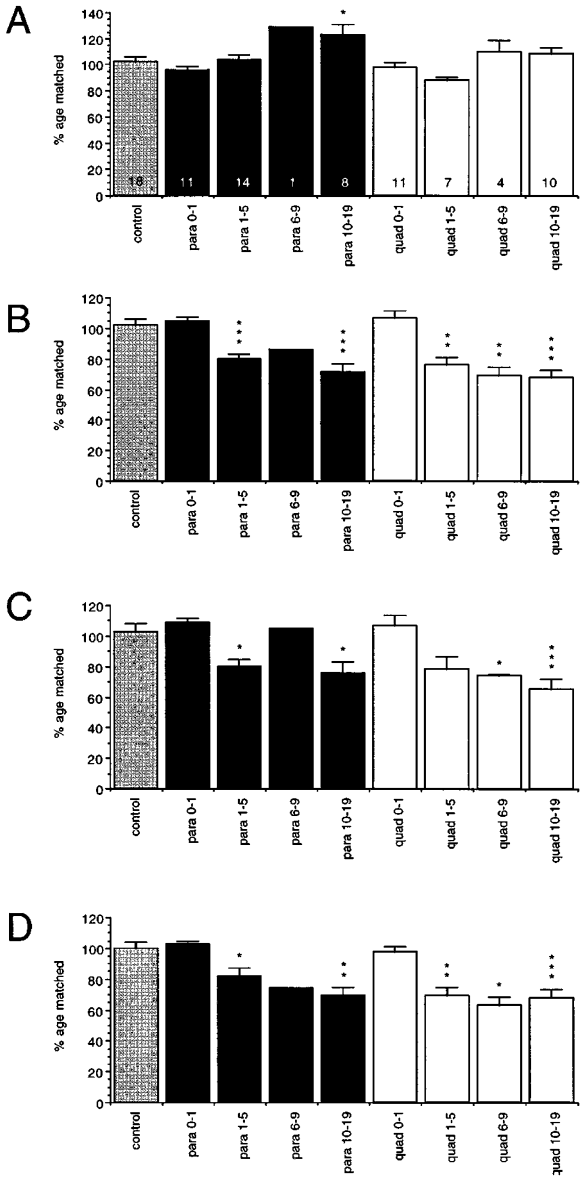

Figure 1 Comparison of the BMDs of the (a) lumbar spine, (b) femoral neck, (c) Ward's triangle, and (d) the greater trochanter in 20–39 year old able-bodied controls and 20–39 year old paraplegic and tetraplegic patients after the patients had been stratified according to the time since injured. * = $P<0.05$; ** = $P<0.01$; *** = $P<0.001$ when compared to controls and to their comparable patients injured for 0–1year

lumbar and femoral regions in the patients and able-bodied controls 60^{+} years of age. The BMDs in the lumbar region of both the paraplegic and tetraplegic patients regardless of the length of time the patient had been injured were greater than or equal to the BMD of the controls (Figure 3a). Although paraplegic patients injured for 6–9 years and tetraplegic patients injured for 10–19 years had BMDs significantly greater than able-bodied controls ($P=0.014$ and $P=0.034$ respectively), they were not significantly greater than their comparable counterpart injured for less than 1 year. No BMDs from the femoral regions

