The effect of osteoporosis management on proximal humeral fracture

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Hypothesis and background: Proximal humeral fractures comprise 10% of fractures in the Medicare population. The effect, if any, of treating osteoporosis to prevent these fractures has not been determined. The primary objective is to determine the effectiveness of a systematic osteoporosis screening and treatment program on the hazard of developing a fracture over the treatment period. The secondary aim is to determine demographic risk factors.

Methods: This is a retrospective cohort study in a health care organization serving 3.3 million members. Individuals selected for dual-energy x-ray absorptiometry screening were (1) women aged 65 years or older; (2) men aged 70 years or older; and (3) individuals aged 50 years or older who have a history of fragility fracture, use glucocorticoids, have a parental history of hip fracture, have rheumatoid arthritis, use alcohol at a high rate, or are cigarette smokers. Treatment consisted primarily of pharmacologic intervention with bisphosphonates.

Results: Individuals diagnosed with osteoporosis had a hazard ratio of 7.43 for sustaining a fracture over the study period. Patients screened with dual-energy x-ray absorptiometry had a hazard ratio of 0.17 whereas those treated medically had a hazard ratio of 0.55 versus untreated controls. Risk factors that significantly increased the risk of a fracture developing included age, female gender, white race, diabetes mellitus, and history of a distal radius fracture.

Discussion and conclusion: Over the study period, screening and treatment for osteoporosis significantly decreased the hazard ratio for proximal humeral fracture. This information broadens the impact of such programs because current best practices are primarily based on prevention of spine and hip fractures.

Level of evidence: Level III, Retrospective Cohort Design, Treatment Study.

Keywords: Proximal humeral fracture; osteoporosis; fracture prevention; bisphosphonates; fragility fracture; DXA scan

Osteoporosis and secondary fragility fractures represent an increasing burden on society in terms of patient morbidity, lost productivity, and expense to the health care system.17,19,32 The value of osteoporosis screening and pharmacologic treatment to prevent hip and vertebral
compression fractures has been well described\textsuperscript{6,11,26,28} and, over time, has come to form the basis for modern recommendations for screening as well as pharmacologic intervention.\textsuperscript{23,34,37}

There are multiple pharmacologic and nonpharmacologic treatments for reducing the incidence of fragility fractures.\textsuperscript{39} Nonpharmacologic treatments include weight-bearing exercise,\textsuperscript{16} home safety measures, and balance training. Pharmacologic interventions such as vitamin D,\textsuperscript{4} calcium,\textsuperscript{9} calcitonin,\textsuperscript{8} and bisphosphonates\textsuperscript{17} focus on increasing bone mineral density (BMD). Bisphosphonates are the most commonly prescribed intervention for osteoporosis.

Proximal humeral fractures (PHFs) are a substantial cause of morbidity.\textsuperscript{31} Surveys of the US Medicare population found that fractures of the proximal humerus comprise 10\% of all fractures in individuals aged older than 65 years.\textsuperscript{2,3} In a registry of the entire Finnish population, the age-adjusted incidence of PHFs increased significantly from 1970 to 2002. Over a period of 30 years, the incidence increased by over 250\% in female patients and by over 340\% in male patients.\textsuperscript{20} The authors predicted that the incidence would continue to rise. Although the Finnish population may have limited generalizability, it illustrates the dramatic increase in PHFs in the developed world.

Accurate stratification of individuals at risk of PHFs is essential to avoid costly over- or under-treatment. Low BMD, increasing age, female gender, diabetes, white ethnicity, and previous insufficiency fracture have all been shown to be positively associated with the risk of PHF.\textsuperscript{24,30} Postmenopausal status and smoking are associated with other osteoporotic fractures but have not been conclusively linked with PHFs.

The primary aim of this population-based cohort study was to determine the effectiveness of an osteoporosis management program in decreasing the incidence of PHFs. The secondary aim was to establish the relevant demographic and clinical risk factors associated with these fractures.

**Materials and methods**

**Study design and setting**

We conducted a retrospective cohort study including all Kaiser Permanente Southern California (KPSC) enrollees who were aged 60 years or older as of January 1, 2002. KPSC is a not-for-profit community health care organization that provides care to approximately 3.3 million members. Integration of the insurance program, hospitals, and medical groups provides a “closed” study environment for population-based interventions. In 2002, KPSC implemented the Healthy Bones Model of Care, an interdisciplinary osteoporosis prevention and management program. This program identifies health plan members who are at risk of the development of osteoporosis and fragility fractures and provides them screening, prevention, and treatment options.

