Original Article

**Estimation of the 10-year Probability of Osteoporotic Fracture in Postmenopausal Taiwanese Women With FRAX**

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**Abstract**

**Objective:** As the proportion of the aging population rises dramatically, osteoporotic fractures among the elderly have become a global health concern. We assessed the prevalence of osteoporosis and estimated the 10-year probability of osteoporotic fractures among postmenopausal women.

**Materials and Methods:** Patients who were undergoing a checkup at a teaching hospital in eastern Taiwan were invited to participate in this study. A self-administered questionnaire was used to ascertain their demographics, diet, lifestyle, and reproductive and medical histories. The bone mineral density (BMD) of the posterior-anterior lumbar spine (L1–L4) was measured by dual-energy X-ray absorptiometry. A diagnosis of osteoporosis was made according to World Health Organization (WHO) criteria. The 10-year probability of osteoporotic fracture was computed online without BMD data with the WHO Fracture Risk Assessment Tool (FRAX).

**Results:** In total, 475 postmenopausal women were involved in this study. The prevalence of osteoporosis was 37.2% (95% confidence interval (CI)=33.2%, 41.5%). The mean 10-year probabilities of a major osteoporotic or hip fracture were 13.8% (95% CI=10.7%, 16.9%) and 2.2% (95% CI=0.8%, 3.5%), respectively. For women aged ≥70 years, the mean 10-year probability of an osteoporotic fracture was 24.3% (95% CI=13.6%, 35.0%). In total, approximately 17.1% (95% CI=14.0%, 20.5%) of women were at high risk of a major osteoporotic fracture (risk>20%) and 20.3% (95% CI=16.1%, 23.9%) were at high risk of a hip fracture (>5%). Furthermore, one in four osteoporotic women was at high risk of a major osteoporotic fracture.

**Conclusion:** Osteoporosis is common among postmenopausal women, and the risk of osteoporotic fracture is of great concern particularly among older women and vegetarians. Ongoing studies of fracture rates should be followed up, and strategies and research directed at fracture prevention should be prioritized as the proportion of the aged population increases. *(Tzu Chi Med J 2010;22(1):29–35)*

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1. Introduction

Osteoporosis is the most common generalized bone disease related to aging, and constitutes a growing health concern globally (1). The incidence of osteoporosis has risen with increased life expectancy in recent decades. The life expectancy of Taiwanese women has remarkably increased in the last decade, rising from 74.5 years in 1995 to 82.0 years in 2008 (2). In 2008, 10.8% of the female population in Taiwan was aged ≥65 years, and 41.2% of those women were aged over 74 years (2). Postmenopausal women account for an estimated 25% of the total female population in Taiwan (3). Previous studies have found that approximately 19.8% of the elderly residing in urban districts have one or more vertebral compaction fractures (4). In 2001, there were 7000 hip fractures in women (5). Osteoporotic fractures, in particular, lead to significant morbidity and mortality (6–8) as well as poor functional outcomes (9,10). These fractures are also associated with great socioeconomic burdens worldwide (1).

Osteoporosis is no longer regarded as an ineluctable result of aging but as a preventable and treatable disorder (1,11). Low bone mass has been identified as an important risk factor for osteoporosis, analogous to pre-hypertension in heart disease or impaired fasting glucose in diabetes. To direct preventive treatment to the appropriate risk groups, an estimation of the fracture risk is necessary. Recently, a new fracture risk assessment tool (FRAX) was developed from 11 clinical risk factors with or without the use of femoral bone mineral density (BMD) (12,13). A World Health Organization (WHO) scientific group proposed that the 10-year probability for fracture be used to express the fracture risk for clinical assessment (12) and to determine intervention thresholds (13).

In Taiwan, most previous research was devoted to the incidence of hip fractures (4,5,14,15), while studies of the probability of osteoporotic fracture are limited (16,17). In this study, we assessed the prevalence of osteoporosis and estimated the 10-year probability of osteoporotic fracture using clinical risk factors in postmenopausal women.

2. Materials and methods

2.1. Participants and setting

This was a hospital-based study carried out from 2004 to 2005 at a teaching hospital in eastern Taiwan. Subjects who were undergoing health checkups were recruited to participate in this study. All participants gave their consent, and the project was approved by the Protection of Human Subjects Institutional Review Board of the hospital. Subjects were excluded if they had a history of thyroid or parathyroid disorders, or if they had taken medication such as thyroid hormone, bisphosphonates, or selective estrogen receptor modulators. Data were collected from a total of 475 postmenopausal women aged ≥50 years.

