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Risk factors and quality of life for the occurrence of hip fracture in postmenopausal women

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ABSTRACT

Background: To identify the risk factors and changes of quality of life in the first occurrence of hip fracture in Taiwanese postmenopausal women.
Methods: In this case-control study, we enrolled 100 postmenopausal women with accidental first-incident hip fracture and 100 women without hip fracture. The control group was matched to the study group according to age. Evaluation consisted of a questionnaire, an interview to both assess quality of life via a 36-item Short Form Health Survey and document risk factors, a physical examination to record height and body weight, and bone mineral density (BMD) of the hip and spine using dual-energy X-ray absorptiometry (DXA).
Results: The mean age of the patients was 77.9 years old. Compared with the controls, the patients with first-incident hip fracture had a lower level of education, increased body height, higher parity, no experience of estrogen therapy, prior history of diabetes mellitus and rheumatoid arthritis, walking aid use, less weight-bearing exercise, and steroid use. Total hip BMD was a stronger predictor than BMD at different sites. Quality of life was significantly higher in the control group at the baseline and 4-month follow-up.
Conclusions: Quality of life was related to the first-incident hip fracture. The increased risk of falls, lower level of education, and total hip BMD are the strongest predictors of first-incident hip fracture in Asian elderly postmenopausal women.

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At a glance commentary

Scientific background on the subject

Because hip fracture prevalence in Asian postmenopausal women is higher than that of their Western counterparts, Asian postmenopausal women may have certain risk factors for first-incident hip fractures that differ from those of Caucasian women. However, current knowledge regarding these risk factors for hip fractures among Asian women is limited.

What this study adds to the field

Besides risk factors related to fall and lower hip bone mineral density which are similar to those reported in Western women, awareness on osteoporosis prevention and quality of life should be the most important factor affecting the first-incident hip fracture in Asian elderly postmenopausal women.

It has been clearly established that because of estrogen deficiency, postmenopausal women have a higher incidence of osteoporosis and fracture than men. In postmenopausal women, the hip, spine and wrist are the areas most susceptible to fracture. Among these osteoporotic fractures, hip fractures are of greater concern, because they may result in personal disability and mortality and therefore, contribute a higher burden on family and society expenditure.

Although a declined age-adjusted hip fracture rate in most Western countries has been demonstrated over the past decades [1,2], the incidence of hip fracture has increased twofold to threefold in most Asian countries over the past 30 years [3]. Therefore, it is projected that by 2050, more than 50% of all osteoporotic hip fractures will occur in Asia [4]. In addition, patients with hip fracture have a two-fold relative risk of recurrent hip fracture [5]. Thus, preventing first-incident hip fracture should be the most critical issue, particularly in Asian countries.

Risk factor identification is critical for preventing first-incident hip fracture, averting subsequent fractures, and improving both outcome and quality of life after hip fracture. The potential risk factors for hip fracture have been evaluated in the white women and include low bone density, lower body weight, cigarette smoking, caffeine intake, use of long-acting sedatives, and inactivity etc. [6,7]. Because the prevalence of hip fracture in Asian postmenopausal women is higher than that in their Western counterparts, except for Northern Europe, Asian postmenopausal women may have some risk factors for first-incident hip fracture that are different from those of white women. However, current knowledge about the risk factors for hip fracture among Asian women is limited.

According to the recent systemic review, Taiwan not only represents the high-risk area for hip fracture worldwide, but also has the highest incidence of hip fracture as compared with other Asia countries [8]. Thus, determining the risk factors for hip fracture in Taiwanese postmenopausal women is crucial for identifying high-risk individuals in Asian countries, as well as for developing effective strategies for prevention. Therefore, the present study was designed as a case-control study to investigate the risk factors for hip fracture among postmenopausal women with first-incident hip fracture.

Materials and methods

Study design and subjects

In this case-control study, women with hip fracture (study group) were compared with women without hip fracture (control group) to determine whether the potential risk factors and bone mass differed between the two groups. This study was approved by the Medical Ethics Committee of Chang Gung Memorial Hospital. All participants provided an informed consent form.

