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Title:

Relationship between nutritional factors and hip bone density in individuals with chronic stroke

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Abstract

The aim of this study was to investigate the relationship between dietary habits and hip bone health in community-dwelling individuals with chronic stroke. The usual dietary intake of 94 individuals with chronic stroke (30 women, mean age: 59.0 years) was assessed by a 3-day food record within a single week. Dual-energy X-ray absorptiometry was used to measure bone mineral density (BMD) at both hips. The results showed that low hip bone mass was found in 59 and 50 of the participants on the affected and unaffected side respectively. The mean hip BMD was also significantly lower on the affected side than the unaffected side ($P<0.001$). The intake of total fat, carbohydrates, calcium, magnesium, iron, zinc, fiber, folic acid, vitamin B1, B2, B3, B6, C, and K was significantly lower than the respective recommended daily intake values ($P<0.05$). Multiple regression analyses revealed that after adjusting for the effects of age, sex, body mass index, post-stroke duration, side of paresis, motor impairment, physical activity level, walking endurance, total calories intake and total number of medications, intake of protein, fiber, and magnesium remained significantly associated with hip T-score on the affected side, accounting for 4.2%, 4.4%, and 3.2% of the variance respectively. On the other hand, intake of protein and fiber were independently associated with hip T-score on the unaffected side, explaining 2.7% and 5.2% of the variance respectively. The results highlighted the potential relevance of diet modification in maintaining bone health post-stroke, which would require further study.

Keywords:

Osteoporosis; nutrition; cerebrovascular accident; diet; bone mineral density

Introduction

Stroke is one of the most prevalent disabling conditions. A common complication post-stroke is fragility fracture, which could result in increased morbidity and mortality [1,2]. On average, the risk of fracture in stroke patients is approximately 2 to 4 fold higher than that in aged-matched able-bodied individuals [2]. Post-stroke fracture is thus a very serious health concern.

Increasing research effort has been directed toward post-stroke bone health in the past decade. A number of studies have shown an accelerated reduction in bone mineral density (BMD) after the onset of stroke, particularly on the affected (paretic) side [1]. This post-stroke bone change is also considered as a major factor contributing to the increased risk of fragility fracture in this patient population, besides frequent falls [3]. Physiologically, the decline in BMD among stroke patients has been associated with increased bone resorption rate and abnormal calcium metabolism as evidenced by an increased serum level of calcium and bone resorption markers [4].

Many factors may influence bone health post-stroke, including genetic, hormonal, behavioral, mechanical and nutritional risk factors [5,6]. Among all these, mechanical and nutritional factors are highly modifiable and may be the key targets of intervention for optimizing bone health post-stroke. Mechanical factors have been quite well studied. Generalized skeletal unloading from increased bed rest and impaired mobility status, muscle atrophy and weakness have been shown to be associated with compromised bone mass among individuals with stroke [1].

After a stroke, changes in functional status, mental health, and even swallowing function may affect dietary habits and hence nutritional intake. Studying the relationship between nutritional factors and bone health post-stroke is thus clinically relevant. Evidence has shown the correlation of calcium, Vitamin D, Vitamin K, and Vitamin C with BMD, especially among post-menopausal women [6-8]. Surprisingly, in contrast to the mechanical factors, the relationship between nutritional factors and BMD in the stroke population is extremely understudied.

Only a few studies have examined the phenomenon of vitamin D and K deficiency and its influence on bone health in the stroke population [9-11]. The evidence rated to the relationship between vitamin D and bone health post-stroke is inconclusive. Sato et al. [10] showed that the sunlight-exposed group had much better outcomes in metacarpal BMD and 25-hydroxyvitamin D (25(OH)D) level and lower hip fracture rate than the sunlight-deprived group, although the National Health and Nutritional Examination Survey (NHANES) study showed that serum 25(OH)D level was not significantly associated with BMD among stroke patients, after adjusting for other confounding factors. Sato et al [9] was the only study that examined the role of vitamin K in post-stroke bone health and found that BMD of the second metacarpal was associated with serum vitamin K levels in people with stroke. However, the influence of other nutritional factors on bone health among individuals with stroke has been largely ignored in research.

To fill the knowledge gap in this field, the current study was undertaken to investigate the relationship between dietary habits and hip bone health in community-dwelling individuals with chronic stroke.

Methods

Study design

This was a cross-sectional exploratory study. All participants in the stroke group were required to attend two separate assessment sessions. In the first session, apart from demographic data, participants were evaluated for physical functioning. They were also taught how to use the 3-day food record. The BMD testing took place in the second session, which was held within two weeks after the first session.

Participants

A sample of individuals with stroke was recruited from the community by advertising the study in a local university and stroke patient self-help groups. The inclusion criteria were: diagnosis of stroke, stroke onset more than 3 months, living at home, 18 years old or above, and able to understand simple verbal commands. The exclusion criteria were: other coexisting neurological disorders, or unstable medical conditions, or were taking medications for treatment of osteoporosis.

Measurements

Demographics data and participant interviews: Body weight (kg) and standing height (m) were recorded (Health O Meter, Alsip, IL) to enable us to compute the body mass index (BMI in kg/m^2). Information on clinical and personal factors such as age, gender, medications, menopausal status and sunlight exposure (average number of hours per day) was acquired by face-to-face interviews.

Dietary intake: Usual dietary intake of all participants was assessed by a 3-day food record (2 days of weekday and 1 day of weekend) within a single week. This is a validated dietary assessment tool for elderly population [12] and its reproducibility has been established [13]. Participants were advised to choose typical days for recording. Participants were taught how to use 3-day food record to document their food intake in detail for the 3 days. After the receipt of the completed document via mail, the information recorded was rechecked by conducting individual telephone interview of each participant by the same assessor who was well trained by an experienced dietitian. The additional food or snacks consumed between meals, portion sizes for the food taken and supplement consumption (e.g. vitamin D and calcium) were also checked. The verified information was analyzed by computer software (Food Processor SQL version 9.8, ESHA, USA) by an experienced dietitian. Mean daily intake of all macronutrient and micronutrients, as well as the total energy (kcal/day), were calculated.

