Strategies for the Prevention of Hip Fracture

Margaret Gourlay, MD, Florent Richy, MSc, Jean-Yves Reginster, MD, PhD

Hip fractures are associated with 10% to 20% excess mortality in the first year and cause functional disability in most survivors. An estimated 17% of white women in the United States will sustain a hip fracture after the age of 50 years. Despite the availability of evidence-based guidelines for hip fracture prevention, routine screening and preventive measures have not been incorporated into standard primary care practice. Many physicians lack adequate knowledge to initiate bone mineral density testing and treatment with preventive medications to decrease the incidence of osteoporosis and fractures. Furthermore, patients are less likely to request information about bone health than about diseases for which systematic screening and prevention protocols have been established. This review describes preventive measures to decrease hip fracture in postmenopausal women, including screening by bone mineral density testing, risk factor assessment, and chemoprevention. Existing guidelines are summarized, and dilemmas regarding their implementation are discussed. Am J Med. 2003;115:309-317. ©2003 by Excerpta Medica Inc.

ONE IN 6 WHITE WOMEN IN THE UNITED STATES WILL SUSTAIN A HIP FRACTURE AFTER THE AGE OF 50 YEARS (1). In 1995, hip fractures led to approximately 300,000 hospitalizations, resulting in direct medical expenditures of $8.6 billion for inpatient care, $3.9 billion for nursing home care, and $1.3 billion for outpatient services (2). The Third National Health and Nutrition Examination Survey reported that osteoporosis at the hip, a predictor of hip fracture risk, affects more than 6 million women in the United States, and osteopenia affects up to an additional 17 million (3). Considering the potential mortality and morbidity in an aging population, the Healthy People 2010 Initiative included osteoporosis among its 28 focus areas (4).

About three quarters of all hip fractures occur in postmenopausal women, and most research has focused on postmenopausal women aged 60 years or older. For this reason, our review focuses on strategies for preventing hip fracture in this group of patients. Because there are insufficient data from controlled clinical trials on hip fracture risk in nonwhite women, the National Osteoporosis Foundation recommends that the risk factors currently identified for white women be used for others on an individual basis to determine the need for bone density testing and treatment (5).

PREVENTION STRATEGIES

Screening

Bone mineral density testing to detect osteoporosis and the assessment of risk factors have been studied as approaches to screening in women at high risk of hip fracture. There is limited evidence regarding the potential use of newer testing methods, such as quantitative ultrasound, and bone turnover markers, in screening.

Bone mineral density testing. Bone mineral density is reported using two types of scores. The T-score is a standard deviation measurement that compares the patient’s bone mineral density with the mean value in a reference population of young healthy adults. It is calculated using the following formula: $T\text{-score} = \frac{(\text{bone mineral density of participant–mean bone mineral density of reference population})}{\text{standard deviation of bone mineral density of reference population}}$ (6). By World Health Organization (WHO) criteria (7), osteoporosis is defined as a T-score $\leq -2.5$ at any site, and osteopenia as a T-score between −1 and −2.5 at any site. The Z-score compares the patient’s bone mineral density with an age-matched reference population. This score is helpful in elderly patients, because low bone density values become more prevalent with increasing age.

T-scores measured by dual-energy X-ray absorptiometry have been validated against fracture outcomes. Central dual-energy X-ray absorptiometry, which measures bone density at the lumbar spine and hip, is the preferred test because femoral bone density is a better predictor of hip fracture risk than bone density at other sites (8). Peripheral dual-energy X-ray absorptiometry (at the distal radius, heel, or finger) was shown to be predictive of fractures in a study of postmenopausal women aged 50 years or older who had been recruited from primary care practices in 34 states (9); however, peripheral measures were not compared with central dual-energy X-ray absorptiometry values.

