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ORIGINAL ARTICLE

Reduced hip bone mineral density is related to physical fitness and leg lean mass in ambulatory individuals with chronic stroke

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Abstract Following a stroke, the reduced level of physical activity and functional use of the paretic leg may lead to bone loss and muscle atrophy. These factors and the high incidence of falls may contribute to hip fractures in the stroke population. This study was the first to examine total proximal femur bone mineral content (BMC) and bone mineral density (BMD) and their relationship to stroke-specific impairments in ambulatory individuals with chronic stroke (onset >1 year). We utilized dual-energy X-ray absorptiometry (DXA) to acquire proximal femur and total body scans on 58 (23 women) community-dwelling individuals with chronic stroke. We reported total proximal femur BMC (g) and BMD (g/cm^2) derived from the proximal femur scans, and lean mass (g) and fat mass (g) for each leg derived from the total body scans. Each subject was evaluated for ambulatory capacity (Six-Minute Walk Test), knee extension strength (hand-held dynamometry), physical fitness [maximal oxygen uptake (VO_2max)] and spasticity (Modified Ashworth Scale). Results showed that the paretic leg had significantly lower proximal femur BMD, lean mass and percent lean mass, but higher fat mass than the non-paretic leg for both men and women. Proximal femur BMD of the paretic leg was significantly related to ambulatory capacity ($r=0.33$, $P=0.011$), muscle strength ($r=0.39$, $P=0.002$), physical fitness ($r=0.57$, $P<0.001$), but not related to spasticity ($r=-0.23$, $P=0.080$). Multiple regression analysis showed that lean mass in the paretic leg was a major predictor ($r^2=0.371$, $P<0.001$) of the paretic proximal femur BMD. VO_2max was a significant predictor of both paretic proximal femur BMD ($r^2=0.325$, $P<0.001$) and lean mass in the paretic leg ($r^2=0.700$, $P<0.001$). Further study is required to determine whether increasing physical fitness and lean mass are important to improve hip bone health in chronic stroke.

Keywords Aerobic capacity · Cerebrovascular accident · Osteoporosis · Physical activity · Rehabilitation

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Introduction

Following a stroke, individuals sustain a higher incidence of falls than the reference population [1, 2]. Balance deficits, muscle weakness, poor motor recovery and reduced functional mobility are contributing factors [3, 4, 5]. Following a stroke, the reduction of weight-bearing physical activity and functional use of the paretic lower extremity may lead to other devastating complications, such as osteoporosis and muscle atrophy [6, 7, 8, 9]. Reduction in bone mineral levels and muscle atrophy, coupled with a high incidence of falls, may contribute to the two to four times higher risk of hip fractures in individuals with stroke when compared with the reference population [8, 10, 11].

Stroke was first used as a model of disuse osteoporosis by Prince et al. [12] and Iversen et al. [13]. It is well known that removal of the mechanical stimuli from muscle forces and weight-bearing activity leads to bone loss [13, 14]. Individuals with stroke typically suffer varying extents of motor paralysis on one side of the body (hemiparesis). By comparing the affected and the non-affected limbs, one can study the effects of disuse on bone demineralization while providing appropriate control for the different cofactors (i.e., environmental, genetic), which may affect bone metabolism in different subjects [15].

Ramnemark et al. [16] have previously reported a 12.2% decrease in proximal femur bone mineral density (BMD) on the paretic side within the 1st year following a stroke. A significant 7% decrease in total leg bone mineral content (BMC) and 3% decrease in lean mass of the paretic leg have also been reported at 1 year post-stroke [7]. However, very few studies have examined changes in BMC, BMD and soft tissue composition in the legs beyond 1 year following stroke.

There are several important reasons to investigate bone health and soft tissue composition changes in community-dwelling, ambulatory chronic stroke survivors (onset >1 year). First, most fractures following stroke occur in the chronic stage (median time for first fracture: 2.4 years) [10]. Second, independent ambulators make up a large proportion (80%) of community-dwelling chronic stroke survivors [17]. These individuals may have a higher risk of falls because the majority of falls occur during walking [1]. Third, the percentage of fallers is higher among individuals with stroke who live in the community [2, 18] when compared with both those who live in stroke rehabilitation settings [5, 19] and the older adult reference population [2]. Finally, BMD at various sites at the hip continued to decrease on the paretic side during the second half of the 1st year following stroke despite recovering walking function [7, 16, 20]. It is very possible that bone health may continue to decline beyond the 1st year post-stroke and thus further increase the risk of hip fractures.

