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Original Article

Osteoporosis and risk of fracture in men with spinal cord injury

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Study design: Cross-sectional study to evaluate bone mineral density (BMD) and fracture history after spinal cord injury (SCI).
Objectives: To determine frequency of osteoporosis and fractures after SCI, correlate extent of bone loss with frequency of fractures after SCI, and determine fracture risk in SCI patients.
Setting: The Hines Veterans Affairs Hospital in Hines, Illinois, USA.
Methods: Femoral neck BMD was measured in 41 individuals with a history of traumatic or ischemic SCI using dual-energy X-ray absorptiometry (DEXA Lunar Whole Body Densitometer Model).
Results: Twenty-five patients (61%) met the World Health Organization (WHO) criteria for osteoporosis, eight (19.5%) were osteopenic, and eight (19.5%) were normal. Fracture after SCI had occurred in 14 patients (34%). There were significant differences between the femoral neck BMD and SCI duration in patients with a fracture history compared to those without. For patients in the same age group, each 0.1 gm/cm^2 and each unit of standard deviation (SD) (*t*-value) decrement of BMD at the femoral neck increased the risk of fracture 2.2 and 2.8 times, respectively. Considered simultaneously with age, duration of SCI, and level of SCI, BMD was the only significant predictor of the number of fractures.
Conclusion: Osteoporosis and an increased frequency of fractures occur after SCI. Measurement of femoral neck BMD can be used to quantify fracture risk in SCI patients.
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Keywords: osteoporosis; bone mineral density (BMD); fracture; risk of fracture; spinal cord injury (SCI); dual energy X-ray absorptiometry (DEXA)

Introduction

Osteoporosis, a condition characterized by low bone mass and deterioration of the skeletal microarchitecture, is a known consequence of spinal cord injury (SCI).[1,2] Decline in bone mineral density (BMD) has been detected radiologically in the paralyzed limbs of patients as early as 6 weeks after SCI.[3] Bone loss is then noted to progress over 12 to 16 months after SCI prior to stabilizing.[4–6] The significance of osteoporosis is that it results in skeletal fragility and increased risk of fractures.[7,8] Bone loss after SCI is reported to reach 'fracture threshold' at 1 to 5 years after injury.[9] Complications from fracture and its treatment can lead to long term hospitalization, increased costs, and increased disability. Thus, guidelines for osteoporosis screening and management in SCI patients are relevant and need to be developed.

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The advent of bone densitometry has provided a means to measure bone mass and quantify 'fracture risk' before a fracture occurs.[7] Most studies of fracture risk, however, are limited to the general population. The goals of this study were to evaluate BMD and fracture history after SCI, to determine the frequency of osteoporosis and fractures after SCI, to correlate the extent of bone loss with the frequency of fractures after SCI, and to determine 'fracture risk' in this patient population.

Subjects and methods

Subjects were recruited from the SCI outpatient clinics, the SCI inpatient units, and the SCI Residential Care Facility of the Hines Veterans Affairs Hospital from July 1999 to March 2000. The study sample was limited to male patients with a history of traumatic or ischemic SCI. Participants with a history and radiological evidence of instrumentation, spondyloarthro-

pathy, or heterotopic ossification involving the area of investigation were excluded from the study. All study participants were medically stable upon inclusion into the study, and each gave informed consent.

Each patient was evaluated by history and physical exam. The history was obtained by direct patient interview and chart review. Data recorded consisted of patient's age, height, weight, SCI history, and fracture history. SCI history included date of onset of SCI, cause of SCI, level of SCI, and extent of SCI (complete *vs* incomplete). Fracture history focused on the number of fracture events after SCI, cause of fracture, location of fracture, and duration of SCI at the time of fracture occurrence. A fracture event was defined as the moment of occurrence of a fracture involving one or more bones. Level and completeness of SCI were assessed on physical examination using the American Spinal Injury Association (ASIA) Classification.