In September 2002, the United States Preventive Ser-
vices Task Force issued a recommendation that all women aged 65 years or older, as well as women aged 60 to 64 years who are at increased risk of osteoporotic fractures, be screened routinely for osteoporosis using bone density testing (grade B recommendation) (10). This recommendation was based on a systematic review of 1248 articles selected from an initial 10,174 English-language citations from MEDLINE (1966 to May 2001), HealthSTAR (1975 to May 2001), the Cochrane databases, supplemental searches, and expert recommendation. The report identified no studies demonstrating the effectiveness of screening in reducing osteoporotic fractures. Most of the data were collected from women in their late 60s or older. Notably, a meta-analysis of 23 publications from 11 prospective cohort studies showed the pooled relative risk of hip fracture to be 2.6 (95% confidence interval [CI]: 2.0 to 3.5) per 1 SD decrease in femoral neck bone density (11). Assuming this relation between fracture risk and bone density, the relative risk of hip fracture of a patient with a T-score of −1 would be 1.65, which would correspond to a lifetime risk of 28% to 33% depending on age (12).

The Task Force Evidence Review presented screening outcomes based on age-specific prevalence rates of osteoporosis, with an assumed 70% adherence rate based on reports from clinical trials. The number needed to screen to prevent one hip fracture ranged from 7446 in women aged 50 to 54 years to 143 in women aged 75 to 79 years, whereas the number needed to treat to prevent one hip fracture was 227 in the 50- to 54-year-old group and 41 in the 75- to 79-year-old group. These estimates were based on the following assumptions: risk reduction of 37% for hip fracture and 50% for vertebral fracture consistent with trials of bisphosphonates, and estimated adherence rate of 70% based on reports of adherence and side effects from treatment trials, assuming less optimal adherence in the general population.

Risk factor assessment. Risk factor assessment has been studied as a means of enhancing the predictive value of bone density (13,14). The World Health Organization Collaborating Center for Public Health Aspects of Osteoarticular Disorders in Liege, Belgium, tested the use of a 10-item prescreening questionnaire for 3998 subjects aged 20 years or older who were referred for bone density measurement at an outpatient osteoporosis center (15). All patients underwent prescreening and bone density testing (gold standard test); a score of ≥1 (one or more osteoporosis risk factors) was considered a positive result. If the questionnaire had been applied only to patients aged 61 years or older, the positive predictive value for osteoporosis at the total hip would have been 15% and the negative predictive value would have been 93%. The prescreening strategy in this group of older patients would reduce overall screening costs by 23% by excluding patients with a low likelihood of osteoporosis.

An analysis of four osteoporosis risk assessment tools found that all methods predicted low bone mass in postmenopausal women equally well (16). The tools were applied to data from two studies in the United States and two in The Netherlands. Specificity for identifying T-scores meeting WHO criteria for osteoporosis ranged from 37% to 58% (depending on the risk instrument) when sensitivity was approximately 90%. The Osteoporosis Self-Assessment Tool, a simple index based on age and weight (0.2[age−weight], where a score ≤−1 denotes higher risk and >−1 denotes low risk), was the easiest to calculate and performed as well as more complex measures.

Other potential screening methods. Quantitative ultrasound is a radiation-free method of measuring bone characteristics that may relate more to quality than to density. Some parameters (e.g., broadband ultrasound attenuation and the speed of sound of the calcaneus) have been shown to be independent predictors of fractures in older women (17,18). However, because treatment studies of fracture have relied on hip dual-energy X-ray absorptiometry rather than quantitative ultrasound, this method has not been used as a standard for screening or diagnosis.

The United States Preventive Services Task Force assessed the potential for bone biochemical turnover markers (alkaline phosphatase [serum total and bone specific], serum osteocalcin or bone Gla protein, and two propeptides of type I procollagen) in bone mineral density screening (19). These markers were not found to be associated with an increased risk of fracture. Studies correlating marker levels and bone loss did not show a trend.

Benefits and Disadvantages of Screening

Screening could potentially decrease the suffering associated with hip fractures, the costs associated with hospitalization, and the disability and long rehabilitation periods after hospital discharge. Screening to detect and treat high-risk patients may prevent the cascade of declining health after an incident fracture.

However, the benefits of screening must also be weighed against its potential harms. Patients with false-positive tests may receive inappropriate treatment. Some medications have serious adverse effects. For example, hormone replacement therapy was considered a safe and cost-effective first-line therapeutic agent for osteoporosis, but was later associated with adverse events due to chronic use (20,21). There is also a potential for misallocation of resources if more lives could be saved or improved by better management of other diseases.