Most studies in chronic stroke included relatively small samples of subjects and consisted of individuals with a wide range of capabilities [21, 22, 23]. No study has examined both proximal femur bone mineral levels and soft tissue composition in the lower extremities of community-dwelling, ambulatory individuals with chronic stroke. Further, it is unknown how these parameters relate to various stroke-specific impairments. As bone formation is stimulated by muscle forces [24], lean mass may potentially be an important predictor of proximal femur BMD. In addition, stroke-specific impairments such as reduced ambulatory capacity, leg muscle weakness, physical inactivity and spasticity may also be important predictors. Identification of the stroke-related factors that influence proximal femur BMD and soft tissue composition of the paretic leg may help clinicians devise appropriate treatment to enhance bone health in this group. The purposes of this study were to: (1) compare the total proximal femur BMC and BMD, lean mass and fat mass between the paretic and non-paretic leg in ambulatory individuals with chronic stroke and to healthy reference values and (2) determine the relationship of these parameters to common stroke-specific impairments such as reduced ambulatory capacity, muscle weakness, decreased physical fitness and spasticity. We studied the total proximal femur BMD as it is the best predictor for hip fractures [25, 26].

Materials and methods

Sample size calculation

The computer program G Power was used to calculate the sample size required for multiple regression analyses [27]. If up to six variables were modeled at an effect size =0.35 (large) at an alpha level of 0.05 and power of 0.90, a minimum of 57 subjects are required.

Subjects

Community-dwelling individuals with stroke were recruited on a volunteer basis. All subjects had to fulfill the following inclusion criteria: (1) had one single stroke only, (2) had a post-stroke interval of 1 year or more, (3) were independent in ambulation with or without a walking aid (i.e., no supervision or physical assistance from a person), (4) were 50 years of age or older, and (5) were living at home (not institutionalized). Potential subjects were excluded if they (1) had other neurological conditions in addition to stroke, (2) had significant musculoskeletal conditions (i.e., amputations, total knee or hip replacements), (3) had unstable cardiovascular disease, (4) had a Folstein Mini Mental Status Examination (MMSE) score <22 [28], (5) had any metal implants in the lower extremities or (6) were taking prescribed medications that affect bone metabolism. Eligible subjects gave informed, written consent to participate in the study. Written permission was also obtained from the primary care physician before an individual was accepted into the study. The study was approved by the local hospital and university research ethics committees. The study was conducted according to the Helsinki Declaration for human experiments.

Dual-energy X-ray absorptiometry

All subjects underwent three separate scans on the same day—total body and bilateral proximal femurs using dual-energy X-ray absorptiometry (DXA; Hologic QDR 4500, Hologic Inc., Waltham, Mass.). All scans were performed by the same technician using standard procedures (Hologic Users Manual). In order to maintain the standard position of the legs throughout the scanning procedures, a Velcro strap was placed around the ankles. We reported total proximal femur BMC (g) and BMD (g/cm^2) as the primary outcomes. Lean mass (g) and fat mass (g) of the paretic and non-paretic leg were derived from the total body scan. Percent lean mass of each leg was then calculated [lean mass ×100%/(lean mass + fat mass)]. In terms of the precision of our DXA scanner, the coefficients of variation (CV) for proximal femur BMC and BMD were 0.90% and 0.44%, respectively. The CV for left leg and right leg lean mass as well as left and right leg fat mass were 1.0, 0.7, 3.1 and 2.9%, respectively.

Six-Minute Walk Test

Although the majority of community-dwelling stroke survivors regain the ability to ambulate independently [17], ambulatory capacity is compromised to varying extents in these individuals. Eng et al. [29] have previously reported that functional walk distances in older individuals with chronic stroke were less than 50% of those for the reference population. The reduced ambulatory capacity in these individuals may significantly impact on bone health. The Six-Minute Walk Test (6MWT) was used to assess ambulatory capacity [30]. The total distance walked (meters) was recorded.

Leg muscle strength

Another factor that may influence bone health in stroke is reduced muscle strength. For example, in individuals with chronic stroke, the torque generated by the knee extensors of the paretic side has been reported to be only half of that generated by the non-paretic side [31]. We used hand-held dynamometry (Nicholas MMT, Lafayette Instruments, Lafayette, Ind.) to evaluate isometric knee extension strength. Subjects were instructed to sit upright in a chair with back support. The knee was placed in 90° flexion and subjects were asked to perform a maximal isometric contraction of knee extension. Three trials were performed on each side. The force values obtained (N) in each leg were averaged. Hand-held dynamometry has been shown to be a reliable method to measure leg muscle strength in stroke [32].

Physical fitness

Different subjective or self-report measures have been used to estimate the level of physical activity, which has been related to bone health [33, 34]. In this study, we used a standardized and objective measure, namely maximal oxygen uptake (VO_2max), as an indictor of physical work capacity. VO_2max is accepted as the standard measure of cardiorespiratory fitness (ACSM, 2000) and is associated with the level of habitual physical activity [35, 36]. As low VO_2 max is commonly observed in people with stroke, it may be an important factor in bone health in this group [37].