Radiological studies of the lumbar spine, both hips and both lower limbs were done to document the presence or absence of the exclusion criteria conditions, to confirm the patient's fracture history, and to document previously undetected fractures.

The standard protocol for Dual Energy X-ray Absorptiometry (DEXA, Lunar Whole Body Densitometer Model) was utilized to selectively measure the BMD of the femoral neck. The left femoral neck BMD was measured, unless unobtainable, then BMD of the right femoral neck was used. BMD values were reported as g/cm^2, and as standard deviations (SD) from the mean peak bone mass of sex-matched young adults in the Lunar database (*t*-value).

The World Health Organization (WHO) standard was used to classify patients into three BMD groups: normal, osteopenic, and osteoporotic. Analysis of Variance (ANOVA) was used to compare these groups. Patients were also grouped into two fracture groups: those with a history of fracture after SCI, and those without.

These two groups were subjected to the Student's *t*-test and Chi-Square Analysis. Statistical significance was considered if $P<0.05$. Logistic regression was used to determine 'fracture risk'. Poisson regression was used to model the number of fractures per patient as a function of age, duration of SCI, level of SCI, and BMD.

Results

Of 49 patients recruited, eight patients were subsequently excluded from the analysis. Among the eight patients, one had extensive HO of both hips, another had previous surgical removal of bilateral femoral heads, and two had radiological evidence of severe spondyloarthropathy encompassing the area to be measured. The DEXA scan could not be performed in two patients, one because of problems with mobility secondary to recent fracture, and the other because of severe bilateral hip contractures, and two patients withdrew from the study for personal reasons. Of the eight patients excluded, three had a history of fracture after SCI. Of the 41 participants remaining in the study, ages ranged from 27 to 83 years (median age = 55 years, mean age = 56.0 ± 13.3 years). Duration of SCI varied from 0.7 to 54.9 years (median duration = 14.9 years, mean duration = 17.8 ± 14.1 years). Level of SCI ranged from C2 to L1 (Table 1).

BMD values obtained ranged from 0.158 to 1.205 g/cm^2 (median BMD = 0.657 g/cm^2) (Table 1). Twenty-five participants (61%) met the WHO criteria for osteoporosis, eight (19.5%) were osteopenic, and eight (19.5%) were normal. There was a statistically significant difference among the three BMD classes in terms of age and duration of SCI. Patients with normal BMD were younger than the other two groups ($F=3.90$, $P<0.05$; mean age normal BMD = 45.00 years, mean age osteopenia = 59.75 years, mean age osteoporosis = 58.24 years), and those with osteoporosis had a longer duration of SCI than the normal BMD group ($t=2.47$, $P<0.05$) (Figure 1). Also, there was a trend towards a greater number of fracture events after SCI for the osteoporosis group compared to the other two groups ($F=3.18$, $P=0.053$; mean number of fracture events for osteoporosis, osteopenia, and normal BMD = 0.96, 0.125 and 0.125, respectively) (Figure 2).

A history of fracture after SCI had occurred in 14 (34%) of the 41 patients (Table 2). The number of separate fracture events per patient ranged from 1 to 4, with a total of 26 fracture events for 14 patients. Duration of SCI at occurrence of first fracture event varied from 1 to 54 years. The majority of the fractures (84.6%) involved the lower limbs, with 62.5% of these fractures occurring below the knee, and 37.5% above the knee. In the lower limbs, fractures occurred more frequently on the right (61.5%) than on the left (38.5%), particularly above the knee where nine of 10 fractures occurred on the right. Falls were the most common cause of fracture.

Of the 14 participants with a fracture history, 12 (85.7%) had osteoporosis, one (7.1%) had osteopenia, and one (7.1%) had normal BMD. There was a significant difference between the BMD of those with a history of fractures (mean BMD = 0.504 g/cm^2), and those without (mean BMD = 0.786 g/cm^2; $t=4.09$, $P<0.001$) (Figure 3). Those with a history of fractures also had a significantly longer duration of SCI (mean SCI duration = 24.8 years), compared to those with no history of fractures (mean SCI duration = 14.3 years; $t=2.39$, $P<0.05$) (Figure 4). There was a difference at the trend level between the two fracture groups on the basis of age ($t=1.80$, $P=0.08$) (Figure 4), but no difference between the two fracture groups in terms of level and extent of SCI (Table 3).