Members selected for dual-energy x-ray absorptiometry (DXA) screening are (1) women aged 65 years or older; (2) men aged 70 years or older; and (3) all individuals aged 50 years or older who (a) have a history of fragility fracture, (b) use glucocorticoids for 3 months or more at doses of 5 mg or greater, (c) have a parental history of hip fracture, (d) have rheumatoid arthritis, (e) use alcohol at a high rate (≥3 oz/d), (f) are cigarette smokers, and (g) have other causes of secondary osteoporosis. Members identified as being at increased risk are screened by DXA scan. Prevention and treatment options include screening for vitamin D deficiency and vitamin and mineral supplementation; use of evidence-based pharmacologic interventions; lifestyle changes, such as increased exercise and smoking cessation; and fall-reduction interventions, such as classes and fall-proofing homes.

**Study measures**

For each member of the cohort, we collected the following from electronic administrative and clinical data sources: (1) demographic information, including age, sex, and self-reported race/ethnicity; (2) enrollment information; (3) inpatient and outpatient encounter information, including diagnosis and procedure codes for each encounter; (4) claims information from outside providers; (5) referral information; (6) radiology records; and (7) pharmacologic treatments. We were able to extract diabetes status, osteoporosis status, osteoporosis screening status, and history of fragility fractures from inpatient and outpatient encounter data before cohort inception.

**Outcome measure**

For each subject, the first occurrence of a PHF occurring between 2002 and 2008 was identified by International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) discharge diagnosis codes 812.0 to 812.19. Fractures identified from the electronic records were verified and validated through chart review by the authors. Patients with a history of PHF before 2002 were excluded from the analysis.

**Exposure measure**

Two components of the osteoporosis management program were assessed for their association with hip fracture incidence: screening for osteoporosis and pharmacologic intervention for osteoporosis.

Patients were considered to have been screened for osteoporosis if they had a BMD test conducted during the study period, regardless of the BMD test results. Patients were considered to have received pharmacologic intervention for osteoporosis if they had been prescribed bisphosphonates, calcitonin, estrogens, selective estrogen receptor modulators, miscellaneous hormones, or sex hormone combinations. For patients who went on to sustain a PHF, the prescriptions must have predated the fracture by at least 6 months for the patient to have been considered exposed before the fracture.

**Covariates and potential confounders**

Age was categorized as 60 to 69 years, 70 to 79 years, and 80 years or older for descriptive purposes and was entered as a
continuous variable in the multivariate model. Race was a dichotomous variable (white vs nonwhite) because further delineation of racial data was not collected by the health plan during this study period.

Diagnosis of osteoporosis was identified from clinical data and hospital discharge data. Patients were classified as having osteoporosis if they had an ICD-9-CM discharge diagnosis recorded with code 733.0x (osteoporosis) or had a BMD test score indicating osteoporosis or low bone mass requiring treatment (lowest T-score < -2.5 from spine L1-L4, either femoral neck, or either total femur) any time during the study period.

Hospital discharge diagnosis codes were also used to identify fractures of the hip (ICD-9-CM code 820.xx) or distal radius (ICD-9-CM codes 813.4-813.54). These fractures must have occurred before the PHF to be considered a risk factor for PHF. As with the PHF outcomes, all reports of hip or distal radius fracture were validated by chart review.

Statistical analysis

Patient demographic and clinical risk factors were described using counts and proportions for categorical data and means or medians for continuous data. The $\chi^2$ test of proportions was used to compare the proportions of patients with incident PHFs by demographic categories, osteoporosis diagnosis categories, screening status for osteoporosis, and pharmacologic intervention for osteoporosis. All reported $P$ values are 2 sided with a statistical significance level set at $\alpha = .05$.

Kaplan-Meier curves were plotted to examine differences in time to PHF for subjects by screening and treatment status. Differences in survival curves were assessed for statistical significance using the log-rank test.

To estimate the associations between the osteoporosis management program indicators (pharmacologic treatment for osteoporosis and screening status for osteoporosis) and incident PHFs, we built a multivariable model using Cox proportional hazards methods, adjusting for age, race, sex, diabetes status, and history of hip or distal radius fracture. Subjects were censored in the analysis if they died or dis-enrolled from KPSC.

We also considered a priori the possibility that screening status and treatment status might interact in a way affecting the outcome. Therefore, we also built a multivariable model that included combinations of screening and treatment status, adjusted for the same covariates listed earlier.