To measure VO_2max, each subject underwent a maximal cycle ergometer test on the Excalibur cycle ergometer (Lode B.V. Medical Technology, Groningen, The Netherlands). Subjects wore a face mask and oxygen consumption (VO_2) was continuously measured using a portable metabolic unit (Cosmed K4 b^2 system, COSMED Srl, Rome, Italy). A 12-lead electrocardiography system was used to monitor the cardiac activity by a physician (Quark C12, COSMED Srl, Rome, Italy). The testing protocol was dependent upon the capability of the individual [38]. The workload started at 20W with increments of 20 W/min for 27 subjects who were mildly impaired, whereas the workload started at 10 W with increments of 10 W/min for the other 31 subjects who were more severely impaired [35, 38]. Subjects were instructed to pedal at approximately 60 revolutions per minute (rpm). The test was terminated when maximal effort was attained, which was indicated by a respiratory exchange ratio of >1.0 or a plateau in VO_2 (<150 ml/min) and volitional fatigue (decline in cycling rate <30 rpm) [35]. Since the metabolic unit performed breath-by-breath gas analysis, the VO_2 data were averaged at a rate of every 15 s to obtain a more accurate measure of the VO_2max. The maximal value (ml/min) obtained was considered to be the VO_2max.

Spasticity

Increased spasticity is related to a higher degree of asymmetry in walking, characterized by decreased single limb support time of the paretic leg [39] and may thus potentially lead to decreased mechanical loading of the paretic leg. Resistance to passive movements in the paretic foot was evaluated by the Modified Ashworth Scale of Spasticity (0: no increase in muscle tone, 4: affected part rigid in flexion and extension). The Modified Ashworth Scale of Spasticity is a reliable tool to assess muscle tone in individuals with stroke [40].

Statistical analysis

The data from the third National Health and Nutrition Examination Survey (NHANES III) were used as the reference sample to calculate the T-score [41], as recommended by Kanis and Gluer [42]. According to the criterion set by the World Health Organization (WHO), a subject was classified as having osteopenia or osteoporosis if proximal femur BMD was below 1.0 (T-score <-1.0) or 2.5 SD (T-score <-2.5) below the young reference population, respectively [42]. Gender-specific reference data were used to calculate the T-scores, in accordance with the official positions adopted by the International Society for Clinical Densitometry [43]. Data from the NHANES III study were also used to calculate total proximal femur Z-scores, to compare our subjects with the age and gender-matched population [44]. For example, a Z-score of -1 indicates a proximal femur BMD value of 1.0 SD below the age and gender-matched population.

Paired *t* -tests were used to examine whether there were side-to-side differences in proximal femur BMC, BMD, lean mass and fat mass. Normal distribution of different variables was checked by descriptive statistics (e.g., skewness and kurtosis) and visual inspection of histograms. Pearson's moment correlations were used to determine the relationship among the variables that were normally distributed: (1) paretic proximal femur BMC and (2) BMD, (3) lean mass and (4) fat mass in the paretic leg, (5) 6MWT distance, (6) paretic knee extension strength, (7) VO_2max, (8) age and (9) height. Spearman's rho correlations were used for (1) spasticity and (2) post-stroke duration (not normally distributed). A point-biserial correlation coefficient was used to quantify the relationship between gender (a dichotomous variable) (male $=0$, female $=1$) and other variables.

Stepwise multiple regression analyses were performed to identify significant predictors of proximal femur BMD and lean mass on the paretic side. To further examine the relative contribution of lean mass and fat mass to the difference in proximal femur BMD between the two sides, an additional stepwise multiple regression analysis was performed to predict the side-to-side difference in proximal femur BMD, using the side-to-side difference in lean mass and fat mass as predictors. A predictor was entered into the model at $P \leq 0.05$ and was removed at $P > 0.1$. All statistical analyses were performed using SPSS11.5 software (SPSS Inc.) using a significance level of 0.05 (two-tailed).

Results

Subject characteristics

Sixty-three subjects (36 men, 27 women) volunteered to participate in the study. Of these, five (1 man, 4 women) were taking bone resorption inhibitors and were excluded from the study. As a result, data from 58 community-dwelling individuals with chronic stroke were included. Subject characteristics are listed in Table 1. Seventeen subjects used a walking aid (wheeled walker, $n=5$; crutch, $n=1$; quad cane, $n=3$; cane, $n=8$) and nine subjects used an ankle foot orthosis for ambulation. On average, the knee extension strength of the paretic leg was 72.9% of the non-paretic leg.