2.2. Survey development

A self-administered questionnaire was designed and used to collect information on demographic characteristics, lifestyle, medical history, and reproductive history. The menstruation history was assessed with questions on the age of menarche, date of the last period, the age of menopause, and operative history of the ovaries. Menopause was defined as no menstrual period for more than 1 year or with an answered age of menopause. The clinical risk factors were comprised of age, sex, body mass index (BMI), long-term glucocorticoid use, parental history of hip fracture, history of fragility fractures, smoking, alcohol consumption (>5 units/day), secondary osteoporosis arising from rheumatoid arthritis, early menopause (onset at <45 years), and chronic liver disease.

The fracture risk assessment tool, FRAX, was based on the BMD of the femoral neck combined with the following clinical risk factors: age, sex, weight, height, smoking, glucocorticoid use, rheumatoid arthritis, secondary osteoporosis, excessive alcohol consumption, and a personal or family history of fracture. It is available online (12) and gives an estimate of the 10-year risk of osteoporotic fracture since December 2007. We retrieved an individual’s relevant data and assessed each participant’s 10-year probability of major osteoporotic (hip, spine, forearm, or humeral fracture) and hip fracture without the BMD online.

2.3. Data collection

Participants completed the questionnaires individually. The height and weight of subjects were measured by nurses. Body weight was measured without shoes in light indoor clothing. The BMD of the posterior-anterior lumbar spine was measured by dual-energy X-ray absorptiometry (DXA) using a QDR 2000 densitometer (Hologic, Waltham, MA, USA). The coefficient of variation of our machine was 1.0% for the lumbar spine. The mean value of bone density of the lumbar spine (L1–L4) was labeled as the subject’s BMDL. Self-reported disorders such as type 1 diabetes, untreated long-standing hyperthyroidism, premature menopause (<45 years), chronic malnutrition, malabsorption, and chronic liver disease were recorded as part of the questionnaire.
2.4. Measurement of variables

The WHO established the following definitions based on bone-mass measurements at the spine, hip, or wrist in white postmenopausal women. Subjects were categorized into three groups based on their bone-mass assessment by a T-score as follows: those with a T-score of $\geq -1.0$ were defined as “young normal”, those with a T-score between $-1.0$ and $-2.5$ were defined as having “osteopenia”, and those with a T-score of $\leq -2.5$ were defined as having “osteoporosis” [1]. Participants with probabilities of $>20\%$ for any major osteoporotic fracture or $>3\%$ for a hip fracture were defined as being at high risk of fracture [18].

2.5. Statistical analysis

The age-specific mean and standard deviation (SD) of the BMDL were calculated for age groups stratified by 5-year intervals. Frequency, percentages, and 95% confidence intervals (CIs) were used to assess the prevalence of osteoporosis. The mean and standard deviation were used to compare numerical variables. The Mantel-Haenszel $\chi^2$ test for trends was used to assess whether the proportions of osteoporosis and fracture risk were related to aging. A $t$ test was used to compare the means of the probability of osteoporotic fracture between subjects diagnosed with and those without osteoporosis. All statistical analyses were performed using SAS release 9.1.3 (SAS Institute Inc., Cary, NC, USA), and $p$ values of $<0.05$ were considered statistically significant. Values are expressed as mean±SD.

3. Results

3.1. Characteristics of participants

Within the group of 475 postmenopausal women, the mean age was 60.9±7.2 years. One-third of the subjects were aged between 55 and 60 years, and 28.4% were aged $\geq 65$ years. The mean age at menopause was 51.8±5.9 years, and the average duration since the onset of menopause was 10.2±7.9 years. Approximately 15.8% ($n=75$) of women reported some history of ovarian-related surgery. The mean body weight was 57.9±8.9 kg, and the mean height was 153.6±8.7 cm, with a mean BMI of 24.5±3.3 kg/m². A total of 3.4% of women had a BMI of $<19.0$ kg/m² and 39.6% recorded a BMI of $>25$ kg/m². One-third (36.4%) were vegetarian. The mean BMI of vegetarians was significantly lower than that of non-vegetarians (23.9 vs. 24.8 kg/m², $p=0.0005$).