Using logistic regression to evaluate the effects of BMD and age on the probability of fracture, the estimated logistic regression model for probability of fracture was: estimated logit = $1.55 + (0.05)(\text{AGE}) - (0.79)(-\text{BMD})$. The odds ratio for occurrence of fracture based on actual BMD was 2.2 ($c=0.86$, $P=0.006$) with a 95% confidence interval (CI) between 1.25 and 3.89. That is, for patients in the same age group, each 0.1 g/cm^2 decrement of BMD at

Table 1 Data for each patient included in the study

Age (years)	*SCI duration (years)*	*SCI level*	*ASIA score*	*BMD* (g/cm^2)	t-*value*	*Number of fracture events after SCI*
27	2.4	T1	D	0.982	−0.7	0
29	1.1	L1	A	1.037	−0.3	0
35	14.6	C5	A	0.432	−4.9	2
39	8.1	T3	A	0.785	−2.2	0
42	19.1	C4	D	1.066	0.0	0
44	11.8	C6	B	1.037	−0.3	0
44	20.6	C4	A	0.396	−5.2	4
46	0.13	C5	D	1.033	−0.3	0
46	25.4	C5	D	1.205	1.0	0
47	1.3	L1	B	0.734	−2.6	0
47	14.9	T6	A	0.766	−2.3	0
48	3.5	C5	C	0.644	−3.8	0
49	10.6	C5	A	0.557	−3.9	0
49	14.9	C5	B	0.344	−5.59	2
50	3.2	L1	A	0.470	−4.6	1
51	7.7	C6	A	0.484	−4.51	0
51	8.2	L1	C	0.622	−3.44	0
51	26.4	C2	B	0.940	−1.0	0
51	31.4	T4	A	0.657	−3.2	2
52	33.7	C5	A	0.420	−5.0	2
55	14.3	C5	A	0.669	−3.1	0
55	33.8	T6	A	0.699	−2.9	0
56	1.2	C5	B	1.138	0.5	0
59	37.7	C6	B	0.601	−3.6	0
59	38.3	C6	A	0.647	−3.3	0
60	30.4	C6	B	0.251	−6.3	4
61	11.8	C6	B	0.763	−2.4	0
63	21.2	T6	A	0.437	−4.87	3
64	8.8	C5	C	0.544	−4.0	0
66	16.7	C6	B	0.735	−2.6	0
66	47	L1	A	0.633	−3.36	0
67	17.4	T12	D	0.760	−2.4	0
68	15.6	C7	D	0.803	−2.1	1
70	0.7	L1	A	0.848	−1.71	0
70	4.9	L1	A	1.038	−0.25	1
70	5.1	T6	A	0.539	−4.1	0
70	43.1	L1	A	0.432	−4.9	1
75	12	C5	D	0.763	−2.4	0
79	32.2	T10	A	0.158	−7.01	1
80	54.9	T8	A	0.580	−3.8	1
83	26	T8	A	0.637	−3.33	1

SCI = spinal cord injury; T = thoracic; L = lumbar; C = cervical; ASIA = American Spinal Injury Association; BMD = bone mineral density

the femoral neck increased the risk of fracture 2.2 times. Using the *t*-value in place of actual BMD in the above equation, the odds ratio obtained was 2.8 (c = 0.86, $P = 0.007$, 95% CI: 1.32, 5.89). Thus, for each unit *t*-value decrement of BMD at the femoral neck, the risk of fracture increased 2.8 times. The odds ratio for age in either equation was 1.05 (95% CI: 0.98, 1.13). Although the CI for age included 1 and was not significant, age was retained in this model because the model predicted fracture more accurately with this variable included.