This study enrolled patients who were admitted to Keelung Chang Gung Memorial Hospital for an accidental first-incident hip fracture from March 2014 to April 2016. Patients were excluded if they were (1) severely cognitively impaired and completely unable to follow orders, (2) terminally ill, or (3) refused to participate. A total of 100 postmenopausal women were included in the study group.

To obtain a control group with a similar background as the study group, 100 postmenopausal women (without hip fracture) undergoing general health evaluation were recruited from the Gynecology Outpatient Clinic of Keelung Chang Gung Memorial Hospital from March 2014 to April 2016. The control group was matched to the study group according to age.

Assessment of risk factors

Questionnaire and interview

All participants underwent in-person interviews: the study group during admission and the control group at the outpatient clinic. We determined their level of education, body height and weight, age at menopause, parity, history of fracture, parental history of fractures, current or previous therapy with estrogen within the past year, smoking habits, alcohol and coffee intake, calcium supplement, sun exposure more than 30 min per day, and weight-bearing exercise three or more times per week, as well as whether they underwent bilateral oophorectomy before the age of 45. We also examined whether the participants had physician-diagnosed fractures, hyperthyroidism, diabetes mellitus, chronic disease (including coronary heart disease, renal disease, epilepsy, parkinsonism, and cancer), rheumatoid arthritis, stroke, cataracts or glaucoma, and visual impairment or using walking aids. Furthermore, we evaluated their current medication, including hormone therapy, steroid, psychological medication (such as tranquilizers, anti-anxiety medication, and anti-psychological medication), osteoporosis medication, and diuretics (including thiazide diuretic, and behyd).

Assessment of quality of life by using 36-item Short Form Health Survey (SF-36)

The 36-Item Short Form Health Survey (SF-36) is a general health-based survey of quality of life [9], which contains 36

items of self-reported aspects of health. In addition to a single-item measure of health transition (HT), the SF-36 comprises eight physical and mental dimensions of health namely: physical functioning (PF), role limitations due to physical health (RP), bodily pain (BP), general health perceptions (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE) and mental health (MH), which are also combined into physical and mental component summary scales (PCS and MCS, respectively). In this study, the Taiwanese version of the SF-36 questionnaire was used to calculate the summary scales [10], which was administered to the last 100 participants both in the study (50) and control (50) groups. The patients recalled their condition (SF-36) from the 4 weeks before fracture, and controls recalled their condition from the time preceding their inclusion. These data were used as baseline measures for both groups. The same data collection performed at the baseline was repeated after 4 months.

Examination

Body weight, height, and bone mineral density (BMD) were measured. Baseline lumbar spine and hip BMD were measured using a dual energy X-ray absorptiometry (DXA) instrument (GE-Lunar, iDAX, Madison, WL, USA) installed at Keelung Chang Gung Memorial Hospital.

Statistical analyses

Summary statistics for the study variables were calculated and compared between the study and control groups. Descriptive statistics were expressed as mean and standard deviation for continuous variables, and as frequency and percentage for categorical variables. Independent t tests were used to assess the differences in numerical variables between the two study groups, and chi-squared tests were used to examine the differences in categorical variables. Multiple logistic regression analysis was used to calculate multivariate-adjusted odds ratios (ORs) of the study variables associated with hip fracture. In multiple regression analyses, regression diagnostics, such as residual analysis, and multicollinearity were performed to ensure model robustness. Paired samples *t* tests were used to compare the SF-36 score between the baseline and 4-month follow-up in the patients and controls. All statistical analyses were performed using the Statistical Analysis System (SAS) software, version 9.1 (SAS Institute, Cary, North Carolina).

Ethical approval

This study was approved by Institutional Review Board of Chang Gung Medical Foundation (IRB:103-0582B; IRB:103-6635B, IRB: 201600490B0, and IRB: 201600772B0).