Table 1 Subject characteristics

Variable	Mean ± SD
Subject demographics	
Gender (male/female)	35/23
Paretic side (left/right)	38/20
Race (White/Asian/Black)	37/20/1
Post-stroke duration (years)	5.6 ± 5.1
Age (years)	65.5 ± 8.8
Mass (kg)	77.7 ± 15.8
Height (cm)	169.3 ± 10.7
Secondary outcome measures	
6MWT distance (m)	312.2 ± 131.5
Knee extension strength (Newtons)	
Paretic leg	188.7 ± 71.3
Non-paretic leg	256.9 ± 86.4
VO_2max (ml/min)	1,372.7 ± 515.9
VO_2max (ml/kg/min)	22.3 ± 4.7
Spasticity (median)	1

Bone mineral levels and soft tissue composition

Proximal femur BMD on the paretic side was significantly lower than on the non-paretic side for both male and female subjects (Table 2). A similar trend exists for proximal femur BMC, but the difference was not

Table 2 Comparison between paretic leg and non-paretic leg. Δ: difference. *CI* confidence interval

Variable	Paretic leg	Non-paretic leg	Δ between legs (95%CI)	*P*	Percent Δ between legs
Proximal femur BMC, g					
Male	40.805 ± 9.005	41.619 ± 7.952	−0.882 (−2.08,0.323)	0.146	−2.3
Female	24.271 ± 6.117	25.095 ± 5.578	−0.824 (−1.716, 0.068)	0.069	−3.6
Proximal femur BMD, g/cm^2					
Male	0.91 ± 0.14	0.95 ± 0.11	−0.033 (−0.051, −0.014)	0.001	−3.7
Female	0.76 ± 0.16	0.80 ± 0.15	−0.037 (−0.062, −0.012)	0.005	−4.8
Lean mass, g					
Male	9,076.63 ± 1,552.03	9,550.73 ± 1,307.98	−474.10 (−696.89, −251.30)	< 0.001	−5.2
Female	6,080.19 ± 1,155.48	6,354.75 ± 1,251.30	−274.55 (−469.69, −79.42)	0.008	−4.0
Fat mass, g					
Male	3,038.75 ± 1,385.38	2,959.30 ± 1,411.94	79.44 (4.66, 154.22)	0.038	3.6
Female	4,349.81 ± 1,384.83	4,229.17 ± 1,430.18	120.64 (31.80, 209.49)	0.010	3.8
Percent lean mass, %					
Male	75.53 ± 5.96	77.08 ± 5.77	−1.55 (−2.30, −0.796)	< 0.001	−2.0
Female	59.15 ± 6.73	60.98 ± 6.84	−1.82 (−2.84, −0.80)	0.001	−2.9

statistically significant. The distribution of proximal femur BMD T-scores for both legs is illustrated in Fig. 1. In the paretic proximal femur, 52 and 17% of female subjects met the criteria for osteopenia and osteoporosis, respectively. The corresponding values for the non-paretic side were 65 and 4%. The proportion of male subjects with osteoporosis was lower. Only two men (6%) had osteoporosis on the paretic side compared to none on the non-paretic side. A large percentage of male subjects had osteopenia, however. Osteopenia was present in 43 and 40% of male subjects in the paretic and non-paretic proximal femur, respectively.

The Z-score distribution is shown in Fig. 2. Approximately 26% of women and 26% of men had a Z-score <-1 in the paretic proximal femur (Fig. 2a). A lower percentage of women (13%) and men (9%) had a Z-score <-1 in the non-paretic proximal femur (Fig. 2b).

Soft tissue composition was also significantly different between the two legs. Both lean mass and percent lean mass were significantly lower in the paretic leg than in the non-paretic leg for both male and female subjects. In contrast, fat mass was significantly higher in the paretic leg than in the non-paretic leg (Table 2).

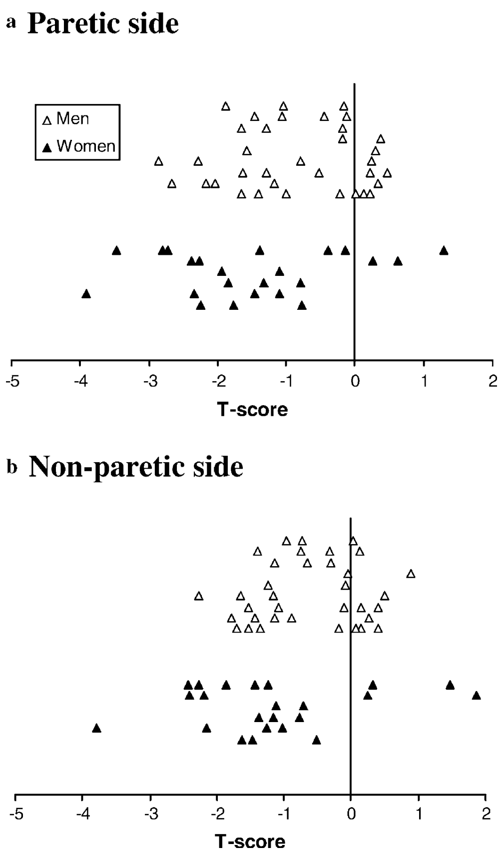

Fig. 1 Distribution of proximal femur T-scores. Proximal femur T-scores for the (**a**) paretic side and (**b**) the non-paretic side were indicated by *open triangles* (men) and *solid triangles* (women). Each *triangle* represents a single subject