Logistic regression was also computed with the study population stratified into three age groups and three SCI duration groups as profiled in Tables 4 and 5. Using these groupings, age and duration of SCI were shown not to be significant predictors of fracture. With the age groups and SCI duration groupings removed from the model, the odds ratios for BMD and *t*-value were 2.1 (c = 0.84, $P = 0.004$, 95% CI: 1.27, 3.43) and 2.6 (c = 0.836, $P = 0.002$, 95% CI: 1.35, 4.93), respectively. Thus, for two patients who are comparable in age and duration of SCI, every 0.1 g/cm^2 decline in femoral neck BMD increased the likelihood of a fracture 2.1 times, while each unit decline in *t*-value increased the likelihood of a fracture 2.6 times.

Using Poisson regression, BMD was found to be the only significant predictor of the number of fractures. The model for prediction of the number

Table 2 Characteristics of patients with fracture history

Age (years)	*BMD* (g/cm^2)	t-*value*	*Number of fracture events*	*Location of fracture*	*Cause of fracture*	*SCI duration at time of fracture (years)*
35	0.432	−4.9	2	L thumb	Caught in lift	7
				L big toe	Bumped door	7
44	0.396	−5.2	4	R distal tibia/fibula	Fall	6
				R distal femur/R midshaft tibia	Fall	9
				2nd/3rd finger, R hand	Pushed wheelchair brake handle	11
				R patella	Fall	20
49	0.344	−5.59	2	R proximal femur	ROM exercises	11
				R distal tibia	ROM exercises	11
50	0.470	−4.6	1	L medial malleolus	Bumped door	3
51	0.657	−3.2	2	B distal tibia/fibula	MVA	2
				L distal tibia/fibula	Fall	22
52	0.420	−5.0	2	L shoulder	Fall	12
				R hip	Leaned forward after a fall	32
60	0.251	−6.3	4	R foot	ROM exercises	1
				R distal femur	R leg dropped, hit edge of bed	5
				Fingers, R hand	Pulled at chest drawer	5
				R proximal femur	Fall	23
63	0.437	−4.87	3	R proximal femur	Fall	8
				R distal tibia	Unknown	Unknown
				L distal tibia	Unknown	Unknown
68	0.803	−2.1	1	L distal tibia	Fall	16
70	1.038	−0.25	1	L distal tibia	Fall	3
70	0.432	−4.9	1	R tibia/fibula	Fall	10
79	0.158	−7.01	1	R proximal femur	Fall	21
80	0.850	−3.8	1	L distal tibia/L proximal fibula	Bumped wall	54
83	0.637	−3.33	1	L proximal femur/R distal femur/L tibia/L fibula	MVA	17

BMD = bone mineral density; L = left; R = right; B = both; ROM = range of motion; MVA = motor vehicle accident; SCI = spinal cord injury