Results

Comparison of clinical characteristics between patients with hip fractures and controls

Table 1 presents the characteristics of the participants. The mean age of the participants was 77.9 years. Compared with the controls, the patients with first-incident hip fractures had a significantly lower level of education ($p = 0.0000$); increased body height ($p = 0.0006$); higher parity ($p = 0.0387$); no experience of estrogen therapy ($p = 0.0082$); prior history of diabetes mellitus ($p = 0.0499$) and rheumatoid arthritis ($p = 0.0180$); walking aid use ($p = 0.0000$); less weight-bearing exercise three times per week ($p = 0.0008$); and steroid use ($p = 0.0323$). Although there was no significant difference on bone mineral density (BMD), the correlation of total hip BMD with the risk of hip fracture was stronger than that of BMD at other sites (spine and femoral neck) [Table 2].

Compared with the study group, the control group had a significantly higher prevalence of chronic disease ($p = 0.0333$), including coronary heart disease, renal disease, epilepsy, Parkinsonism, and cancer, and a habit of daily coffee intake ($p = 0.0169$).

Multivariate analysis

The ORs and 95% confidence intervals (CIs) estimated using multivariate logistic regression analysis for all the predictor variables revealed that the level of education, walking aid use (OR 6.121; 95% CI 2.548–14.700; $p = 0.000$), total hip BMD (OR 0.571; 95% CI 0.400–0.816; $p = 0.002$), and body height (OR 1.190; 95% CI 1.102–1.285; $p = 0.000$) were the only significant risk factors for first-incident hip fractures [Table 3].

Differences in health-related quality of life between patients and controls at baseline and 4-month follow-up

At the baseline, the patients with first-incident hip fractures had significantly lower scores for the SF-36 domains, namely PF ($p = 0.000$), RP ($p = 0.010$), BP ($p = 0.005$) GH ($p = 0.000$), VT ($p = 0.003$), SF ($p = 0.007$), RE ($p = 0.000$), MH ($p = 0.006$), and HT ($p = 0.049$), as well as PCS ($p = 0.000$) and MCS ($p = 0.012$). At the 4-month follow-up, the patients still had significantly lower scores for all SF-36 domains (including PCS and MCS), except for RP, as compared with the controls [Fig. 1]. However, compared with the baseline, patients with hip fractures had significantly increased scores for PCS ($p = 0.033$) and decreased scores for MH ($p = 0.047$) at the 4-month follow-up.

Discussion

This study demonstrated that in addition to higher parity, no experience of estrogen therapy, prior history of diabetes mellitus and rheumatoid arthritis, less weight-bearing exercise three times per week, and steroid use, the risk factors considered to be the main determinants of first-incident hip fracture in Taiwanese postmenopausal women included walking aid use, higher body height, lower level of education, and total hip BMD. In addition, quality of life, including physical and mental components, played a crucial role in the occurrence of first-incidence hip fracture.

The incidence of hip fracture is generally accepted to increase exponentially with age. This study further confirmed that most hip fractures occur in older postmenopausal women. More than 95% of hip fractures are caused by falling [11]. The present study revealed several significant risk

Table 1 Characteristics of the study population.