Chemoprevention

Chemopreventive strategies to reduce hip fractures focus on the prevention and treatment of osteoporosis. Preventive measures involve prescribing medications in high-
Calcitonin. Calcitonin is not considered a first-line agent for osteoporosis treatment, largely owing to limitations in a randomized controlled trial that tested its efficacy in preventing fractures (29). A 37% decrease in the risk of vertebral fracture was seen in patients taking 200 IU of salmon calcitonin nasal spray, but there was no notable decrease in those taking 400 IU/d. Interpretation of these results is difficult because of the lack of dose response, partial unblinding of the study, and the high dropout rate (59%). Still, intranasal calcitonin can be a useful adjunct to other treatment agents because it has an analgesic effect after vertebral fracture.

Bisphosphonates. Alendronate and risedronate are first-line agents for the prevention and treatment of osteoporosis. A randomized placebo-controlled trial of alendronate showed a 59% reduction in vertebral fractures after 12 months (P <0.001) and a 53% reduction in hip fractures after 18 months of continuous dosing (P = 0.01) (30). Similarly, a trial of risedronate demonstrated a significant reduction in hip fracture risk (relative risk \[RR\] = 0.7; 95% CI: 0.6 to 0.9) after a mean of 2 years of therapy (31). The overall efficacy of risedronate was primarily due to a reduction in hip fractures in women aged 70 to 79 years who had osteoporosis and vertebral fractures at baseline (RR = 0.4; 95% CI: 0.2 to 0.8). No effect was seen in women aged 70 to 79 years who had low bone density and no prevalent fractures, or in women aged 80 years or older. Meta-analyses of alendronate and risedronate confirmed these findings (32); the numbers needed to treat during 2 years for a high-risk population (based on bone mineral density) were 72 (95% CI: 61 to 99) for alendronate and 96 (95% CI: 75 to 151) for risedronate.

Minor gastrointestinal adverse effects occur in up to one third of women taking bisphosphonates, but serious adverse effects, such as esophageal ulceration or perforation, are very rare (33).

Selective estrogen receptor modulators. A meta-analysis of seven randomized trials of raloxifene demonstrated a reduction in vertebral fractures, but not nonvertebral fractures (34). Unlike estrogen, raloxifene has been associated with a decreased risk of breast cancer (35) and a decreased risk of cardiovascular events in women with increased cardiovascular risk at baseline (36). Raloxifene may cause vasomotor symptoms rather than alleviate them. It is associated with a risk of thromboembolism similar to estrogen (37).

Hormone replacement therapy. An analysis of 1997 and 1998 National Ambulatory Medical Care Survey data showed that estrogen replacement therapy was prescribed, provided, or continued in 79% of 26.2 million ambulatory care visits associated with osteoporosis medication management in women aged 40 years or older (38). Since then, new data on the harms of long-term hormone replacement therapy have been publicized. In 2002, the Women’s Health Initiative reported increases in cardiovascular events, thromboembolism, and breast cancer risk in women taking an estrogen-progestin com-
<table>
<thead>
<tr>
<th>Drug</th>
<th>Indications</th>
<th>Route and Dose</th>
<th>Adverse Effects and Risks</th>
<th>Efficacy to Reduce Fractures</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate</td>
<td>Prevention</td>
<td>Oral, 5 mg/d, or 35 mg once weekly</td>
<td>Abdominal pain, nausea, dyspepsia, esophageal ulcer (rare)</td>
<td>Vertebral, nonvertebral,</td>
<td>Vertebral, nonvertebral, including hip</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>Oral, 10 mg/d, or 70 mg once weekly</td>
<td></td>
<td>Vertebral, nonvertebral,</td>
<td></td>
</tr>
<tr>
<td>Risedronate</td>
<td>Prevention</td>
<td>Oral, 5 mg/d, or 35 mg once weekly</td>
<td>Abdominal pain, nausea, dyspepsia, esophageal ulcer (rare)</td>
<td>Vertebral, nonvertebral,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>Oral, 5 mg/d, or 35 mg once weekly</td>
<td></td>
<td>Vertebral, nonvertebral,</td>
<td></td>
</tr>
<tr>
<td>Raloxifene</td>
<td>Prevention</td>
<td>Oral, 60 mg/d</td>
<td>Deep vein thrombosis, pulmonary embolism, vasomotor symptoms, leg cramps</td>
<td>Vertebral</td>
<td>Decreases breast cancer risk, may decrease risk of cardiovascular events in some patients</td>
</tr>
<tr>
<td>Parathyroid hormone</td>
<td>Treatment</td>
<td>Oral, 60 mg/d</td>
<td>Osteosarcoma (in animal studies), hypercalcemia</td>
<td>Vertebral, nonvertebral</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>Parenteral, 20 μg/d by subcutaneous injection</td>
<td></td>
<td>Vertebral, nonvertebral</td>
<td></td>
</tr>
<tr>
<td>Calcitonin</td>
<td>Treatment</td>
<td>Intranasal, 200 IU/d (alternating nostrils)</td>
<td>Nasal irritation, rhinitis</td>
<td>Vertebral</td>
<td>Analgesic effect after vertebral fracture</td>
</tr>
<tr>
<td>Estrogen, estrogen with progestin</td>
<td>Prevention</td>
<td>Oral, 0.625 mg conjugated equine estrogen ± 2.5 medroxy-progesterone acetate/d</td>
<td>Vaginal bleeding, breast tenderness, risk of breast cancer, deep vein thrombosis, pulmonary embolism</td>
<td>Vertebral ± hip</td>
<td>FDA label warning issued January 9, 2003</td>
</tr>
</tbody>
</table>