3.2. Spine mineral density

The mean BMDL by age group is shown in Fig. 1A. The mean BMD was 0.822±0.14 g/cm². The mean

![Fig. 1 — (A) Mean spinal bone mineral density by age; (B) proportion of osteopenia and osteoporosis according to dual-energy X-ray absorptiometry by age; (C) mean 10-year probability of osteoporotic fracture by age; (D) proportion of women considered to be at high risk of osteoporotic fracture by age.](image-url)
BMD_L was 0.879 g/cm² at the age of 50–55 years and diminished thereafter to 0.848 g/cm² for the 56–60-year age group. The mean BMD_L exhibited a marked decrease in subjects aged > 65 years. The second significant age-related decline was noted after an age of 70 years, with mean BMD_L values falling from 0.780 to 0.733 g/cm². BMD testing revealed that 37.2% (95% CI = 33.2%, 41.5%) of women had osteoporotic processes affecting the spine. The prevalence of osteoporosis increased with age (21.6% at 50–54 years, 28.8% at 55–59 years, 46.2% at 60–64 years, 58.4% at 65–69 years, and 62.9% at ≥ 70 years). The Mantel-Haenszel χ² test for trends produced a value of 33.8 (p < 0.001; Fig. 1B). The mean BMD_L was significantly lower among vegetarians (0.795 ± 0.14 g/cm²) than non-vegetarians (0.837 ± 0.14 g/cm²). The prevalence of osteoporosis was significantly higher among vegetarians (49.7%; 95% CI = 42.3%, 57.2%) than non-vegetarians (30.1%; 95% CI = 24.9%, 35.7%; Table 1).

### Table 1 — Prevalence of osteoporosis and estimated probability of an osteoporotic fracture* according to vegetarian status

<table>
<thead>
<tr>
<th>Vegetarian</th>
<th>No (n=302)</th>
<th>Yes (n=173)</th>
<th>χ² test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Results of lumbar BMD testing (DXA)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal bone density</td>
<td>68</td>
<td>22.5</td>
<td>31</td>
</tr>
<tr>
<td>Osteopenia</td>
<td>143</td>
<td>47.4</td>
<td>56</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>91</td>
<td>30.1</td>
<td>86</td>
</tr>
<tr>
<td>10-year probability of an osteoporotic fracture</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any major fracture &gt; 20% (%)</td>
<td>40</td>
<td>13.5</td>
<td>41</td>
</tr>
<tr>
<td>Hip fracture &gt; 3% (%)</td>
<td>52</td>
<td>17.2</td>
<td>44</td>
</tr>
</tbody>
</table>

*Probability of osteoporotic fracture was calculated using FRAX without BMD data. BMD = bone mineral density; DXA = dual-energy X-ray absorptiometry; FRAX = Fracture Risk Assessment Tool.

3.3. **Self-reported clinical risk factors**

The proportions of participants positive for various clinical risk factors included 18.1% with a history of prior fracture, 14.7% with a parental history of fracture, and 1.6% with a history of long-term oral glucocorticoid use. Among those patients with disorders causing secondary osteoporosis, 16.1% (n=53) had undergone early menopause (at the age < 45 years), while no participants had a history of type 1 diabetes, malnutrition, rheumatoid arthritis, or untreated chronic hyperthyroidism. Eight women reported being on steroid medications at the time of the study. There were no current smokers within the sample population, and only eight women had ever smoked. No participants reported consuming alcohol in excess of three units daily.

3.4. **The 10-year probability of osteoporotic fracture**

Since the femoral head but not spinal BMD was proven to be valid using the FRAX tool, we calculated the risk without BMD data. Of the variables that were inputted into FRAX, age, sex, body weight, height, and seven other clinical risk factors were entered and used to calculate individual fracture risk. The mean 10-year probability of a major osteoporotic or hip fracture was 13.8% (95% CI = 10.7%, 16.9%) and 2.2% (95% CI = 0.8%, 3.5%), respectively. A significantly higher risk was noted among more elderly women (Fig. 1C). The mean probability of a major osteoporotic fracture was 24.3% (95% CI = 15.6%, 35.0%) among women aged ≥ 70 years compared with 9.9% (95% CI = 2.5%, 17.3%) in women aged 55–59 years, and 15.7% (95% CI = 8.8%, 22.6%) in women aged 60–65 years. The mean probability of a hip fracture was 2.2% (95% CI = 0.6%, 5.04%) in the 60–69-year age group and 6.5% (95% CI = 0.4%, 12.6%) in women aged ≥ 70 years.

In total, 17.1% (95% CI = 14.1%, 20.9%) of women were at high risk (> 20%) of a major osteoporotic fracture and 20.3% (95% CI = 16.7%, 23.9%) were at high risk (> 3%) of a hip fracture over the next 10 years. Not surprisingly, the risk of osteoporotic fracture was higher among older women. Approximately one in five women aged 60–65 years were at high risk of osteoporotic fracture compared with that in one in two women aged ≥ 70 years (Fig. 1D).