Variables	Patient group (N = 100)	Control group (N = 100)	*p*-value
Age	78.7 ± 9.0.	77.1 ± 6.1	0.1314
Education level			0.0000
unschooled	51 (52%)	21 (21%)	
primary school	29 (30%)	53 (54%)	
Secondary or higher education	18 (18%)	24 (25%)	
Body Weight (kg)	54.0 ± 9.2	52.7 ± 8.9	0.3295
Body Height (cm)	153.2 ± 6.1	150.1 ± 6.3	0.0006
Body mass index (kg/m^2)	23.1 ± 3.7	23.4 ± 3.5	0.6792
Age at menopause	48.7 ± 5.5	50.4 ± 7.7	0.0885
Parity	4.5 ± 2.1	3.9 ± 1.8	0.0387
Bilateral oophorectomy prior to 45 y/o	6 (6%)	7 (7%)	0.7887
Estrogen therapy	9 (9%)	23 (23%)	0.0082
Prior history of fracture	37 (38%)	32 (33%)	0.4227
Parental history of fracture	6 (6%)	8 (8%)	0.5927
Prior history of hyperthyroidism	5 (5%)	12 (12%)	0.0832
Prior history of diabetes mellitus	33 (34%)	21 (21%)	0.0499
Chronic diseases[a]	32 (33%)	47 (48%)	0.0333
Rheumatoid arthritis	16 (17%)	6 (6%)	0.0180
Prior history of stroke	17 (17%)	9 (9%)	0.0821
Prior history of cataracts or glaucoma	48 (50%)	55 (55%)	0.4812
Prior history of visual impairment	23 (24%)	15 (15%)	0.1128
walking aids	50 (51%)	16 (16%)	0.0000
Current smoking	7 (7%)	5 (5%)	0.5275
≥3 alcoholic beverages/day	0 (0%)	1 (1%)	1.000
Coffee intake every day	6 (6%)	17 (17%)	0.0169
Calcium supplement	25 (26%)	36 (36%)	0.1206
Sun exposure over 30 min/day	41 (42%)	39 (39%)	0.6823
Weight-bearing exercise ≥3 times/week	22 (23%)	45 (45%)	0.0008
Steroid use ≥3 months and ≥5 mg/day	7 (7%)	1 (1%)	0.0323
Psychological medication[b]	31 (32%)	25 (25%)	0.2790
diuretics[c]	16 (16%)	9 (9%)	0.1141
Bone mineral density			0.2900
T-score[d] ≤ −2.5	69 (72%)	64 (66%)	
−2.5 < T-score < −1	24 (25%)	25 (26%)	
T-score ≥ −1	3 (3%)	8 (8%)	

[a] Chronic diseases include coronary heart disease, renal disease, epilepsy, parkinsonism, and cancer.
[b] Psychological medication includes tranquilizers, anti-anxiety medication, and anti-psychological medication.
[c] Diuretics include thiazide diuretic, and behyd.
[d] T-score: measure bone mineral density in the hip and spine by DXA.

factors, particularly higher body height, history of rheumatoid arthritis, and walking aid use, that increase the likelihood of a fall. Because falls commonly result from a combination of risk factors [12,13], the variation in a person's socio-demographic factors and the effectiveness of interventions should be considered. In the present study, the control group had a higher incidence of chronic diseases, hyperthyroidism and cataracts or glaucoma, most of which are also recognized as the risk factors for falls. However, the control group also had a higher average level of education, more regular exercise, and higher total hip BMD. It should be investigated whether the difference is due to the awareness of the patients and their family on how to prevent falling and subsequent hip fracture or other factors in the control group.

Table 2 Association of bone mineral density with First Incident Hip Fractures.

BMD site	Patient group (N = 100)	Control group (N = 100)	*p*-value
Lumbar spine	0.84 ± 0.17	0.86 ± 0.20	0.987
Total hip	0.65 ± 0.16	0.73 ± 0.14	0.000
Femoral neck	0.60 ± 0.19	0.63 ± 0.11	0.198
Lumbar spine T-score	−2.08 ± 1.40	−1.98 ± 1.53	0.602
Total hip T-score	−2.47 ± 1.25	−1.78 ± 1.11	0.000
Femoral neck T-score	−2.61 ± 1.59	−2.38 ± 0.92	0.212

Table 3 Multivariate adjusted odds ratios for the major risk factors of first-incident hip fracture in postmenopausal women.

Variables	Adjusted OR	95% CI	*p*-value
Education			
primary school vs Unschooled	0.251	0.107–0.592	0.002
Secondary or higher education vs unschooled	0.338	0.128–0.891	0.028
Walking aids	6.257	2.708–14.457	0.000
Total hip T-score	0.554	0.402–0.763	0.000
Body height	1.179	1.095–1.268	0.000