Hip bone density: Dual-energy X-ray absorptiometry (DXA; Hologic Inc., Bedford, MA) was used to scan the hip on each side. The hip region was chosen because it is the most common site of fracture among stroke survivors [3] and is often used for diagnosing osteoporosis [14]. All DXA scans were performed by the same technician with more than 5 years of experience. Each hip scan automatically generated several variables including hip bone mineral content (BMC, in g), BMD (in g/cm^2), T-score and Z-score.

Self-perceived change in dietary habit: Self-perceived change in dietary habit after the onset of stroke was measured by the Global Rating of Change score (GRC: 0-10). A higher score was indicative of a greater change. (0: no change in the dietary pattern at all; 10: dietary pattern was totally different after stroke)[14]. Besides, the specifics of dietary habit changes were asked (e.g., eating less or more). The GRC scale offers a flexible, quick, and simple method of self-assessed rating of their change in condition in clinical settings [14].

Physical activity level: The Physical Activity Scale for the Elderly (PASE) questionnaire was used to estimate the physical activity level [15]. The questionnaire consists of 10 items to assess the physical activities of different intensities for the previous 7 days, with a possible score range from 0 to 400. A higher PASE score is indicative of a higher physical activity level. PASE has been shown to have good test-retest reliability and validity [15].

Motor impairment: The severity of motor impairment in the affected lower limb was measured by the Chedoke-McMaster Stroke Assessment (CMSA)[16]. The leg and foot were evaluated by a 7-point scale, with a higher score indicating better motor recovery. The scores of the leg and foot were summed to yield a composite score (possible score range: 2-14). CMSA has good reliability and validity for measurement of motor recovery in stroke patients [16].

Walking endurance: The Six Minute Walk Test (6MWT) was administered. Participants were instructed to "walk as far as possible in an enclosed corridor over 6 minutes" and the walking distance covered in the 6 minutes was measured. 6MWT has good test-retest reliability among individuals with stroke (ICC=0.99) [17].

Sample size calculation

Sample size estimation was made based on an alpha of 0.05 and power of 0.8. To detect a significant association between 4 nutritional variables of interest and hip BMD after accounting for 10 other relevant factors (age, gender, body mass index, post-stroke duration, side of paresis, motor impairment, physical activity level, walking endurance, total calories intake and total number of medications) (medium effect size $f^2=0.15$), a minimum sample size of 94 individuals with stroke would be required.

Statistical analysis

Data analysis was performed by using PASW Statistic 18.0 (SPSS Inc., Chicago, IL) and the level of significance was set at $p<0.05$ (two-tailed) unless otherwise stated. Paired t-test was used to compare the hip BMD and T-score between the affected and unaffected sides. One sample t-test was used to compare the T-score and Z-score from 0 (i.e., the mean of the respective reference population).

One-sample t-tests were used to compare the mean value of each nutritional variable with the recommended daily intake value provided by the Chinese Dietary Reference Intakes (Chinese DRI 2014) [18]. If a particular nutritional variable is not listed in the Chinese Dietary Reference Intake document, the recommended value provided by the United States Dietary Reference Intake (US DRI 2010) would be used for comparison [19]. Pearson correlation coefficient (r) was used for preliminary analysis to examine the bivariate association between hip T-score on each side (dependent variables) and the nutritional variables. Those variables that yielded a p value <0.10 in bivariate correlation analysis were then entered into the hierarchical regression model, after accounting for the effects of age, gender, BMI, post-stroke duration, side of paresis, PASE score, CMSA score, 6MWT distance, and total number of medications. Total calories intake was also entered as a covariate to assess the effects of diet composition independent of energy intake. To avoid multicollinearity, bivariate correlations among the nutritional variables were checked. If moderate or high correlations were found, separate regression models would be used to predict hip T-score.

Results

Characteristics of participants

Ninety-five individuals with stroke (65 men, 30 women) were enrolled in the study. One of the participants withdrew from the study because he returned to England for living after the bone scan, and was thus unable to complete the 3-day food record. Complete data sets of 94 stroke patients were used for subsequent analysis.

The characteristics of the participants are displayed in Table 1. There was no significant difference between the proportion of participants with left-sided paresis (58.5%) and those with right-sided paresis (41.5%)(Chi-square=2.723, p=0.099). Overall, the lower limb function was moderately impaired, as indicated by the CMSA score (mean=8.3, SD= 2.5). The physical activity level (mean PASE score=88.3, SD=61.0) was low, compared with able-bodied individuals of similar age previously reported by Chad et al. (men: mean=154.3, SD=80.4; women: mean=137.9, SD=76.7) [20].

Hip bone health profile

Total hip BMC, BMD, T-score and Z-score on the affected side were significantly lower than the corresponding values on the unaffected side ($p<0.001$) (Table 1). The proportion of individuals with osteoporosis on the affected side nearly doubled that on the unaffected side. The Z-score on the affected side (-0.565) was also significantly different from zero ($p<0.001$), indicating that the mean hip BMD value in the affected leg was significantly lower than that of the age-matched reference database.

Nutritional status

Three participants required their family member who lived with them to complete the 3-day food record because of the communication problems arising from expressive dysphasia. Two participants required meals service from a non-governmental organization because they were unable to prepare the meals by themselves. The results of the 3-day food record are displayed in Table 2. The mean intake of carbohydrates, calcium, iron, magnesium, zinc, Vitamin B1, Vitamin B2, Vitamin B3, Vitamin C, Vitamin K, folic acid and fiber was lower than the recommended intake ($p<0.05$). The mean intake of total fat, protein and sodium, on the other hand, was higher than the corresponding recommended intake values ($p<0.001$).

Self-perceived dietary habit changes

The mean GRC score was 4.7 (SD=2.5). The three most frequent changes in dietary habit reported were reduction in fatty food intake (41.5%), total amount of food consumption (38.3%) and salty food intake (19.1%) (Table 3).