Of the 99 women diagnosed with a normal bone density, 10% (95% CI = 8.4%, 15.9%) were at high risk of osteoporotic fracture. Among subjects who were evaluated as being osteopenic or osteoporotic in the bone-density tests, 13.6% (95% CI = 8.9%, 18.4%) and 24.8% (95% CI = 18.4%, 31.2%), respectively, were considered to be at high risk (Table 2). The mean probability of an osteoporotic fracture was significantly
higher among osteoporotic subjects diagnosed with spinal DXA \( (t\text{-}test, p<0.01) \) compared to those with normal bone density. Vegetarians were found to have a higher risk of osteoporotic fracture compared to non-vegetarians. The proportion of high risk of a major osteoporotic fracture was 23.7% and that of the hip was 25.3% among vegetarians (Table 1).

### 4. Discussion

In this study, approximately one-third of postmenopausal women were diagnosed with osteoporosis by spinal DXA, with a trend toward an increasing prevalence with increasing age. By utilizing several clinical risk factors, we found that the estimated 10-year probability of osteoporotic fracture also increased with age. Fracture risk was substantially higher among the elderly. A greater fracture risk was also noted among those diagnosed with osteopenia or osteoporosis. Based on these findings, we recommend the application of the Caucasian risk profile to calculate the absolute fracture risk in Taiwanese women. At present, screening for osteoporosis is not covered by the current health policies in Taiwan. Bone-density examinations are limited to individuals who have been diagnosed or received treatment for osteoporosis. Therefore, physicians may need to use other tools for initial risk assessments. The tool of osteoporosis self-assessment in Asians (OSTA), based on clinical variables such as weight and age, has been developed \( (19) \). The feasibility of using the OSTA was examined in our previous study \( (20) \). Using FRAX, the fracture risk is now easily assessable in a clinical setting. Improved assessment of fracture risk, combined with tailored therapies for at-risk patients, is necessary to increase the proportion of these patients receiving appropriate bone-sparing therapies \( (21,22) \). Our findings suggest that age and BMI can simultaneously be used to assess the osteoporosis and fracture risk, if no information on other clinical risk factors is available.

Although the probability may be underestimated, it may be helpful in providing a rough estimation during consultation to guide women in making a decision of whether to pay for a DXA examination or undergo treatment.

The prevalence of other clinical risk factors for osteoporosis such as smoking, excessive alcohol consumption, chronic steroid use, and secondary osteoporosis varies among different populations. In the present study, 16.1% of women had an early onset of menopause. In Taiwan, it is estimated that approximately one-third of all women will have had a hysterectomy by the age of 55 years, and that 20.2% of these will have been for inappropriate reasons \( (23) \); it is unknown whether an oophorectomy was simultaneously performed. Further studies are required to determine the causes of early menopause in Taiwanese women. In addition, postmenopausal women who are naturally or surgically rendered menopausal should be assessed.

The term “previous fractures” refers to fractures arising spontaneously or from trauma, which in a healthy individual would not result in a fracture. Parental hip fractures refer to a history of hip fracture in the subject’s mother or father. In our study, one in five women reported having a history of a previous fracture, and one in seven had a history of parental fracture. The high proportion of previous or parental fractures raised some concerns. It is possible that these findings were affected by recall bias or the participants’ misunderstanding of the questions. Since our data were collected before the FRAX tool was made public, we could not clarify our questions with WHO definitions. We suggest that future studies should be more cautious about the definitions of these questions and provide clarification of the response options.

BMD accounts for approximately 80% of the variance in bone strength \( (24) \), and is an important predictor of fractures. Bone fracture risk significantly increases when the BMD falls below 1g/cm\(^2\) \( (25) \).

### Table 2 — Mean age, body mass index, and probability of fracture from results of a bone mineral density test*  

<table>
<thead>
<tr>
<th>Results of the bone mineral density test</th>
<th>Normal ((n=99))</th>
<th>Osteopenia ((n=199))</th>
<th>Osteoporosis ((n=177))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (yr)</td>
<td>58.0 ± 5.8</td>
<td>60.4 ± 7.1</td>
<td>63.2 ± 7.2</td>
</tr>
<tr>
<td>Mean body mass index (kg/m(^2))</td>
<td>25.1 ± 3.6</td>
<td>24.7 ± 3.3</td>
<td>25.9 ± 3.1</td>
</tr>
<tr>
<td>Mean bone mineral density (g/cm(^2))</td>
<td>1.021 ± 0.1</td>
<td>0.848 ± 0.1</td>
<td>0.681 ± 0.1</td>
</tr>
<tr>
<td>Mean probability of a major osteoporotic fracture (%)</td>
<td>11.4 ± 7.1</td>
<td>15.0 ± 8.2</td>
<td>16.0 ± 9.1</td>
</tr>
<tr>
<td>Mean probability of a hip fracture (%)</td>
<td>1.4 ± 1.6</td>
<td>1.9 ± 2.4</td>
<td>2.9 ± 3.0</td>
</tr>
<tr>
<td>Probability of a major osteoporotic fracture &gt;20% (%)</td>
<td>10 ± 10.1</td>
<td>27 ± 13.6</td>
<td>44 ± 24.7</td>
</tr>
<tr>
<td>Probability of a hip fracture &gt;3% (%)</td>
<td>11 ± 11.1</td>
<td>27 ± 13.6</td>
<td>58 ± 32.8</td>
</tr>
</tbody>
</table>