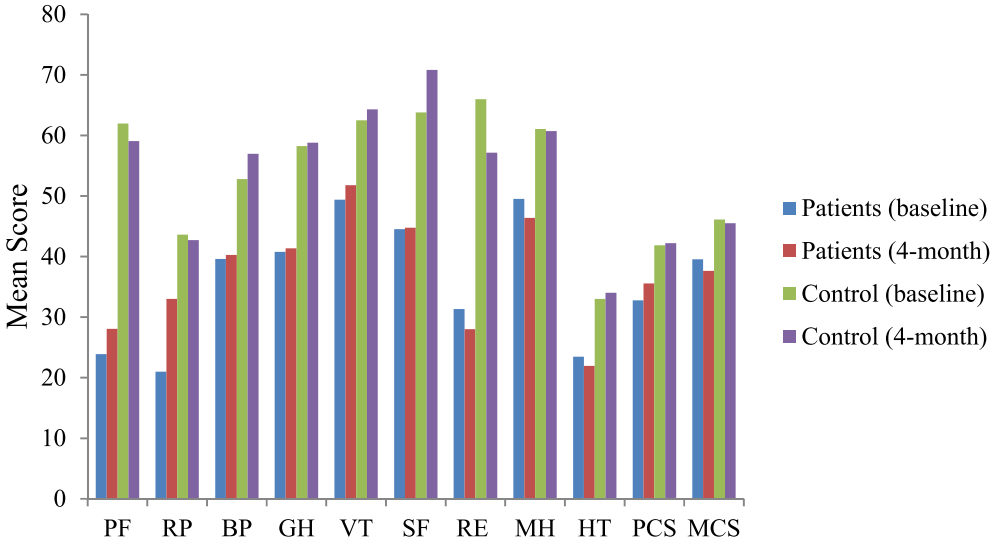

Fig. 1 Mean scores (95% confidence intervals) by using the 36-Item Short Form Health Survey (SF-36) at the baseline and 4-month follow-up in patients with hip fractures (n = 50) and controls (n = 50). In addition to health transition (HT), the SF-36 comprises eight domains: physical functioning (PF), role limitations due to physical health (RP), bodily pain (BP), general health perceptions (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE) and mental health (MH), which are also combined into physical and mental component summary scales (PCS and MCS).

The correlation between the level of education and either bone mass or the risk of fractures remains controversial. Shaw [14] found no significant associations between BMD and the level of education in a cross-sectional study of healthy volunteers in Taiwan. By contrast, Ho et al. [15] demonstrated that a higher level of education was independently associated with improved BMD and a lower prevalence of osteoporosis among postmenopausal Chinese women. Colon-Emeric et al. [16] also observed a positive association between the level of educational and the risk of hip fracture among ambulatory non-Hispanic white men. Recent analysis demonstrated that low socioeconomic status was associated with an increased incidence of hip fracture [17,18]. The present study further demonstrated that the lower level of education is a significant main determinant of first-incident hip fracture. Awareness on osteoporosis and general health should be the most critical issue for preventing hip fracture.

It has been clearly established that low bone mass is associated with an increased risk of fracture. In a large meta-analysis of prospective cohort studies, the relative risk of hip fractures was assumed to be 2.6 per 1 standard deviation decrease in bone density [19]. In the present study, 97% patient group and 92% control group had low bone mass. However, after further analysis of BMD at different sites, only total hip BMD was found to be significantly related to first-incident hip fracture and was demonstrated to be one of the major risk factors. The recently published 10-year follow-up multicenter Study of Osteoporotic Fractures (SOF) [20] and a meta-analysis from Canada, Europe, Japan and Australia [21] have also shown that the prediction of the hip fracture risk from hip BMD measurement has the highest RR value and is the most effective type of DXA examination. Therefore, when performing DXA to evaluate BMD, it is more appropriate to evaluate not only spine but also hip BMD, particularly in older patients.

A meta-analysis of randomized controlled trials in older adults reported that the combination of weight-bearing exercise and progressive resistance training was the most effective method for preserving BMD and preventing bone loss at clinically relevant sites such as the hip and spine [18]. The present study also showed that women with less weight-bearing exercise three times per week had a higher incidence of hip fracture. Numerous lifestyle risk factors, disease, and medication, such as smoking, alcohol and coffee consumption, calcium supplement use, sun exposure more than 30 min per day, hyperthyroidism, diabetes mellitus, steroid, psychological medication, and diuretics, are believed to affect BMD and hip fracture. In this study, diabetes mellitus and steroid use increased the risk of first-incident hip fracture. Except for coffee consumption, other risk factors did not exert significant effects, which may be attributed to the culture difference between Taiwan and Western countries, as well as to the limited sample size.