FDA = Food and Drug Administration.
tion for primary prevention, and the data safety monitoring board stopped the trial early (20). A smaller ongoing arm has enrolled women who have had hysterectomies and are using estrogen alone; this cohort has not reported the same level of adverse outcomes as of mid-2003. In light of these data, the United States Preventive Services Task Force issued a general recommendation against the routine use of estrogen and progestin for the prevention of chronic conditions in postmenopausal women (grade D recommendation), and concluded that the evidence was insufficient to recommend or warn against the use of unopposed estrogen for chronic disease prevention (grade I recommendation) (39). Women taking estrogen-progestin in the Women’s Health Initiative study had a significantly lower risk of hip fracture (hazard ratio = 0.66; unadjusted 95% CI: 0.45 to 0.98; adjusted 95% CI: 0.33 to 1.33) compared with the placebo group. Despite this finding, the Task Force encourages clinicians to discuss with their patients alternative strategies for preventing osteoporosis and fractures. A 2003 trial showed that combination therapy with hormone replacement and alendronate greatly improved bone density at the spine and total hip as compared with monotherapy with either agent (40). However, this study was not adequately powered to examine fracture as an outcome or to measure differences between treatment groups in the occurrence of rare, serious adverse events such as venous thrombosis.

Most management guidelines for osteoporosis have not been revised since the announcement of these findings. The implications for health care policy are uncertain regarding the safety of various forms of unopposed estrogen (e.g., conjugated equine estrogen, transdermal estrogen) for osteoporosis prevention and treatment, as well as regarding the management of patients who have taken estrogen or estrogen-progestin agents for extended periods without experiencing adverse consequences. A shift to increased use of agents such as bisphosphonates and selective estrogen receptor modulators is expected. A randomized controlled trial showed that a 10-mg daily dose of alendronate can increase or maintain bone mineral density after discontinuation of hormone replacement therapy (41).

Parathyroid hormone. Parathyroid hormone (teriparatide) was approved by the Food and Drug Administration in 2002 for the treatment of osteoporosis. Its efficacy was supported by a randomized trial in which 1637 postmenopausal women with prior vertebral fractures received 20- or 40-μg injections of parathyroid hormone daily for 17 to 18 months (42). Both treatment groups showed a notably lower risk of fractures. Women who received the 20-μg dose had 65% (95% CI: 45% to 78%) fewer vertebral fractures and 53% (95% CI: 12% to 75%) fewer nonvertebral fractures. Similarly, women who received the 40-μg dose had 69% (95% CI: 50% to 81%) fewer vertebral fractures and 54% (95% CI: 14% to 75%) fewer nonvertebral fractures.

Osteosarcoma has been observed in rats who had been exposed to high doses of parathyroid hormone for most of their lifespan (43), but not in humans.