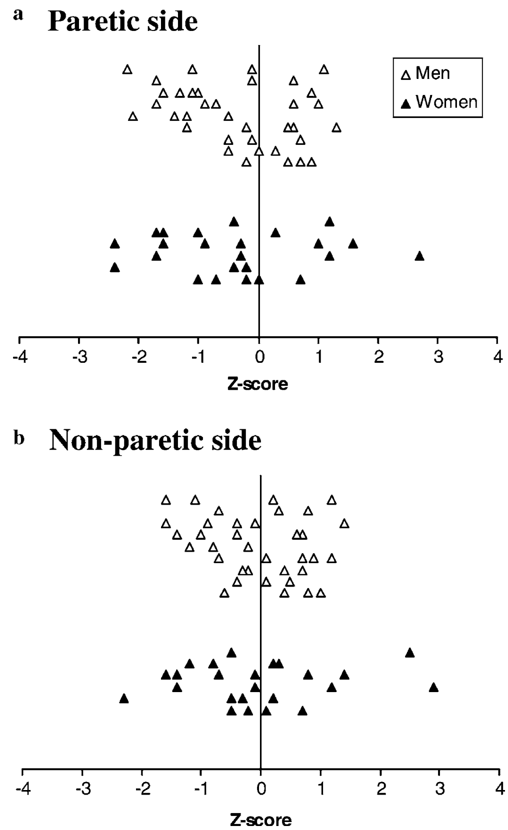

Fig. 2 Distribution of proximal femur Z-scores. Proximal femur Z-scores for the (**a**) paretic side and (**b**) the non-paretic side were indicated by *open triangles* (men), and *solid triangles* (women). Each *triangle* represents a single subject

In general, the side-to-side differences in bone mineral level and soft tissue composition were consistent across ethnicities. In both, Caucasian ($n=37$) and Asian subjects ($n=20$), significantly lower proximal femur BMD (Caucasian: $P=0.014$; Asian: $P<0.001$), lean mass (Caucasian: $P=0.007$, Asian: $P<0.001$) and percent lean mass (Caucasian: $P=0.002$; Asian: $P<0.001$), but higher fat mass (Caucasian: $P=0.007$; Asian: $P=0.010$) were obtained in the paretic leg when compared with the non-paretic leg. The side-to-side difference in proximal femur BMC was significantly different in Asian subjects ($P=0.004$), but not in Caucasian subjects ($P=0.597$).

Influence of stroke-specific impairments on bone mineral levels and soft tissue composition

Proximal femur BMD on the paretic side was significantly correlated with height, gender, paretic leg lean mass, knee extension strength, 6MWT distance and VO_2max (Table 3), and these factors were used as the independent variables in the first stepwise multiple regression model. Although age is related to hip BMD in healthy older adults [41, 44, 45], it was not included in the model due to a non-significant pair-wise correlation.

Table 3 Correlations with proximal femur BMC, BMD, lean mass and fat mass of the paretic leg

Variables	Proximal femur BMC	Proximal femur BMD	Lean mass	Fat mass
Demographics/soft tissue composition				
Height	0.77**	0.52**	0.82**	−0.22
Post-stroke duration	0.01	0.04	−0.02	0.17
Age	−0.01	−0.11	−0.14	−0.17
Gender	−0.72**	−0.47**	−0.73**	0.43**
Lean mass	0.78**	0.61**	-	0.01
Fat mass	−0.03	0.17	0.01	-
Stroke-related impairments				
Ambulatory capacity (6-min walk test)	0.25	0.33*	0.22	−0.04
Muscle strength (paretic knee extension)	0.41**	0.39**	0.50**	−0.05
Physical fitness (VO_2max)	0.69**	0.57**	0.84**	−0.05
Spasticity (Modified Ashworth Scale)	−0.21	−0.23	−0.21	0.05

**$P < 0.005$

Results showed that paretic leg lean mass was the only significant predictor of proximal femur BMD on the paretic side, accounting for 37.1% of its variance [$F(1,56) = 32.991$, $P < 0.001$] (Table 4, model 1). Height, gender, 6MWT distance, knee extension strength and VO_2max were excluded from the stepwise regression model ($P > 0.1$).