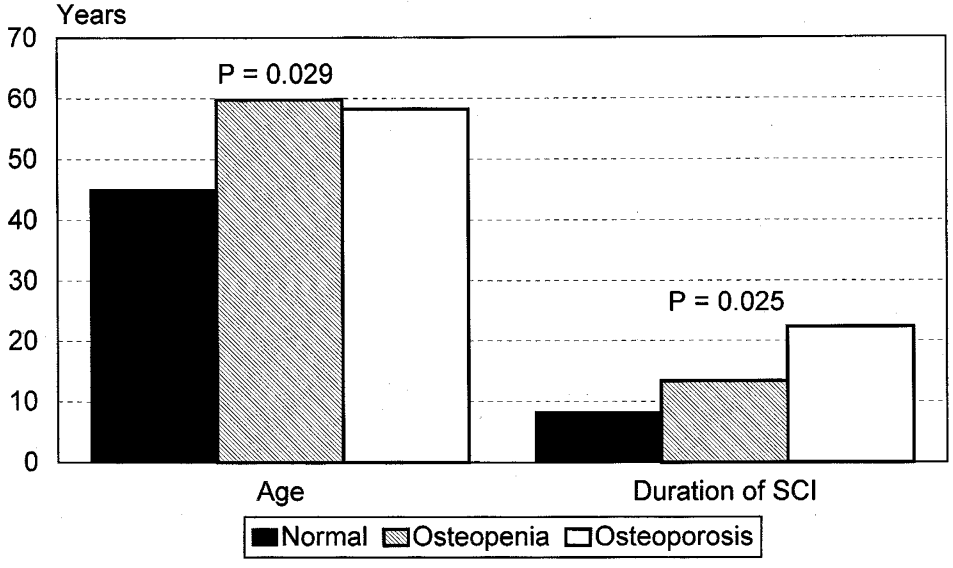

Figure 1 Distribution of BMD groups in terms of mean age and mean duration of SCI

of fractures per patient was: predicted number of fractures = predicted fracture rate per year × SCI duration, where predicted fracture rate per year = exponential (−1.43 − 3.5882 × BMD) (Figure 5).

Table 3 Comparison of fracture and non-fracture groups

	Fracture (n = 14)	*Non-fracture* (n = 27)	P-*value**
Age (years)	61.0 (14.7)	53.3 (12.0)	0.08
SCI duration (years)	24.8 (14.2)	14.3 (12.9)	0.02
BMD	0.50 (0.23)	0.79 (0.20)	0.0002
t-value	−4.4 (1.7)	−2.2 (1.6)	0.0002
ASIA score (%)			
A	78.6	40.7	
B	14.3	25.9	
C	0	11.1	
D	7.1	22.2	0.12
Level of fracture (%)			
Cervical	42.9	59.3	
Thoracic	35.7	22.2	
Lumbar	21.4	18.5	0.57

*Student's *t*-test *P* value reported for continuous variables, Chi square *P* value for categorical variables. Continuous variables summarized by mean (SD)

Table 4 Distribution of BMD by age group

Age (years)	n	*Fracture Mean* (SD)*	n	*No fracture Mean* (SD)*
Less than 50	3	0.39 (0.04)	11	0.90 (0.21)
50 to 61	4	0.45 (0.17)	9	0.73 (0.20)
62 or greater	7	0.58 (0.28)	7	0.69 (0.12)

*Values in table are average BMD (SD) in g/cm^2

Table 5 Distribution of BMD by SCI duration group

SCI duration (years)	n	*Fracture Mean* (SD)*	n	*No fracture Mean* (SD)*
Less than 10	2	0.75 (0.40)	12	0.78 (0.22)
10 to 20	4	0.49 (0.21)	9	0.79 (0.16)
21 or greater	8	0.45 (0.18)	6	0.79 (0.24)

*Values in table are average BMD (SD) in g/cm^2

Discussion

In the past decade, osteoporosis moved from a disease of fractures to a disease of fracture risks.[7,8,10] The advent of bone densitometry provided a means to measure bone mass and quantify fracture risk before a fracture occurred.[7] Prospective studies identified an inverse relationship between BMD and fracture risk, with fracture risk lowest when BMD was highest, increasing 2–3-fold for each standard deviation (SD) decrement in BMD at the spine and hips, and to a lesser extent at the wrist.[7] The predictive value of bone density for the development of fractures was determined to be comparable to that of blood pressure for stroke, and better than that of serum cholesterol for coronary artery disease.[1,11]

The current approach to osteoporosis prevention is selected measurement of BMD in at risk populations.[7,10] Quantification of fracture risk in these