Associations between nutritional factors and bone health

Based on the results of the bivariate correlation analysis, only the intake of protein ($r=0.224$; $p=0.030$), magnesium ($r=0.238$; $p=0.021$), fiber ($r=0.260$; $p=0.011$) and sunlight exposure ($r=0.209$; $p=0.043$) were selected as independent variables in subsequent multivariate regression analysis to predict hip T-score on the affected side. On the other hand, the intake of protein ($r=0.195$; $p=0.060$), fiber ($r=0.266$, $p=0.010$), iron ($r=0.186$, $p=0.073$), magnesium ($r=0.196$, $p=0.059$), and sunlight exposure ($r=0.238$; $p=0.021$) were used for multivariate regression analysis to predict the hip T-score on the non-paretic side. To avoid multicollinearity, correlations among these nutritional factors were checked. It was found that magnesium had a strong correlation with protein ($r=0.77$, $p<0.001$) and moderate correlation with fiber ($r=0.46$, $p<0.001$) and iron intake ($r=0.577$; $p<0.001$). Therefore, magnesium was entered into a separate regression model. After adjusting for the effects of age, gender, BMI, post-stroke duration, side of paresis, PASE score, CMSA score, 6WMT distance, total calories intake, and total number of medications, the intake of protein and fiber (Table 4, model 1), and magnesium (Table 4, model 2) remained independently associated with T-score of the hip on the affected side ($p<0.05$), accounting for 4.2%, 4.4%, and 3.2% of the variance, respectively. Overall, the two models explained a total of 42.9% (Table 4, model 1) and 37.4% (Table 4, model 2) of the variance in hip T-score on the affected side respectively. The association of sunlight exposure with hip T-score on the affected side was not significant after adjusting for the effects of other factors.

On the unaffected side (Table 5, model 1), the intake of protein ($p=0.021$) and fiber ($p=0.006$) was independently associated with the hip T-score after adjusting for the effects of potential confounders, and accounted for 2.7% and 5.2% of its variance respectively. This model accounted a total of 48.2% of the variance in non-paretic hip T-score. Intake of magnesium, on the other hand, was no longer significantly associated with the hip T-score on the unaffected side in multivariate analysis ($p=0.119$) (Table 5, model 2).

Discussion

This was the first study to investigate the relationship between nutritional factors and bone health in stroke patients. Our results showed that intake of fiber, protein and magnesium may be important nutritional factors that underlie bone health among individuals with stroke.

Bone health of individuals with stroke

Our results showed that the hip bone mass on the affected side was significantly lower in the unaffected side, a finding consistent with previous studies [1]. Our participants generally had poorer hip bone health in the affected leg when compared with the age-matched reference population, as revealed by the Z-scores.

Fiber intake and bone health

Fiber intake was independently associated with hip T-score on both sides. Our results showed that the average daily fiber intake was less than half of the recommended intake, and in fact, all but two patients had a lower fiber intake than the recommended value. In addition, the relationship between dietary fiber intake and the hip T-score on both sides was positive, indicating that those with lower dietary fiber intake tended to have lower hip BMD than their counterparts with relatively higher dietary fiber intake within the sample. Our results were in contrast with previous reports which showed that fiber intake was negatively associated with total hip and total spine BMD among female adults, and that dietary fiber may be detrimental to bone health by decreasing calcium absorption [21,22]. What may potentially explain the discordance in results? Dietary fibers consist of a mix of insoluble and soluble fibers which may show opposite effects on calcium absorption [23]. Brans' insoluble fiber fraction bounds to calcium ion and thus decreases the bioavailability of calcium [24]. The calcium-binding capacity of the bran cereal altered the usual inverse relationship between calcium load and fractional absorption among healthy premenopausal women [25]. Oxalate in green leafy vegetables could also form insoluble complexes with calcium but it was shown to have relatively little influence on calcium absorption [26]. In contrast, ingestion of inulin (soluble fiber) and soluble maize fiber was found to increase the apparent absorption and balance of calcium [27]. In addition, sugar beet fiber (partly soluble fiber) consumption improved calcium balance, without modification of its absorption after the 28-day study period [27]. Food rich in fiber such as fruits and vegetables may protect bone health by providing abundant sources of vitamin C, vitamin K and trace minerals, promoting an alkaline environment to reduce urinary calcium excretion and favoring the intake of phytoestrogen, a weak plant source hormone which stimulates the effect of estrogen on bone metabolism (i.e., reducing bone resorption and increasing bone formation) [27,28].

We were unable to differentiate between insoluble and soluble fiber intake. However, given that fiber intake was positively correlated with T-score of both hips, and that close to 15% of our participants reported an increased consumption of fruits and vegetables after stroke, we speculated that insoluble fiber make up only relatively small proportion of total fiber consumed by our participants. Beneficial effects of phytoestrogen, fruit and vegetable consumption on bone mass may have outweighed the possible interference of calcium absorption by increased fiber intake.

Protein intake and bone health

Protein intake was also independently associated with hip T-score on both sides. Although the protein intake was on average higher than the recommended level, there was substantial variability among the participants. A good proportion of the participants (28.7%) actually had a lower protein intake than the recommended value (Table 2). The relationship between protein intake and bilateral hip BMD was positive, indicating that those who had a higher protein take tended to have higher hip BMD than their counterparts with relatively lower protein intake within the sample. This finding was in contrast with the earlier studies, which showed a negative relationship between protein intake and BMD [29,30]. It was thought that a high protein diet may lead to a high endogenous acid load and urinary calcium loss [29,30]. More recent studies, however, have demonstrated the beneficial effect of protein on bone health in older adults [31,32]. It was found that low intake of protein for 4 days (<0.8g/kg) caused in reduction in intestinal calcium absorption, resulting in increased serum parathyroid hormone and calcitriol (1,25-[OH]2D) that persisted for 2-4 weeks [32]. A diet with 1.0 to 1.5 g protein/kg, in contrast, was found to be associated with normal calcium metabolism [32]. It was suggested that dietary protein may benefit bone health by promoting insulin-like growth factor 1 production, suppressing parathyroid hormone, and stimulating muscle protein synthesis [33].