Because of the significant relationships of lean mass to knee extension strength ($r = 0.50$, $P < 0.001$) and VO_2max ($r = 0.84$, $P < 0.001$), there is the potential that the regression procedure may have removed these factors from the model because of their close relationship to the best predictor (lean mass). Thus, in the second stepwise regression model, the same variables in model 1 were entered except paretic leg lean mass (Table 4, model 2). In this model, VO_2max was the only significant predictor of paretic proximal femur BMD, accounting for 32.5% of the variance [$F(1,56) = 26.926$, $P < 0.001$]. Height, gender, 6MWT distance and knee extension strength were removed from this model ($P > 0.1$).

The third regression model was used to predict lean mass based on its significant correlations with height, gender, knee extension strength and VO_2max (Table 3). VO_2max and height were significant predictors of lean mass in the paretic leg, with VO_2max accounting for 70.0% of its variance (Table 4, model 3). Adding height to the model accounted for an additional 9.4% of the variance in paretic leg lean mass [$F(2,55) = 105.828$, $P < 0.001$]. Gender and knee extension strength were removed from the regression model ($P > 0.1$). Regarding fat mass in the paretic leg, it was significantly correlated with gender only (Table 3) and hence no multiple regression analysis was performed.

In the last regression model, we used the side-to-side difference in lean mass and fat mass to predict the side-to-side difference in paretic proximal femur BMD (Table 4, model 4). Side-to-side difference in lean mass, but not side-to-side difference in fat mass, was a significant predictor of side-to-side difference in paretic proximal femur BMD, accounting for 9.9% of its variance [$F(1,56) = 6.161$, $P = 0.016$].

Discussion

Comparison with the reference population

Our data showed that many individuals with chronic stroke had osteopenia or osteoporosis in the proximal femur, with a higher degree of bone loss in the paretic leg (Fig. 1). It may be related to the preferential use of the non-paretic leg during functional activities. For example, it is common that more weight is borne by the non-paretic leg during standing or walking activities in individuals with stroke [46, 47]. A substantial proportion of our subjects also had low proximal femur BMD values when compared to the age- and gender-matched population (Fig. 2). The results indicate that stroke has a major impact on bone health.

Table 4 Multiple regression analyses for predicting proximal femur BMD and lean mass of the paretic leg

Dependent variable	Predictors	r^2	r^2 change	β	P for each predictor
1. Proximal femur BMD[a]	Paretic leg lean mass	0.371	0.371	0.609	< 0.001
2. Proximal femur BMD[b]	VO_2max	0.325	0.325	0.570	< 0.001
3. Paretic leg lean mass[c]	VO_2max	0.700	0.700	0.507	< 0.001
	Height	0.794	0.094	0.450	< 0.001
4. Side-to-side difference in proximal femur BMD[d]	Side-to-side difference in lean mass	0.099	0.099	0.315	0.016

[a]Excluded variables: height, gender, 6MWT distance, paretic knee extension strength, VO_2max; [b]excluded variables: height, gender, 6MWT distance, paretic knee extension strength; [c]excluded variables: gender, paretic knee extension strength; [d]excluded variable: side-to-side difference in fat mass

Lower hip BMD is associated with a higher risk of hip fracture. An individual with a T-score of −1 SD at the hip would have a 2.6-fold higher relative risk of hip fracture [42, 48]. Based on the prevalence of osteopenia and osteoporosis in the proximal femur on the paretic side (Fig. 1), 43% of men and 52% of women would have at least a 2.6-fold increase in hip fracture risk (osteopenia; T-score between −1.0 and −2.5). An additional 6% of men and 17% of women would have a greater than 10-fold ($2.6^{2.5}$) increase in hip fracture risk (osteoporosis; T-score <2.5) [42]. However, the actual risk of hip fractures would presumably be much higher due to the presence of additional risk factors such as a high incidence of falls [19] and physical impairments (i.e., poor balance, reduced motor control) [3, 4, 5]. This is of particular concern on the paretic side, because proximal femur BMD is lower in the paretic leg (Table 2), and the majority of fractures occur on the paretic side [11, 49].

Side-to-side differences in bone mineral levels and soft tissue composition

Previous studies in stroke patients have reported a 1.3–8.8% side-to-side difference in BMD at various sites in the legs [15, 16, 20, 22, 23, 50, 51, 52]. However, comparison with other studies is extremely difficult for several reasons. First, these studies reported data from patients in different stages of stroke recovery such as acute [22], subacute [15, 23, 50, 51], and chronic [15, 50]. Second, many studies included subjects who were non-ambulatory [16, 20, 22, 51, 52]. Third, BMD was measured at different sites in the lower extremity in different studies such as the femoral neck [15, 20, 51, 52], trochanter [20], proximal femur [16], total femur [16], first metatarsus [21] and whole leg [6, 50]. This is the first study to examine total proximal femur BMC and BMD in community-dwelling, independent ambulators with chronic stroke.