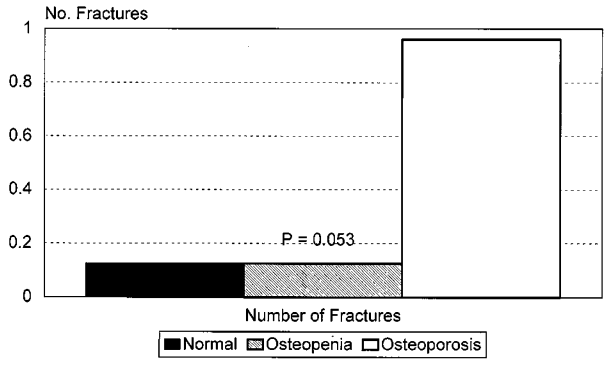

Figure 2 Distribution of BMD groups in terms of mean number of fractures

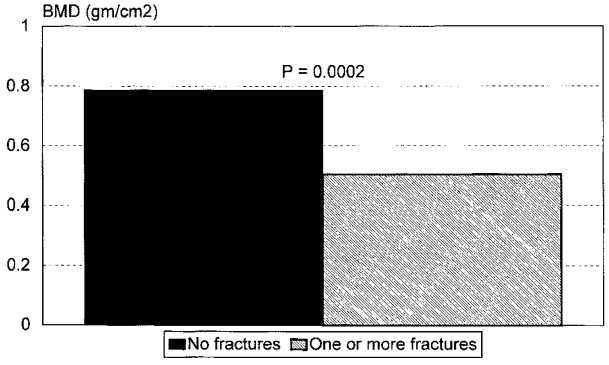

Figure 3 Distribution of fracture groups in terms of mean BMD (g/cm^2)

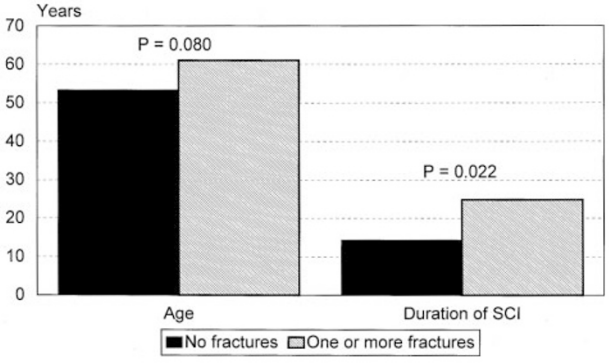

Figure 4 Distribution of fracture groups in terms of mean age and mean duration of SCI

populations is considered to be of value in determining need for treatment.[7] In the general population, postmenopausal women have been determined to be at greatest risk for osteoporotic fractures, with 13% to 18% of women 50 years and older fitting the WHO criteria for osteoporosis, and another 37% to 50% with less than normal BMD.[1] Thus, it is advocated that all postmenopausal women 65 years and above, who have not been previously screened, should

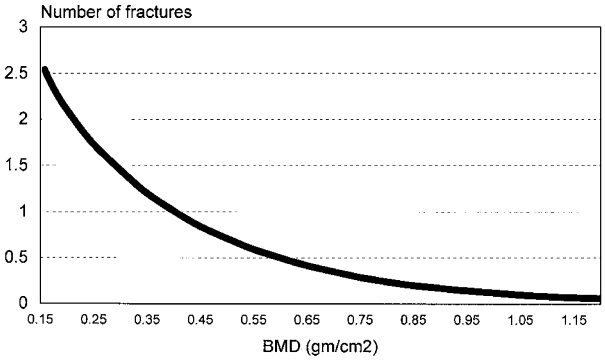

Figure 5 Predicted number of fractures *vs* BMD (g/cm^2), for patient with duration of SCI = 17.5 years

undergo densitometry.[10] Initiating treatment is then recommended for BMD of 2 or more SD below the mean.[1]

The SCI population is also considered at high risk for development of osteoporosis. Within months following injury, decline in BMD is detected in the paralyzed limbs of SCI patients.[4,5] Bone loss then progresses over several months, stabilizing at 12 to 24 months after SCI at values 60% to 70% of normal in the femoral neck, and 40% to 50% of normal in the proximal tibia.[4–6,12] In a cross-sectional study evaluating BMD in SCI, Szollar *et al* reported that bone loss was detectable by densitometry in all age groups by 12 months post-injury, and that decline in BMD reached fracture threshold at 1 to 5 years after SCI.[9] Fracture threshold has been defined in the literature as a BMD of 1 g/cm^2.[13]