Magnesium intake and bone health

Magnesium intake was significantly associated with hip bone health on the paretic side in our multivariate analysis. The average magnesium intake among our participants was much lower than the recommended intake. Indeed, all but one of the participants had a magnesium intake below the recommended value. Magnesium is found in whole grains, vegetables, nuts seeds, dairy products, coffee, and chocolate [34]. The intake of these food sources may be deficient among our participants. The relationship between magnesium intake and hip T-score on the affected side was a positive one, indicating that those who had relatively higher magnesium intake tended to have better paretic hip bone health than their peers who had lower magnesium intake. The finding was in agreement with previous studies on post-menopausal women [35], which also reported a positive correlation between magnesium intake and BMD. Our results also extended the finding of previous work which demonstrated that magnesium was a significant predictor of rate of change of total body BMD among premenopausal women [36]. Although the beneficial effect of magnesium on bone health was shown in observational studies, experimental studies examining the effects of magnesium supplementation on bone health were small-scaled, with conflicting results [37,38]. More studies are needed to confirm the association of magnesium with bone health post-stroke.

While association of hip BMD with intake of fiber and protein was significant on both sides, this was not the case for magnesium, which showed significant correlation with hip BMD on the paretic side only. Although the effects of nutritional factors are supposedly systemic, previous research has shown that these factors may have differential effect in different skeletal sites. For example, Chan et al. [21] showed that vitamin E level was associated with total spine BMD, but not total hip BMD in young adult women. Sato et al. [9] showed that the association of BMD of the second metacarpal with vitamin K levels was significant on the paretic side only in chronic stroke patients. A similar phenomenon was observed in the relationship between bone health and vascular health in stroke patients. Large artery elasticity, a systemic factor, was found to be only associated with bone strength index of the radius diaphysis on the paretic side, but not on the non-paretic side among individuals with chronic stroke [39]. It is possible that the stroke impairments that specifically affect the paretic side may cause the bone on that side to be more susceptible to the influence exerted by certain systemic factors, including the nutritional variables.

Overall, the intake of protein, fiber and magnesium accounted for a small part of variance of the hip T-score (2-5%). Given that bone metabolism is influenced by a multitude of factors, the fact that a single nutrient could account for 2-5% is quite substantial. The magnitude of the influence of nutritional factors on bone health found in this study was indeed quite similar to previous research in other populations. For example, Chan et al. [22] showed that in young adult women, intake of fiber was significantly associated with total spine BMD, accounting for 2.4% of the variance. Orchard et al. [35] also showed that those who consumed >442.5mg of magnesium per day had significantly higher hip BMD and whole body BMD by 3% and 2% respectively, compared with their peers who consumed <206.5 mg of magnesium per day.

Other factors

Age and female sex were significant predictor of hip T-score in our stroke patients, which extended the findings of previous studies that BMD decreased with age [40] and that more severe bone loss occurred among female stroke survivors [41].

Surprisingly, we did not find a positive correlation between calcium intake and hip BMD. Our finding was thus consistent with the National Health and Nutrition Examination Survey, which reported little or no difference among 1,384 healthy elderly in the measurement of femoral or lumbar BMD across a wide range of daily calcium intakes, from a mean of 400 mg/d (Q1) to 2000 mg/d (Q5) [42]. It was also suggested that little calcium from foods and supplements was going to bone mineral and being retained in the skeleton [42]. However, our results were in contrast with the results of previous studies involving middle-aged and elderly women [6] and elderly men [43], which showed a positive relationship between calcium intake and bone health. The discrepancy might be due to the difference in participant characteristics (stroke Vs able-bodied). The fact that bioavailability of calcium was affected by other dietary factors may also contribute to the discordance in results. Brans' insoluble fiber fraction can be one of the factors as it could bind to calcium to form insoluble complexes [24,25] and have a dramatic effect on decreasing calcium bioavailability. The calcium and phosphorus ratio was 0.7:1 for our stroke participants, which was far lower than the recommended ratio (1.6:1) [19]. The high phosphorous and low calcium consumption may impair the synthesis of the active metabolite of vitamin D and disrupt calcium absorption [44]. This may confound the relationship between calcium intake and BMD.

Our results found a significant bivariate correlation between sunlight exposure and hip T-score on both sides. However, the association was no longer significant in multivariate analysis. Unexpectedly, the degree of motor recovery (CMSA score), PASE and 6MWT were not significant predictors of hip T-score. These measures did not specifically measure the frequency and intensity of lower limb loading activities, which may partly explain the non-significant results.

Clinical and research implications

Diet modification after stroke is usually focused on secondary prevention of stroke (i.e., blood pressure and weight control, etc.). However, using diet modification as a way to promote bone health among individuals with stroke has been largely neglected. Our findings showed that magnesium, fiber, protein were associated with hip BMD. In addition, the level of intake of magnesium and fiber was particularly low, leaving room for potential intervention. Nutritional intervention in the form of patient education and prescription of supplements may be an important component of stroke care. To date, very few studies have investigated the effects of nutritional intervention on bone outcomes in the stroke population [1,11]. More research is needed in this important field.

Limitations

This study had several limitations. Firstly, the results were generalizable to community-dwelling individuals with stroke only. The dietary habits and BMD may be very different for those who are institutionalized. Secondly, the nutrition data was obtained by self-report food record only and the analysis (e.g., vitamin D) was limited by the database of the ESHA software. The PASE and GRC scores were based on self-report, and were thus susceptible to measurement bias. However, these were validated assessment tool and should provide a reasonable estimate of the variables being measured [15,16]. Thirdly, our regression models explained only 37-48% of the variance in hip T-score on both sides, suggesting that other factors that may have important effect on bone health were not captured in our analysis. Finally, a cross-sectional design was used. While we found significant associations between hip BMD and certain nutritional factors, no causal relationship was established. We also could not rule out the possibility that the events that occurred before stroke (e.g., dietary habits or lifestyle before stroke) may already have exerted important influence on hip BMD. However, the effects of these factors on hip bone health, if any, would be bilateral. The fact that the hip BMD on the affected side was significantly lower than the unaffected side has clearly demonstrated the impact of stroke on hip bone health, which is also well documented in other studies [1]. In addition, to conduct a longitudinal study that involves a similar number of individuals with stroke as in this study and the measurement of change of different factors before and after stroke, a large number of individuals (likely to be in the order of 100,000 people) will need to be assessed, because the incidence of stroke was approximately 300 per 100,000 person-years [45] and only a certain proportion of the new stroke cases would fulfill our eligibility criteria. While it is acknowledged that a longitudinal study design and a larger sample size may increase the rigor of the results, it was infeasible due to our constraints in time, manpower and budget. Despite the cross-sectional design, our study was an important first step to understanding the role of nutrition in post-stroke bone health. The results have provided some preliminary yet important insight into the nutritional status and its potential influence on bone health in the chronic stroke population, and may pave the way for further research using a larger sample size and longitudinal design.