Overall, we found a 4.1% side-to-side difference in proximal femur BMD (Table 2). This is in contrast to previous studies in healthy subjects, which found no significant (0.1–1.5%) side-to-side difference in proximal femur BMD [53, 54]. Stroke-related impairments thus have considerable impact on bone health in the paretic leg.

Our results showed a significant 4.7% side-to-side difference in lean mass, indicating muscle atrophy in the paretic leg. This finding is comparable to those found by Ryan et al. [55] (3.5%; post-stroke duration = 3 years) and Iversen et al. [6] (5.4%; post-stroke duration = 23–38 weeks). We also found that the paretic leg had a significant 3.7% greater fat mass when compared with the non-paretic leg. In contrast, no significant change in fat mass at 1 year post-stroke was reported in a previous study [7]. Nevertheless, our results lend support to the findings by Ryan et al. [55], who used computed tomography to demonstrate that in individuals with chronic stroke, there was increased fat content in and around the muscle fibers in the paretic leg. The observed soft tissue composition changes in the paretic leg (i.e., muscle atrophy, increased fat content) may be a function of the reduced fitness level secondary to a sedentary lifestyle following stroke [55] and reduced weight-bearing during daily functional activities [46, 47].

Influence of stroke-specific impairments

Paretic leg lean mass was the most significant predictor of total proximal femur BMD on the paretic side. Moreover, the side-to-side difference in paretic leg lean mass was also the best predictor of side-to-side difference in proximal femur BMD. This muscle-bone relationship has been found in other populations, such as post-menopausal women [56], middle-aged [57] and older adults [58, 59]. Our results thus suggested that increasing or maintaining muscle mass in the paretic leg may have a protective effect on proximal femur bone health in individuals with chronic stroke.

It has been previously reported that VO_2max is a major predictor of proximal femur BMD in elderly women [60]. We identified VO_2max as a strong determinant of both the paretic proximal femur BMD and paretic leg lean mass in older individuals with chronic stroke. Reduction in VO_2max is related to decreased habitual physical activity in healthy populations [36]. Our finding thus highlights the importance of physical activity and fitness on muscle and bone health in individuals with stroke. Low VO_2max is common following stroke [37], and the mean VO_2max value obtained in this study was only at the 10th percentile of the age-matched healthy population for both men and women [35]. The observed low fitness level reflects a sedentary lifestyle or decreased physical activity level, despite that all subjects are independent in ambulation. Reduced physical activity, when coupled with the preferential use of the non-paretic side for weight-bearing [46, 47], may explain the more compromised bone and muscle health status in the paretic leg when compared with the non-paretic leg.

Ambulation has been identified as a significant determinant of hip BMD in older adults [59]. The importance of ambulatory ability on bone and muscle health in stroke was shown by Jorgensen et al. [20], who reported that those who stayed wheelchair bound at 1 year post-stroke had a 13% reduction in femoral neck BMD on the paretic side, whereas those who relearned to walk at 2 months only had an 8% decrease of the same. Another study in stroke showed that those who relearned to walk at 2 months post-stroke had no significant reduction of lean mass on the paretic side at 1 year post-stroke [7]. In contrast, those who remained non-ambulatory at 2 months lost 5–6% of lean mass on the paretic side at 1 year [7].

Our results, however, showed that ambulatory capacity (6MWT distance) only had a low correlation with proximal femur BMD on the paretic side ($r = 0.33$)

and had no significant correlation with paretic leg lean mass ($r = 0.22$). The difference in results may be due to several reasons. First, all of our subjects were independent ambulators, whereas the subjects in their study included those who were non-ambulatory or who required physical assistance by another person. Second, different outcome measures were used to indicate ambulatory capacity. The Functional Ambulation Category (FAC) was used in their study to classify the level of ambulatory independence based on the amount of human assistance needed (1 = wheelchair bound; 6 = independent on both level and uneven surfaces), whereas we used the 6MWT to measure walking distance. Lastly, the stronger determinant of VO_2max may have reduced the effect of the 6MWT distance in the model. Improvement in VO_2max is related to the interactions among factors such as frequency, duration and intensity of physical activities [35]. A longer distance walked during the 6MWT does not necessarily mean that an individual regularly participates in activities at a level sufficient to induce an increase in VO_2max.