In addition to aging, the impact of menopause on the risk of hip fracture is recognized to be associated with the significant bone loss because of estrogen deficiency. Thus, factors related to menopause may affect the risk of hip fracture. Many studies, including the initial Women's Health Initiative (WHI) trial [22], an observational study [23], and a meta-analysis of 22 clinical trials [24], have consistently reported a significant reduction in the risk of hip fracture among current or ever users of menopausal hormone therapy (MHT) compared with never users. In this study, we also found a similar effect of MHT on hip fracture. In addition, early menopause is widely believed to be a long-term risk factor for osteoporosis and fracture. However, in the present study, age at menopause and bilateral oophorectomy prior to 45 y/o was not significant risk factors for hip fracture, which is consistent with some reports [25]. The difference between this result and those

reported in other studies [6,26] may result from adjustment for age, which is one of the main determinants of hip fracture.

Because pregnancy causes pronounced changes in the levels of sex steroids and other hormones involved in calcium homeostasis, many studies demonstrated that parity is associated with a reduced hip fracture risk [27]. However, the actual effect of parity on osteoporotic fracture risk is uncertain, because lifestyle factors and the socioeconomic condition during pregnancy may also play a crucial role. Similar to our previous study that showed an inverse relationship between parity and BMD in Taiwanese postmenopausal women [28], the present study also revealed increasing parity resulting in a higher incidence of first-incidence hip fracture. The difference in the effects of parity between Eastern and Western countries may be associated with variability in the socioeconomic condition present decades ago.

The most significant implication of our findings is related to awareness on osteoporosis prevention and health care. This implication can be further confirmed by the difference on quality of life between the study and control groups. Rohde et al. also reported that the patients with hip fracture had lower global quality of life before fracture occurrence than did the controls [29]. Similar to other investigations using SF-36, our study also has some similar limitations and possible selective response shift, because the patients self-evaluated their "pre-fracture" SF-36 after the fracture had occurred. To minimize the recall problem, SF-36 assessments in the present study were performed with the shortest possible time lag during admission for the fracture event, which has been demonstrated to be crucial for a more accurate report of quality of life [30]. Although significant improvement of physical component summary after a 4-month follow-up in patient group may imply possible selective reporting bias, the general quality of life at the baseline and 4-month follow-up was still lower in the patient group than that in the control group. The surgery and rehabilitation may improve some of physical problems in patients with hip fracture, which still influenced the mental health as shown by the significant reduction of mental health score after 4-month follow-up in the study group.

In addition to the aforementioned recall problem, one limitation of this study is the limited sample size. The advantage of enrolling controls from a hospital in this study is that this enrollment afforded an improved assessment of the general condition and ensured the same source population as patients to reduce the possibility of selection bias. The strengths of the study are its prospective design, and that all participants were completely investigated using clearly defined methods.

In conclusion, many risk factors, particularly increased risk of falls and low hip BMD, for the first-incident hip fracture in Taiwanese postmenopausal women were identified in the present study, which are similar to reports in Western women [6,7]. However, the present study revealed that the level of awareness to health care should be considered as the main factor contributing to the difference in the risk of hip fracture between Western and Eastern countries. Thus, increasing awareness on osteoporosis prevention through education should be prioritized to prevent the first-incident hip fracture in Asian postmenopausal women.

Summary

This study demonstrated that in addition to higher parity, no experience of estrogen therapy, prior history of diabetes mellitus and rheumatoid arthritis, less weight-bearing exercise three times per week, and steroid use, the risk factors considered to be the main determinants of first-incident hip fracture in Taiwanese postmenopausal women included walking aid use, higher body height, lower level of education, and total hip BMD. In addition, quality of life, including physical and mental components, played a crucial role in the occurrence of first-incidence hip fracture.

Conflicts of interest

All authors declare they have no conflicts of interest.

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