Conclusion

The intake of fiber and magnesium was very low in people among community-dwelling individuals with chronic stroke. These nutrients, in addition to protein intake, were significantly associated with hip bone health in this population. Diet modification may have the potential in maintaining or improving hip bone health post-stroke and should warrant further study.

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Disclosure Statement

The authors declare that they have no conflicts of interests.

Authorship

Author #1 contributed to statistical analysis of data, interpretation of data and prepared the first draft of the paper. Author #2 designed the study and contributed to the acquisition of data, statistical analysis, and interpretation of data. Authors #3 and #4 contributed to the acquisition of data, and interpretation of data. Author #5 designed the study, interpretation of data, and was responsible for project management. He is guarantor. All authors revised the paper critically for intellectual content and approved the final version. All authors agree to be accountable for the work and to ensure that any questions relating to the accuracy and integrity of the paper are investigated and properly resolved.

Compliance with Ethical Standards

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

*Informed consent***:** Informed consent was obtained from all individual participants included in the study.

References

1. Eng JJ, Pang MYC, Ashe MA (2008) Balance, falls, and bone health: Role of exercise in reducing fracture risk after stroke. J Rehabil Res Dev 45:297-314.
2. Melton LJ, Brown RD, Achenbach SJ, O'Fallon WM, Whisnant JP (2001) Long-term fracture risk following ischemic stroke: A population-based study. Osteoporos Int 12:980-986.
3. Dennis MS, Lo KM, McDowall M, West T (2002) Fractures after stroke: frequency, types, and associations. Stroke 33:728-734.
4. Sato Y (2000) Abnormal bone and calcium metabolism in patients after stroke. Arch Phys Med Rehabil 81:117-121.
5. Pocock NA, Eisman JA, Hopper JL, Yeates MG, Sambrook PN, Eberl S (1987) Genetic determinants of bone mass in adults. A twin study. J Clin Invest 80:706-710. Doi: 10.1172/JCI113125
6. Ilich JZ, Brownbill RA, Tamborini L (2003) Bone and nutrition in elderly women: protein, energy, and calcium as main determinants of bone mineral density. Eur J Clin Nutr 57:554-565. Doi: 10.1038/sj.ejcn.1601577
7. Freudenheim JL, Johnson NE, Smith EL (1986) Relationships between usual nutrient intake and bone-mineral content of women 35-65 years of age: longitudinal and cross-sectional analysis. Am J Clin Nutr 44:863-876.
8. Hodges SJ, Akesson K, Vergnaud P, Obrant K, Delmas PD (1993) Circulating levels of vitamin K1 and K2 decreased in elderly women with hip fracture. J Bone Miner Res 8:1241-1245. Doi: 10.1002/jbme.5650081012
9. Sato Y, Tsuru T, Oizumi K, Kaji M (1999) Vitamin K deficiency and osteopenia in disuse-affected limbs of vitamin D-deficient elderly stroke patients. Am J Phys Med Rehabil 78:317-322.
10. Sato Y, Metoki N, Iwamoto J, Satoh K (2003) Amelioration of osteoporosis and hypovitaminosis D by sunlight exposure in stroke patients. Neurology 61:338-342.
11. Sato Y, Iwamoto J, Kanoko T, Satoh K (2005) Low-dose vitamin D prevents muscular atrophy and reduces falls and hip fractures in women after stroke: a randomized controlled trial. Cerebrovasc Dis 20:187-192. Doi: 10.1159/000087203
12. Luhrmann PM, Herbert BM, Gaster C, Neuhauser-Berthold M (1999) Validation of a self-administered 3-day estimated dietary record for use in the elderly. Eur J Nutr 38:235-240.

13. Smith-Warner SA, Elmer PJ, Fosdick L, Tharp TM, Randall B (1997) Reliability and comparability of three dietary assessment methods for estimating fruit and vegetable intakes. Epidemiology 8:196-201.
14. Kamper SJ, Maher CG, Mackay G (2009) Global rating of change scales: a review of strengths and weaknesses and considerations for design. J Man Manip Ther 17:163-170. Doi: 10.1179/jmt.2009.17.3.163
15. Vaughan K, Miller WC (2013) Validity and reliability of the Chinese translation of the Physical Activity Scale for the Elderly (PASE). Disabil Rehabil 35:191-197. Doi: 10.3109/09638288.2012.690498.
16. Gowland C, Stratford P, Ward M , Moreland J, Torresin W, Hullenaar SV, Sanford J, Barreca S, Vanspall B, Plews N (1993) Measuring physical impairment and disability with the Chedoke-McMaster stroke assessment. Stroke 24:58-63.
17. Eng JJ, Dawson AS, Chu KS (2004) Submaximal exercise in persons with stroke: test-retest reliability and concurrent validity with maximal oxygen consumption. Arch Phys Med Rehabil 85:113-118.
18. Chinese Nutrition Society: Chinese Dietary Reference Intakes 2013 Version (2014) Beijing: Science China Press
19. U.S. Department of Agriculture and U.S. Department of Health and Human Services: Dietary Guidelines for Americans, 7th ed. Washington (2010) U.S. Government Printing Office
20. Chad KE, Reeder BA, Harrison EL, Ashworth NL, Sheppard SM, Schultz S, Bruner BG, Fisher K, Lawson JA (2005) Profile of physical activity levels in community-dwelling older adults. Med Sci Sports Exerc 37:1774-1784.
21. Chan R, Woo J, Lau W , Leung J, Xu L, Zhao XH, Yu W, Lau E , Pocock N (2009) Effects of lifestyle and diet on bone health in young adult Chinese women living in Hong Kong and Beijing. Food Nutr Bull 30:370-378.
22. Wolf RL, Cauley JA, Baker CE , Ferrell RE, Charron M, Caggiula AW, Salamone LM, Heaney RP, Kuller LH (2000) Factors associated with calcium absorption efficiency in pre-and perimenopausal women. Am J Clin Nutr 72:466-471.
23. Chen Z, Stini WA, Marshall JR , Martinez ME, Guillen-Rodriguez JM, Roe D, Alberts DS (2004) Wheat bran fiber supplementation and bone loss among older people. Nutrition 20: 747-751. Doi: 10.1016/j.nut.2004.05.015