Previous studies in older adults have found a positive correlation between leg muscle strength and hip BMD [58, 61]. Our results have demonstrated a similar relationship between muscle strength and hip BMD in stroke ($r = 0.39$). This is in agreement with a previous study in patients with subacute stroke (mean onset = 63 days), which showed a significant relationship between femoral neck BMD loss and degree of motor paralysis in the leg ($r = -0.41$) [52]. Overall, the results again point to the importance of muscle health on hip BMD.

Our results only showed a trend for a negative relationship between spasticity and paretic proximal femur BMD, but it did not reach statistical significance ($r = -0.23$, $P = 0.080$). A simple explanation is that our study may have been insufficiently powered to detect a significant relationship. However, the effects of spasticity on hip BMD may be quite complex. Spasticity is related to reduced walking velocity [29] in individuals with stroke, which would in turn cause a reduction in the peak ground reaction force [62]. Moreover, those with more severe spasticity tend to walk with more asymmetry, resulting in a reduced single limb support time of the paretic leg [39]. These factors presumably would reduce the amount of mechanical loading on the paretic leg and may lead to more bone loss. However, the tonic muscle activity due to spasticity may help preserve muscle mass and provide some mechanical loading to the bone. The complex relationships among spasticity, bone mineral level and muscle mass have been demonstrated in patients with spinal cord injury [63]. While muscle mass was better preserved in spinal cord injured patients with spastic paralysis than those with flaccid paralysis, longitudinal changes in BMC were not different between the two groups of patients [63]. The lack of a significant relationship between hip BMD and spasticity reported in our study is also consistent with the study by Jorgensen and Jacobsen [7], who found no significant relationship between spasticity and 1-year changes in total leg BMC in individuals with stroke.

Age was not significantly correlated with proximal femur BMD, in contrast to the healthy population [41, 44, 45]. In addition, post-stroke duration was also not related to proximal femur BMD. These findings indicate that the severity of stroke took precedence over the effects of age and post-stroke duration on proximal femur BMD. It is noteworthy that 20 of our subjects were of Asian ethnicity. However, this should not affect the interpretation of our results. We found that side-to-side differences in BMD and soft tissue composition measures were consistent across ethnicities. Previous studies have shown that most differences in BMC and BMD between Asian and Caucasian populations could be accounted for by body size (i.e., height) rather than true ethnic differences [64, 65]. The prevalence of osteoporosis in older Asian women is also comparable to that in the Caucasian reference [66].

Clinical implications

This study has important clinical implications for stroke rehabilitation. First, a substantial proportion of subjects have osteoporosis in the paretic leg. The prevalence of osteopenia also tends to be high. Osteopenia itself does not result in fractures [67]. However, the departure from healthy BMD values, when coupled with the presence of physical impairments and high incidence of falls, would increase traumatic fractures [67]. Second, given that improving physical fitness (VO_2max) is a strong predictor of paretic proximal femur BMD and lean mass of the paretic leg, physical activities and exercises should be promoted to improve muscle and bone health in the lower extremities. A 6-month resistive training program has been shown to increase muscle mass and improve BMD in the femoral region in healthy young and older adults [68]. The beneficial effects of resistive or aerobic exercises on bone health in the femoral region have been reported in other studies [68, 69, 70, 71, 72]. So far, no study has been conducted to examine the effects of different forms of exercise training on bone health and soft tissue composition in individuals with stroke. Future research is urgently needed in this important area.

Limitations

DXA was used to measure BMC, BMD and soft tissue composition in this study. This technique has its own limitations. Due to its planar nature, DXA is not able to assess the true composition and geometry of bone. Areal BMD only partially corrects for the bone size and therefore tends to overestimate the sex-specific differences due to the larger skeletons in men [74]. In spite of its limitations, DXA remains the most common method of evaluating bone mineral status. Areal BMD is used to diagnose osteoporosis and to predict fracture risk [42]. Reproducibility of DXA in individuals with stroke has also been demonstrated [75].

Lean mass measured by DXA is sensitive to changes in hydration [76]. Edema in stroke patients, if present, is most commonly seen on the paretic side [77]. Overestimation of muscle mass in the paretic leg may occur as a result. Our data showed that the paretic leg had a significantly lower lean mass than the non-paretic leg. Therefore, this potential artifact would not explain our results. Fat mass has also been shown to overestimate BMC [78]. Again, this possible artifact should not affect the interpretation of our results because the paretic leg, with its higher fat mass, still had a lower proximal femur BMC than the non-paretic leg.

Conclusion

This is the first paper to show that many older individuals with chronic stroke have low bone mineral levels in the proximal femur although they were able to ambulate without supervision or physical assistance. Muscle atrophy was also apparent in the paretic leg. We have thus highlighted the potential importance of physical activity and exercise for improving muscle and bone health in the lower extremities of individuals with chronic stroke.

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