Results

We identified 524,612 KPSC enrollees who were aged at least 60 years as of January 1, 2002. Overall, 1.0% of the cohort (n = 5,111) sustained a new PHF during the study period (2002-2008). At-risk patients not screened for osteoporosis had PHFs in greater proportions than did patients who had been screened by DXA scan (1.1% vs 0.8%, $P < .001$) (Fig. 1). PHFs were also more common among patients diagnosed with osteoporosis compared with those without the diagnosis (2.6% vs 0.7%, $P < .001$).

PHFs were significantly more common among women (1.4% vs 0.5% for men, $P < .001$; hazard ratio [HR], 3.13) and white patients (1.4% vs 0.6% for nonwhite patients, $P < .001$). The risk of fracture significantly increased in linear fashion after age 60 years (HR of 1.03 for every year of age >60 years). Fracture occurrence was most common in the oldest patients, with the highest rate among those aged 80 years or older (1.9%). In our study, whites had a significantly higher risk of PHFs, twice the risk (HR, 2.02) of all other ethnicities pooled together.

Both the screened group and the treated group were more likely to be female, to be white, to be diagnosed with osteoporosis, and to have had previous hip or distal radius fractures compared with the unscreened group and the untreated group, respectively (Table I). Considering screening and treatment jointly, however, we found some important differences among the 4 groups. The group that was both screened and treated was more likely to be female, to be white, to be diagnosed with osteoporosis, and to have a history of distal radius fractures compared with the other combinations of screening and treatment (Table II). Those who were treated but not screened were more likely than all other groups to have had a prior hip fracture (5.8%, n = 2,669).

Over the course of the study period, 0.9% of patients not treated with pharmacologic interventions for osteoporosis sustained incident PHFs (Fig. 2) compared with 1.2% of the treated group who had fractures ($P < .001$). The treated group sustained fractures less commonly than the untreated group until about 3.25 years into the study, at which time the treated group sustained more fractures. Finally, when we looked at screening/treatment combinations (Fig. 3), approximately 0.7% of the patients who were screened and untreated sustained PHFs. Those who were screened and treated had a similar experience early in the study period, but by approximately 3.5 years of follow-up, this group began sustaining more PHFs than did the screened and untreated group (1.0% and 0.7%, respectively). The unscreened but treated group sustained incident PHFs most frequently throughout the study period, with 2.9% of this group ultimately having a fracture (Fig. 3). A diagnosis of osteoporosis increased the hazard of fracture (HR, 7.43; 95% confidence interval [CI], 6.88-8.02) more than any other risk factor analyzed.

Adjusting for age, sex, race, history of diabetes, history of hip or distal radius fracture, and diagnosis of osteoporosis, we found that having been screened for osteoporosis was strongly associated with a reduction in the instantaneous risk of incident PHF relative to the unscreened group (HR, 0.17; 95% CI, 0.16-0.19) (Table III). Receipt of pharmacologic intervention for osteoporosis was also strongly associated with a reduction in the risk of PHFs relative to patients who had not received medication treatment (HR, 0.55%; 95% CI, 0.51-0.59) (Table III).

Having a history of hip fracture was not associated with risk of sustaining an incident PHF (HR, 1.01; 95% CI, 0.89-1.14), although prior distal radius fracture significantly increased the hazard of subsequent hip fracture (HR, 1.33; 95% CI, 1.17-1.51) (Table III).
In the multivariable model that included discrete combinations of screening and treatment status, we found that compared with the unscreened and untreated group, all other groups were at substantially reduced risk of incident PHFs (Table III), with screening and treatment combined being most strongly protective against PHFs (HR, 0.09; 95% CI, 0.08-0.10) (Table III).

**Discussion**

In this study, fractures occurred at twice the rate in female patients, and fracture risk increased with age. Patients with osteoporosis were over 7 times more likely to sustain a PHF compared with patients who did not carry the diagnosis. Pharmacologic intervention for osteoporosis cut the rate of PHF almost in half relative to patients who had not received medication treatment.

The group screened for osteoporosis had a dramatically reduced rate of fracture versus the unscreened group. In multivariate models, screening and treatment were each independently associated with substantial reductions in PHF risk. In addition, the group that underwent both screening and treatment had the greatest reduction in risk relative to unscreened subjects.