24. Bergman CJ, Gualberto DG, Weber CW (1997) Mineral binding capacity of dephytinized insoluble fiber from extruded wheat, oat and rice brans. Plant Foods Hum Nutr 51:295-310.
25. Weaver CM, Heaney RP, Teegarden D, Hinders SM (1996) Wheat bran abolishes the inverse relationship between calcium load size and absorption fraction in women. J Nutr 126:303-307.
26. Heaney RP, Weaver CM (1993) Oxalate in vegetables: effect on calcium absorbability. J Bone Miner Res 8:S333.
27. Coudray C, Bellanger J, Castiglia-Delavaud C , Remesy C, Vermorel M , Rayssignuier Y (1997) Effect of soluble or partly soluble dietary fibers supplementation on absorption and balance of calcium, magnesium, iron and zinc in healthy young men. Eur J Clin Nutr 51:375-380.
28. Prynne CJ, Mishra GD, O’Connel MA, Muniz G, Laskey MA, Yan L, Prentice A, Ginty F (2006) Fruit and vegetable intakes and bone mineral status: a cross-sectional study in 5 age and sex cohorts. Am J Clin Nutr 83:1420-1428.
29. Feskanich D, Willett WC, Stampfer MJ, Colditz GA (1996) Protein consumption and bone fractures in women. Am J Epidemiol 143:472-479.
30. Sellmeyer DE, Stone KL, Sebastian A, Cummings SR (2001) the Study of Osteoporotic Fractures Research Group: A high ratio of dietary animal to vegetable protein increases the rate of bone loss and the risk of fracture in postmenopausal women. Am J Clin Nutr 73:118-122.
31. Genaro Pde S, Pinheiro Mde M, Szejnfeld VL, Martini LA (2015) Dietary protein intake in elderly women association with muscle and bone mass. Nutr Clin Pract 30:283-289. Doi: 10.1177/0884533614545404
32. Kerstetter JE, O’Brien KO, Insogna KL (2003) Low protein intake: The impact on calcium and bone homeostasis in humans. J Nutr 133:855S-861S.
33. Mangano KM, Sahni S, Kerstetter JE (2014) Dietary protein is beneficial to bone health under conditions of adequate calcium intake: an update on clinical research. Curr Opin Clin Nutr Metab Care 17:69-74.
34. O’Neil CK, Evans E (2003) Beyond calcium and vitamin D. Clin Rev Bone Miner Metab 2:325-339.
35. Orchard TS, Larson JC, Alghothani N , Bout-Tabaku S, Cauley JA, Chen Z, LaCroix AZ, Wactawski-Wende J, Jackson RD (2004) Magnesium intake, bone mineral density, and fractures: results from the Women's Health Initiative Observational Study. Am J Clin Nutr 99:926-933. Doi: 10.3945/ajcn.113.067488

36. Houtkooper LB, Ritenbaugh C, Aickin M, Lohman TG, Going SB, Weber JL, Greaves KA, Boyden TW, Pamenter RW, Hall MC (1995) Nutrients, body composition and exercise are related to change in bone mineral density in premenopausal women. J Nutr 125:1229-1237.
37. Aydin H, Deyneli O, Yavuz D, Gozu H, Mutlu N, Kaygusuz I, Akalın S (2010) Short-term oral magnesium supplementation suppresses bone turnover in postmenopausal osteoporotic women. Biol Trace Elem Res 133:136-143. Doi: 10.1007/s12011-009-8416-8
38. Doyle L, Flynn A, Cashman K (1999) The effect of magnesium supplementation on biochemical markers of bone metabolism or blood pressure in healthy young adult females. Eur J Clin Nutr 53:255-261.
39. Pang MY, Yang FZ, Jones AY (2013) Vascular elasticity and grip strength are associated with bone health of the hemiparetic radius in people with chronic stroke: implications for rehabilitation. Phys Ther 93:774-85. Doi: 10.2522/ptj.20120378.
40. Cvijetic S, Korsic M (2004) Apparent bone mineral density estimated form DXA in healthy men and women. Osteoporos Int 15:295-300. Doi: 10.1007/s00198-003-1525-x
41. Bainbridge NJ, Davie MW, Haddaway MJ (2006) Bone loss after stroke over 52 weeks at os calcis: influence of sex, mobility and relation to bone density at other sites. Age Ageing 35:127-132.
42. Anderson JJ, Roggenkamp KJ, Suchindran CM (2012) Calcium intakes and femoral and lumbar bone density of elderly US men and women: National Health and Nutrition Examination Survey 2005–2006 analysis. J Clin Endocr Metab 97:4531-4539. Doi: 10.1210/jc.2012-1407
43. Kim KM, Choi SH, Lim S , Moon JH, Kim JH, Kim SW, Jang HC, Shin CS (2014) Interactions between dietary calcium intake and bone mineral density or bone geometry in a low calcium intake population (KNHANES IV 2008–2010). J Clin Endocr Metab 99:2409-2417. Doi: 10.1210/jc.2014-1006
44. Calvo MS, Park YK (1996) Changing phosphorus content of the US diet: potential for adverse effects on bone. J Nutr 126:1168S.
45. Woo J, Ho SC, Goggins W, Chau PH, Lo SV (2014) Stroke incidence and mortality rates in Hong Kong: implications for public health education efforts and heath resource utilisation. Hong Kong Med J 20:S24-29.