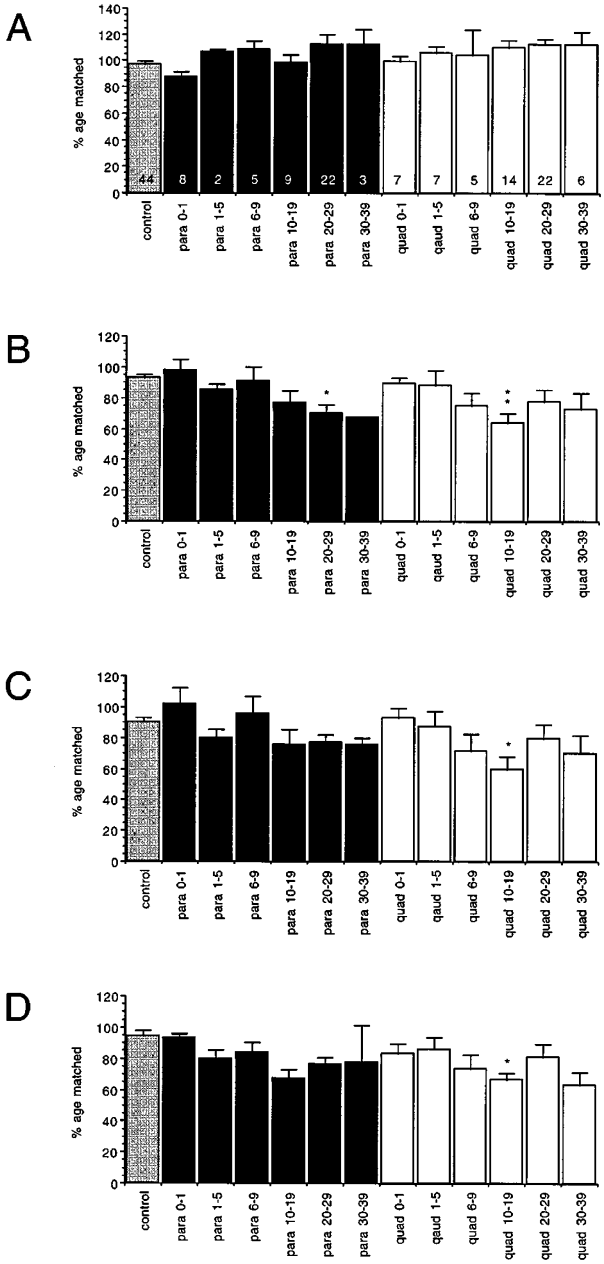

Figure 2 Comparison of the BMDs of the (a) lumbar spine, (b) femoral neck, (c) Ward's triangle, and (d) the greater trochanter in 40–59 year old able-bodied controls and the 40–59 year old paraplegic and tetraplegic patients after the patients had been stratified according to the time since injured. $*=P<0.05$; $**=P<0.01$; $***=P<0.001$ when compared to controls and to their comparable patients injured for 0–1 year

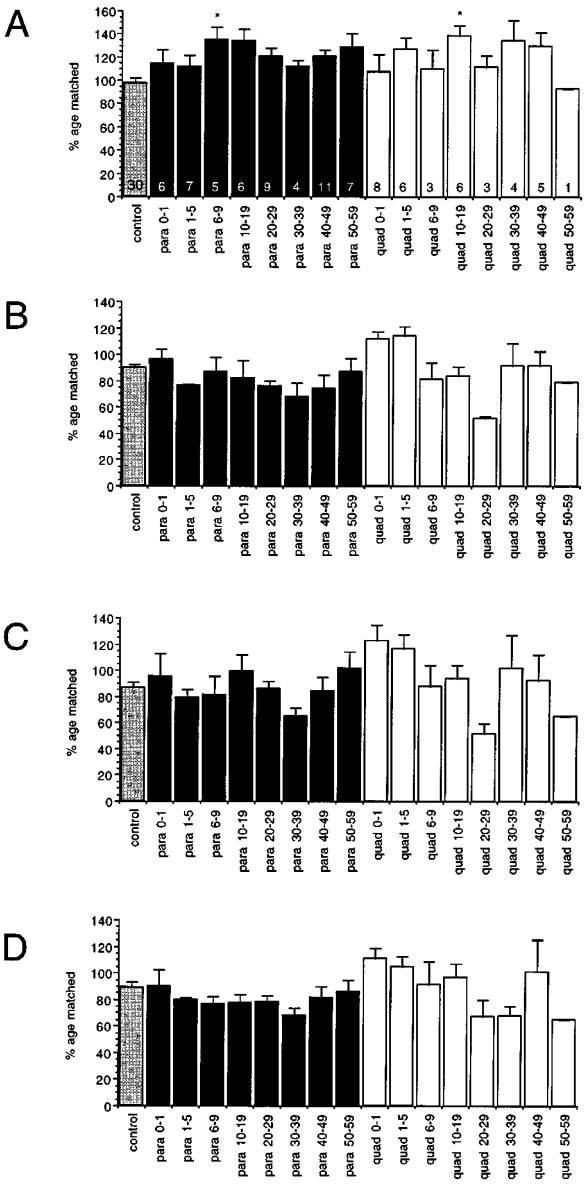

Figure 3 Comparison of the BMDs of the (a) lumbar spine, (b) femoral neck, (c) Ward's triangle, and (d) the greater trochanter in 60^{+} year old able-bodied controls and the 60^{+} year old paraplegic and tetraplegic patients after the patients had been stratified according to the time since injured. $*=P<0.05$; $**=P<0.01$; $***=P<0.001$ when compared to controls and to their comparable patients injured for 0–1 year

of paraplegic patients were significantly different than the controls whereas tetraplegic patients injured for 20–29 years had BMDs significantly lower than the controls and the tetraplegic patients injured for less than 1 year in the femoral neck ($P=0.018$ and $P=0.005$ respectively) and Ward's triangle ($P=0.05$ and $P=0.029$ respectively; Figure 3b–d).