Nonpharmacologic Prevention

Hip protectors may help to reduce the risk of fractures in nursing home residents who are at a high risk of falling (44,45), although some studies have not found these aids to be effective (46) and studies are often inconclusive owing to high rates of noncompliance. Multidisciplinary programs that include education, environmental modification, exercise programs, medication management, and provision of free hip protectors may also reduce falls and fractures among patients in residential care facilities (47).

GUIDELINES AND IMPLEMENTATION

A search of the National Guidelines Clearinghouse and the Cochrane Database in April 2003 revealed three guideline statements addressing the prevention of hip fracture and two statements addressing the prevention of falls (Table 2). Seven practice guidelines relating to osteoporosis screening or prevention and treatment were also identified (52–58). Table 3 summarizes the screening and management guidelines recommended by the National Osteoporosis Foundation (5).

Implementation

Despite the availability of evidence-based guidelines for the prevention of hip fractures and osteoporosis, implementation of preventive measures remains inadequate. Gallagher et al (59) surveyed 1500 women enrolled in an independent practice association model health plan regarding osteoporosis screening and counseling services. Only 12% of women aged 65 years or older had received bone mineral density testing; 34% of postmenopausal women with a history of fracture received testing, and 49% had ever discussed osteoporosis with their health care provider. Thus, even in a group of patients with excellent access to health care, screening was infrequent in patients with multiple risk factors and only half of the women had ever received preventive counseling.

Chemoprevention with calcium and vitamin D is feasible in many in the general population; however, this strategy is underused. Although only 50% to 60% of older adults meet the recommended calcium intake, fewer than 2% of total office visits involving women aged 40 years or older are associated with the use of calcium or vitamin D supplements (38).

Barriers to the Implementation of Guidelines

Limitations of supporting evidence. In the past, physicians may have been reluctant to implement guidelines
for hip fracture prevention because of concerns about the scope and quality of supporting evidence for clinical recommendations. Several of the guidelines were developed for specific patient populations (e.g., nursing home residents, patients living in other countries) and were not meant to be applied to all postmenopausal women in the United States. Although several guideline statements were based on systematic reviews, some were based on traditional reviews of the literature.

The second United States Preventive Services Task Force assessed screening for osteoporosis in postmenopausal women to be a C-level recommendation, that is, based on evidence available at that time, the balance of benefits and harms of screening was too close to justify a general recommendation (60). Subsequently, important data on the efficacy of bisphosphonates and selective estrogen receptor modulating agents were published, and large cohort studies provided new information regarding osteoporosis risk factors. Based on a systematic review and meta-analyses of observational trials and randomized controlled trials, the third Task Force promoted osteoporosis screening to a grade B recommendation in September 2002. The newer evidence and guidelines may prompt primary care physicians to be more receptive to systematic screening in women aged 65 years or older.

**Physician-related factors.** Several studies have shown that many physicians refrain from diagnosing and treating osteoporosis owing to limited knowledge about guidelines and testing methods. In a cross-sectional survey of primary care physicians (internists, geriatricians, and family physicians) at an urban community hospital (61), 72% of physicians never ordered bone densitometry. Self-reported barriers to use included cost, unfamiliarity with guidelines, uncertainty with clinical applicability, minimal effect on treatment decisions, and availability of testing facilities. A small study of primary care physicians and orthopedic surgeons reported that of 23 primary care physicians surveyed, 9 (39%) thought that bone density testing was unnecessary for treatment.