Uluduz D, Adil MM, Rahim B, Gilani WI, Rahman HA, Gilani SI, Qureshi AI (2014) Vitamin D deficiency and osteoporosis in stroke survivors: an analysis of National Health and Nutritional Examination Survey (NHANES). J

Vasc Interv Neurol 7:23–28.

Sato Y, Kuno H, Kaji M, Oshima Y, Asoh T, Oizumi K (1998) Increased bone resorption during the first year after stroke. Stroke 29:1373-1377.

Table 1. Characteristics of participants (n=94)

	Value			
	Mean	SD		
Demographics				
Age, years	58.9	10.7		
Sex (men/women), n	64/30 [a]	--		
No. of postmenopausal women, n	24[a]	--		
Postmenopausal years	8.0	9.5		
Body mass index, kg/m^2	24.8	3.5		
Stroke characteristics				
Post-stroke duration, months	51.5	49.0		
Type of stroke (ischemic/hemorrhagic/ unknown), n	51/ 41/ 2[a]	--		
Affected side of body (left/right), n	55 / 39[a]	--		
Six minute walk distance, meters	264.1	110.9		
Physical Activity Scale for the Elderly (0-400)	88.3	60.0		
Chedoke-McMaster lower limb motor score (2-14)	8.2	2.4		
Medications				
Anti-hypertensive agents, n	57	--		
Anti-diabetic agents, n	23	--		
Hypolipidemic agents, n	44	--		
Anti-coagulants, n	50	--		
Anti-depressants, n	5	--		
Anti-spastic agents, n	4	--		
Analgesics, n	2	--		
Total number of medications	3	2		
Other characteristics				
Sunlight exposure, hours per day	2.1	1.6		
Calcium supplementation, n	5[a]	--		
Vitamin D supplementation, n	1[a]	--		
Bone health	**Affected side**		**Unaffected side**	
	Mean	**SD**	**Mean**	**SD**
Total bone mineral content (g)	26.872***	11.086	27.738	10.826
Total hip bone mineral density (g/cm2)	0.745***	0.195	0.822	0.147
Total hip T-score	-1.471***†	1.344	-1.043†	1.091
Total hip Z-score	-0.565***†	1.217	-0.096	0.933
	Count	**% count**	**Count**	**% count**
Normal/osteopenia/osteoporosis[b]	35/42/17	37.3/44.7/18.1	44/41/9	46.8/43.6/9.6

[a] The values are expressed as the number of individuals.

[b] Normal: T-score ≥-1.0; osteopenia: T-score between -1.0 and -2.5; osteoporosis: T-score ≤ -2.5

Significantly different from the unaffected side: *P<0.05, **P<0.01, ***P<0.001

†Significant different from zero (one sample t-test, P<0.05)

Table 2. Mean total intake of nutrients per day

Nutrient	Mean	SD	Recommended intake	Range of Recommended intake[a]	Number (%) of individuals who had intake below the recommended value
Calories (kcal)	1632.1	431.1	2047.6***[bc]	1501.0-2999.5	81 (86.2%)
Carbohydrates (g)	192.3	57.0	256.0***[bc]	187.6-374.9	84 (89.3%)
Total Fat (% of calories)	34.2	6.9	20-30%***[cd]	---	2 (2.1%)
Cholesterol (mg)	227.8	287.8	<300[e]	---	80 (85.1%)
Protein (g)	77.1	27.5	61.8***[cf]	55-65	27 (28.7%)
Fiber (g)	13.3	5.7	28***[de]	---	92 (97.9%)
Calcium (mg)	500.4	325.6	971.2***[cf]	800-1000	87 (92.6%)
Copper (mg)	0.6	0.8	0.8[c]	---	77 (81.9%)
Iron (mg)	10.2	5.6	12.5***[cf]	12-20	75 (79.8%)
Magnesium (mg)	175.6	61.7	327.0***[cf]	310-330	93 (98.9%)
Phosphorus (mg)	743.8	276.3	713.9[ce]	670-720	45 (47.9%)
Sodium (mg)	2490.4	2168.7	1414.4***[cf]	1400-1500	38 (40.4%)
Zinc (mg)	5.4	2.3	10.9*** [cf]	7.5-12.5	91 (96.8%)
Calcium : phosphorus ratio	0.7 : 1		1.6 : 1[e]	---	---
Vitamin B1 (mg)	1.0	0.5	1.3***[cf]	1.2-1.4	78 (83.0%)
Vitamin B2 (mg)	0.7	0.5	1.3***[cf]	1.2-1.4	86 (91.5%)
Vitamin B3 (mg)	10.3	4.3	15.3***[ef]	14-16	78 (83.0%)
Vitamin B6 (mg)	1.1	0.5	1.6***[cf]	1.4-1.6	79 (84.0%)
Vitamin C (mg)	85.8	58.8	100*[c]	---	62 (66.0%)
Vitamin D (IU)[g]	23.6	22.9	45.9***[cf]	40-60	24 (25.5%)
Vitamin K (µg)	49.4	92.2	80**[c]	---	82 (87.2%)
Folic acid (µg)	215.8	120.2	400***[c]	---	91 (96.8%)

[a] For those variables that have multiple recommended values according to age groups, sex, etc., the overall minimum and maximum recommended values are listed.

[b] There are different recommended intake values for different groups according to age groups, sex and physical activity levels (i.e. low, moderate and high). The value listed here is a single composite recommended value computed based on the distribution of age groups, men/women proportion, and physical activity level of our participants.

[c] Recommended intake value is based on the Chinese Dietary Reference Intake (Chinese DRI 2014).

[d] A mean value of 25.0% was used for comparison with the stroke group (one-sample t-test).

[e] Recommended intake value is based on the United States Dietary Reference Intake (US DRI 2010).