Discussion

Precise and accurate methods for measuring bone mass have only recently been applied to studies in spinal cord injury. These studies are difficult to interpret because of the many methodological variations. They have been based mainly on biochemical studies showing imbalance between anabolic and catabolic functions, occasionally on histomorphometric studies, and only recently on BMCs and BMDs.[1–12,16–20] Spinal cord injury associated bone loss appears by most of these studies to be regional, affecting certain skeletal areas below the level of injury. In all these studies, small numbers of subjects with most injuries for less than 24 years were used. Therefore, the aim of the present study was to determine the BMD in the lumbar spine and hip regions in a large number of male individuals with spinal cord lesions and to investigate the relationship of BMD to the age of the patients, the level of the injury, as well as the age of the injury.

In cross-sectional and longitudinal studies, Biering-Sorenson *et al*[5,6] showed that BMC of the femoral bone was continuously and significantly decreased (25% lower) in spinal cord injured patients between 20 and 55 years of age compared to normal individuals, while the BMC of the lumbar spine was nearly unchanged. These results are similar to our spinal and femoral BMD results for patients between 20–39 years of age. Although there was a 5% decrease in the BMD of the lumbar spine of the 20–39 year old patients, it was not significant: however, the BMDs of all three femoral regions were significantly lower (18% for all three regions) than their able-bodied age matched controls. The BMD of the lumbar spine of both the 40–59 year old and the 60^{+} year old patients were significantly higher (11% and 35%, respectively) than their able-bodied age-matched controls. The BMD of the femoral regions were all significantly lower (approximately 16% in the 40–59 year old patients, but were not different in the 60^{+} year old patients. The only other group of osteoporotic subjects noted to maintain relatively more spinal bone mass is the group of females studied by Steiger *et al*[14] over age 85 years. Biering-Sorenesen *et al*[6] stated that their longitudinal study indicated that normal muscle function and load bearing is necessary to prevent bone mass loss.

Leslie and Nance[12] showed evidence of significant hip demineralization (14%) but normal bone density in the lumbar spine of 14 spinal cord injured male patients injured for 1 to 17 years. Sharp *et al*[9] studying men 5.6 days–48 years post injury, demonstrated that the lumbar spine BMD was maintained at the level of age matched controls. They also showed a BMD decrease of 19% for the hip but did not indicate at which level the hip bone mass stabilized. Uebelhart *et al*[22] measured BMC and BMD of the lumbar spine and the lower limbs of six young male acute spinal cord injury subjects. They found stable bone mass in the lumbar spine in sharp contrast to the lower limbs where the BMC was lower by 7.1% and the BMD by 6.4%. These findings although utilizing different methodologies seem to correlate with our findings.

Conclusion

Spinal cord related changes in bone mass have a different pattern from osteoporosis that occurs as a result of other etiologic factors such as post menopause, endocrine, age related, etc. The lumbar bone mass was found stable with a nonsignificant decline in the tetraplegic population at 1–5 years post-injury in the 20–39 year age group. In all the other age groups the lumbar spine maintained its bone mass even further increasing it with age, regardless of age at the time of injury or level of injury. The bone mass gain on bone densitometry may be explained by degenerative changes in the spine, giving falsely higher values, which raises the questions: (1) if spinal cord injury accelerated the development of degenerative joint disease and (2) if it is falsely increased, why don't we see osteoporotic vertebral fractures to the extent it occurs in post-menopausal osteoporotic women, (3) does degenerative joint disease provide stability preventing osteoporotic vertebral fractures?

The hip area did not show evidence of bone mass loss until after the first year post injury. Following that, the decline was gradual with the lowest bone mass at 19 years following injury regardless of age or level of injury. The pattern of hip bone mass loss was not different in paraplegic patients as opposed to those with tetraplegia.

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