### Table 2. Guidelines for the Prevention of Hip Fractures and Falls

<table>
<thead>
<tr>
<th>Guideline (Reference)</th>
<th>Evidence Review</th>
<th>Target Population</th>
<th>Key Recommendations and Findings</th>
</tr>
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<tbody>
<tr>
<td><strong>CDC Recommendations</strong></td>
<td>Nonsystematic review using electronic databases</td>
<td>Women aged ≥65 years</td>
<td>Prevention of falls through community interventions, nursing-home interventions; injury prevention strategies.</td>
</tr>
<tr>
<td><strong>Scottish Intercollegiate Guidelines Network:</strong> Prevention and Management of Hip Fracture in Older People (49)</td>
<td>Systematic review of evidence available in electronic databases</td>
<td>Older people in Scotland at risk of or with hip fracture</td>
<td>Fall prevention and chemoprevention with calcium and vitamin D for patients with osteoporosis risk factors.</td>
</tr>
<tr>
<td><strong>Hip Protectors for Preventing Hip Fractures in the Elderly (44)</strong></td>
<td>Systematic review of all randomized or quasi-randomized controlled trials</td>
<td>Elderly people in nursing homes, residential care, or supported living at home</td>
<td>Occurrence of hip fractures in 2% (29/1313) for people wearing hip protectors vs. 6% (130/2099) in controls. Could not assess statistical significance.</td>
</tr>
<tr>
<td><strong>American Academy of Orthopedic Surgeons/American Geriatrics Society/British Geriatrics Society: Guideline for the Prevention of Falls in Older Persons (50)</strong></td>
<td>Systematic review of studies available in electronic databases, and via hand searches</td>
<td>Elderly people</td>
<td>Exercise (e.g., tai chi), environmental modification, medication review, and aids, such as canes, walkers, and hip protectors, recommended. Bone-strengthening medications and disease management.</td>
</tr>
<tr>
<td><strong>Barts and the London, Queen Mary’s School of Medicine and Dentistry: Guidelines for the Prevention of Falls in People Over Age 65 (51)</strong></td>
<td>Systematic review using Cochrane review criteria</td>
<td>Ambulatory people aged ≥65 years in the United Kingdom, living at home, in a residential home, or in a nursing home</td>
<td>Tailored exercise programs and tai chi training. Home-based assessments and medical assessments of people who fall. For high-risk residents in residential settings, risk assessment with referral to primary physician if needed.</td>
</tr>
</tbody>
</table>
and 4 (17%) thought that patient frailty was a barrier to testing (62). Moreover, if a bone density test shows an abnormal result, physicians still may not respond with appropriate interventions. A retrospective review of cases from a community teaching hospital found that for patients diagnosed with osteoporosis based on bone density studies, 48% underwent no further investigations to rule out secondary causes of osteoporosis and 11% received no therapy (calcium and vitamin D excluded) (63). Only 11% of patients of internists and 15% of patients of gynecologists were referred to specialists in metabolic bone diseases.

Patient-related factors. Most patients know less about hip fractures and osteoporosis than about other diseases that receive more media attention. Screening protocols for breast cancer and colon cancer are standard in most primary care clinics, and patients are likely to expect and ask for these tests. Because fewer patients request information about bone health, they are less likely to engage physicians in a discussion and receive preventive counseling.

Improving Implementation
Improving the implementation of evidence-based guidelines for hip fracture prevention is not easy. Physician education is important because many physicians are not familiar with these guidelines. Problem-based learning workshops using standardized patients may be an effective educational approach (64). Clinician-oriented bone density test reports can also teach physicians to interpret and use results appropriately. A randomized trial demonstrated that primary care physicians were more likely to understand the bone mineral density definition of osteoporosis and to modify pharmacologic treatment when they received longer clinical bone density test reports written by endocrinologists, as opposed to short technical reports without clinically relevant details (65).

Patient education can be accomplished through community interventions and increased media coverage. Increasing a patient’s knowledge of hip fracture risk can lead to increased physician-patient dialog, which may prompt a physician to consider bone density screening and counseling regarding bone health. A study of an active community education program demonstrated that patient education with resulting enhanced physician-patient dialog led to increased bone density test orders by physicians, whereas didactic lectures did not change physician behavior (66).

CONCLUSION
Despite the availability of evidence-based guidelines for the prevention of hip fractures, systematic screening and preventive interventions have not been incorporated into standard primary care practice in the United States. The reasons for the low level of implementation are largely modifiable, namely, by improving the education of physicians and patients to promote increased screening and appropriate physician response to bone density test results.

The third United States Preventive Services Task Force guidelines for bone density screening and the Women’s Health Initiative trial will have considerable effects on the practice patterns of primary care physicians. Health care policy will evolve as organizations revise outdated recom-
mendations based on new evidence on the effectiveness of osteoporosis screening and preventive interventions. Hopefully, these changes will stimulate physician-patient dialog, ultimately leading to better patient care.

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REFERENCES