* \( t\text{-}test \) was used to compare differences between subjects diagnosed with and those without osteoporosis (normal and osteopenia); all \( p \) values were <0.05. SD = standard deviation.
In Taiwan, a previous prospective study demonstrated a four-fold increase in the risk of mild trauma fractures in subjects below that fracture threshold (26). In the present study, the mean spinal BMD was relatively low, and approximately 80% of subjects were diagnosed with osteopenia or osteoporosis by spinal DXA. These findings show that a substantial proportion of our subjects were at risk of osteoporotic fracture. Consequently, two questions were raised regarding how this health concern should be addressed: which groups should receive treatment and what changes need to be made to current policies? Recent clinical guidelines recognize the inadequacy of BMD alone as the determinant of an intervention threshold and they have proposed the use of different BMD values along with other important risk factors in determining levels of intervention. Therapy is generally recommended for all postmenopausal women with a low T-score value and for those with other risk factors present. Based on guidelines from the Taiwanese Osteoporosis Association (27) and the National Osteoporosis Foundation (NOF) (18), therapy is recommended in postmenopausal women with a T-score of <−1.0 in the presence of one or more clinical risk factors. Also according to the NOF, treatment should be initiated in postmenopausal women if the 10-year probability of hip fracture is >3% or if the 10-year probability of a major osteoporotic fracture is >20%. We found that approximately 15–20% of women aged 60–69 years and 80% of women aged ≥70 years should receive treatment. However, currently, medical treatment for the primary prevention of osteoporosis is not subsidized in Taiwan. In addition, there is limited evidence supporting the efficacy of medical treatment of osteoporosis in Taiwanese women. Since the proportion of the aging population is increasing rapidly, public health policymakers and researchers should devote more attention to this issue.

Since fracture incidence varies by age, sex, race, and geographic region, the FRAX algorithm must be calibrated to different districts using local hip fracture and mortality rates. External validation of the predictive accuracy needs to be carried out and further studied in Taiwan. FRAX was introduced to the public in 2008, and therefore there are limited reports of the predictive value of this tool. Its validity needs to be further assessed with longitudinal studies in different countries. In addition, significant factors associated with falls or low bone mass, such as type 2 diabetes, cardiovascular disease, use of hormone replacement therapy, menopausal symptoms, and use of antidepressants were not taken into account by the FRAX. The clinical use of this tool should be combined with detailed clinical risk assessments. Currently, it can be used as a convenient tool for risk assessment of osteoporotic fractures despite concerns about its accuracy. In our study, participants underwent a medical checkup, and other clinical risk factors such as type 1 diabetes, untreated long-standing hyperthyroidism, chronic malnutrition, and chronic liver diseases were not found. Therefore, the estimation of the probability of osteoporotic risk may be more valid than merely a self-reported assessment.

There were several limitations of our study. First, participants in this study were mainly volunteers and members of the Buddhist Tzu Chi Relief Foundation and generally represented women in the community who have a healthy lifestyle. Our sample was from one hospital and one-third of the women were vegetarians. The effect of a vegetarian diet on bone health is unclear. Our results were also limited to patients undergoing checkups at the hospital. Therefore, the findings cannot be directly applied to the general population. Second, information about lifestyle, reproductive history, previous fracture, and parental hip fracture was self-reported and consequently was subject to recall bias. Since the risk estimation tools used were derived with data from Caucasian females, it is likely that the calculated risk may differ for Taiwanese females. Further studies need to evaluate the application of FRAX in Taiwanese women.

In conclusion, osteoporosis is common among postmenopausal women, and fracture prevention strategies and research should be prioritized as the Taiwanese population ages. The risk of osteoporotic fracture needs to be determined and followed up, particularly among older women and vegetarians. Ongoing studies of the accuracy and feasibility of the FRAX algorithm are crucial for its clinical application.

References

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