[f] There are different recommended intake values for different groups according to age group and sex. The value listed here is a single composite recommended value computed based on the distribution of age and men/women proportion of our participants.

[g] The data on Vitamin D intake is based on 31 stroke participants only.

Significantly different from the mean intake obtained from stroke patients: *$P<0.05$, **$P<0.01$, ***$P<0.001$

Table 3. Self-perceived dietary habit changes

Dietary habit changes	Frequency (n)	Percentage (%)
Decreased intake of fatty food	39	41 .5
Decreased amount of food intake	36	38.3
Decreased intake of salty food	18	19.1
Decreased intake of sweet food	13	13.8
Increased intake of fruits and vegetables	13	13.8
Decreased intake of meat	12	12.8
Increased intake of cereal	9	9.6
Decreased intake of fried food	7	7.4
Decreased dining out	6	6.4
Decreased intake of food with sauce	6	6.4
Decreased intake of rice	5	5.3
Other dietary habit changes	5	5.3
Decreased drinking of beverage	4	4.3
Decreased intake of snack	3	3.2
Required to eat soft food	3	3.2
Stopped alcohol consumption	2	2.1

Table 4. Multiple regression analysis for predicting hip T-score on the affected side

Predictor	R^2 change	B[a]	Beta[b]	Tolerance[c]	*P*
Model 1 (Dependent variable: Hip T-score on affected side)					
F=4.614, R^2=0.429, p<0.001					
Age	0.396[c]	-0.045	-0.359	0.683	0.001**
Sex (men=1, women=2)		-0.796	-0.277	0.681	0.008
Body mass index		0.088	0.229	0.838	0.015*
Post-stroke duration		0.002	0.066	0.798	0.490
Side of paresis (right=1, left=2)		0.065	0.024	0.891	0.789
Physical Activity Scale for the Elderly		0.001	0.057	0.730	0.565
Chedoke-McMaster lower limb motor score		-0.004	-0.007	0.507	0.953
Six minute walk distance		0.003	0.232	0.459	0.067
Total calories intake		-0.001	-0.472	0.300	0.003**
Total number of medications		0.110	0.162	0.852	0.080
Sunlight exposure	0.002	-0.006	-0.008	0.831	0.935
Protein	0.042	0.018	0.367	0.363	0.011*
Fiber	0.044	0.056	0.239	0.777	0.015*
Model 2 (Dependent variable: Hip T-score on affected side)					
F=4.028, R^2=0.374, p<0.001	0.339				
Age		-0.048	-0.383	0.669	0.001**
Sex (men=1, women=2)		-0.897	-0.313	0.682	0.004**
Body mass index		0.065	0.169	0.888	0.074
Post-stroke duration		0.003	0.099	0.814	0.313
Side of paresis (right=1, left=2)		0.149	0.055	0.883	0.559
Physical Activity Scale for the Elderly		0.001	0.047	0.712	0.652
Chedoke-McMaster lower limb motor score		0.025	0.044	0.515	0.718
Six minute walk distance		0.002	0.201	0.456	0.126
Total calories intake		-0.001	-0.257	0.476	0.047*
Total number of medications		0.099	0.146	0.856	0.129
Sunlight exposure	0.002	0.012	0.014	0.828	0.886
Magnesium	0.032	0.005	0.238	0.561	0.048*

[a] B, Unstandardized regression coefficient

[b] Beta, Standardized regression coefficient

[c] All Tolerance values >0.2: indicate no substantial multicollinearity

Predictor variables were significant: *P<0.05, ** P <0.01, *** P <0.001

Table 5. Multiple regression analysis for predicting hip T-score on the unaffected side

Predictor	**R^2 change**	**B^a**	**$Beta^b$**	**Tolerance ^{c}**	***P***
Model 1 (Dependent variable: Hip T-score on unaffected side)					
F=5.251, R^2=0.482, p<0.001					
Age	0.396^c	-0.046	-0.452	0.679	<0.001***
Sex (men=1, women=2)		-0.603	-0.259	0.669	0.011*
Body mass index		0.060	0.191	0.830	0.035*
Post-stroke duration		0.004	0.166	0.798	0.071
Side of paresis (right=1, left=2)		-0.070	-0.032	0.885	0.713
Physical Activity Scale for the Elderly		0.001	0.062	0.672	0.534
Chedoke-McMaster lower limb motor score		-0.033	-0.072	0.507	0.530
Six minute walk distance		0.001	0.149	0.449	0.222
Total calories intake		-0.001	-0.411	0.291	0.008**
Total number of medications		0.109	0.197	0.844	0.029*
Sunlight exposure	0.003	0.001	0.001	0.800	0.991
Iron	0.005	-0.006	-0.028	0.515	0.804
Protein	0.027	0.013	0.325	0.345	0.021*
Fiber	0.052	0.051	0.266	0.727	0.006**
Model 2 (Dependent variable: Hip T-score on unaffected side)					
F=4.017, R^2=0.416, p<0.001					
Age	0.396	-0.048	-0.471	0.669	<0.001***
Sex (men=1, women=2)		-0.675	-0.290	0.682	0.006**
Body mass index		0.039	0.126	0.888	0.165
Post-stroke duration		0.005	0.203	0.814	0.034*
Side of paresis (right=1, left=2)		-0.021	-0.010	0.883	0.914
Physical Activity Scale for the Elderly		0.001	0.053	0.712	0.601
Chedoke-McMaster lower limb motor score		-0.009	-0.020	0.515	0.867
Six minute walk distance		0.001	0.130	0.456	0.302
Total calories intake		-0.001	-0.200	0.476	0.108
Total number of medications		0.098	0.177	0.856	0.057
Sunlight exposure	0.003	0.017	0.025	0.828	0.792
Magnesium	0.018	0.003	0.178	0.561	0.119

[a] B, Unstandardized regression coefficient

[b] Beta, Standardized regression coefficient

[c] All Tolerance values >0.2: indicate no substantial multicollinearity

Predictor variables were significant: *P<0.05, ** P <0.01, *** P <0.001