The results of our study confirm the prevalence of low bone mass and osteoporosis in the SCI population. Four of every five patients evaluated (80%) had less than normal BMD, 75% of whom fit the WHO criteria for osteoporosis. Patients with osteoporosis were older and had a longer duration of SCI than those patients with normal BMD. This corresponds with previous findings that hip BMD declines with increasing age and time after SCI.[12,14]

This study also shows that BMD in the osteoporosis range by WHO standards may be associated with an increased risk of fractures in the SCI population. Though patients with osteoporosis only showed a trend towards a greater number of fracture events after SCI compared to the normal and osteopenic patients, the limited size of the study population may have affected the outcome. Nevertheless, the frequency of SCI patients with a history of fracture in this study was 34%, which is higher than previous reports in the literature of 1% to 9%.[15–21] Also, almost half of the patients (12 of 25) in the osteoporosis group had at least one fracture event after SCI, and 8% (two of 25) had as many as four fracture events. Furthermore, over 85% of the patients with a history of fracture (12 of 14) were classified in the osteoporosis group, with the average femoral neck BMD of patients with a history of fracture (mean BMD = 0.504 g/cm^2) only 64% that of patients with no fracture history (mean BMD = 0.786 g/cm^2). These BMD values were similar to findings by Garland *et al*. who on evaluating knee BMD in SCI patients, found significant differences between the knee BMD of SCI patients with fractures, 0.5502 ± 0.135 g/cm^2, and SCI patients without fractures, 0.6735 ± 0.163 g/cm^2.[13]

Interestingly, though patients with a history of fracture had a significantly longer duration of SCI compared to those with no fracture history, the difference in age between these two groups was only at trend level. Again, the limited size of the sample in this study may have affected the outcome. However, using logistic regression, age was not found to be a significant factor in determining fracture risk, nor was it found to be significantly predictive of the number of fractures per patient using Poisson regression. Nevertheless, despite the lack of a direct relationship between age and fracture risk in this study, age was noted to play a role in the ability of BMD to accurately predict fracture risk using the logistic regression model. In contrast, 'risk of fracture' has been shown to increase with age independent of BMD in the general population.[8]

Furthermore, this study emphasizes the validity of using BMD for predicting development of fractures in SCI patients. BMD was found to be the only significant predictor of the number of fractures in this group of patients, with each 0.1 g/cm^2 and each unit of *t*-value decrement of BMD at the femoral neck increasing the risk of fracture by a factor of 2.2 and 2.8 times, respectively.

Preventing fractures by preventing and managing osteoporosis is, thus, of clinical importance in the SCI population. However, studies attempting to modify risk factors for osteoporosis in SCI patients have had mixed results.[22–30] Also, it has been recommended that preventive pharmacologic intervention of osteoporosis in SCI patients should begin 1 year post-injury.[31] However, most drugs currently approved for prevention and management of osteoporosis in the general population have not been systematically studied in SCI patients. One of the few studies evaluating pharmacologic management of osteoporosis in SCI patients investigated the use of Tiludronate, a biphosphonate. In this study, two doses of Tiludronate, 200 mg/day and 400 mg/day, were compared to a placebo group. Iliac bone mass was measured through histomorphometric analysis. Results revealed decrease of trabecular bone volume in both the placebo and the 200 mg/day group, while bone volume increased in the 400 mg/day group. These changes in bone volume, however, were not statistically significant.[32]

Clearly, more studies in this field are needed. As osteoporosis is highly prevalent in the SCI population, screening for osteoporosis in SCI patients may be advocated, and treatment recommended based on BMD values obtained. However, attempts to detect

early bone loss in this patient population may be futile unless effective methods to prevent and manage osteoporosis after SCI are found.

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