**Demographic findings**

Our findings regarding age, gender, and racial differences in fracture incidence are in line with published literature of risk factors for osteoporotic fractures in the hip and spine. Specifically, the risk of hip fracture increases exponentially at about age 65 years, whereas spine and shoulder fractures have a more linear risk curve. All 3 of these fractures have a propensity for female patients; about 70% cases occur in women. Finally, white...
persons sustain hip and spine fractures at about double the rate of other ethnicities pooled together, a finding that was consistent in our shoulder data. The hip and spine literature has been well established over the past 2 decades, and given the findings of this study, we can consider the shoulder as part of this group of diagnoses in terms of demographic risk factors.

Effect of screening and treatment

Our osteoporosis management program showed a significant decrease in PHF risk by 45% (HR, 0.55) for patients who received pharmacologic osteoporosis treatment. This effect is consistent in magnitude with the hip literature on bisphosphonate efficacy. McClung et al25 conducted a randomized trial of risedronate versus placebo in elderly women with osteoporosis and risk factors for fracture and observed a relative risk of fracture of 0.6 (95% CI, 0.4-0.9) in the treated group compared with untreated individuals.

In our cohort, it would appear that the protective effect of treatment was most profound in the first 3 years (1,100 days) of treatment, at which point the treated group began having more fractures than the untreated group (Fig. 2). The reason for this is that at the beginning of the study, there were few patients in the treatment group. As the observational period progressed, larger numbers of individuals were treated and for more time. It is possible that the treated group was at increased risk of fracture versus the untreated group because of noncompliance, less physical activity, lower bone density, poor response to treatment, or other risk factors and eventually outstripped the untreated group in terms of fracture rate.

The rate of evaluation and management improves when subspecialty and primary care providers work in a coordinated fashion. A study in the Geisinger Health System

<table>
<thead>
<tr>
<th>Table II</th>
<th>Demographic data and clinical characteristics of cohort at risk of sustaining incident PHFs, by jointly considered screening and treatment status for osteoporosis, 2002-2008</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Unscreened [n (%)]</td>
</tr>
<tr>
<td></td>
<td>Untreated</td>
</tr>
<tr>
<td>Total</td>
<td>301,824 (57.4)</td>
</tr>
<tr>
<td>Female</td>
<td>94,913 (31.5)</td>
</tr>
<tr>
<td>White</td>
<td>118,121 (39.1)</td>
</tr>
<tr>
<td>Age 60-69 y</td>
<td>177,985 (59.0)</td>
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<tr>
<td>Age 70-79 y</td>
<td>84,750 (28.1)</td>
</tr>
<tr>
<td>PHF</td>
<td>70,604 (23.4)</td>
</tr>
<tr>
<td>Previous hip fracture</td>
<td>3,304 (1.1)</td>
</tr>
</tbody>
</table>

Figure 2 Unadjusted time to incident PHF for a cohort of persons aged 60 years or greater comparing those who received pharmacologic treatment for osteoporosis with untreated individuals.
showed that a comprehensive, coordinated osteoporosis disease management program leads to a decrease in hip fracture rate and decreases the costs of care.\textsuperscript{29} In a study population of 22,171 women aged older than 55 years, the age-adjusted incidence rate of hip fractures changed from 7.9 to 5.1 per 1,000 person-years over a 5-year period after implementation of the program.

The medical and financial rationale behind modern osteoporosis screening programs is largely based on cost-benefit analysis from hip and spine fracture data.\textsuperscript{34,37,38} Although we did not specifically examine costs, adding the benefit of reducing the expense and morbidity of PHF rates by pharmacologically treating osteoporosis further increases the benefit of these programs for the same cost. Despite clear benefits, implementation of screening and treatment guidelines has been inconsistent. Multiple authors have reported that the rate of evaluation and management of osteoporosis remains poor after fragility fractures.\textsuperscript{10,13}

**Limitations**

This study has limitations that must be considered. We collected the data retrospectively from large administrative databases, which have limitations regarding capturing fracture cases, screening status, disease severity, and interventions. The inclusion of all individuals in the insurance plan reduced selection bias common in a retrospective cohort study design.

The subjects in this study were not randomized to screening or treatment groups but were enrolled based on risk factors for osteoporosis or fragility fractures, including a prior hip or distal radius fracture. This potentially introduces bias as to the type of patients who were screened. It is unlikely that the act of screening itself reduces the fracture rate; rather, the patients who were screened likely had a higher fracture risk than unscreened patients. The overall effect of treatment was similar in screened and unscreened patients (the HR was 0.55 for treatment in the unscreened group, and the difference between the HR of screened and treated of 0.09 and the HR of screened and untreated of 0.19, which is 0.47, was near the 0.55 HR observed in the untreated group). The main finding of this study is that pharmacologic treatment is effective at reducing PHFs.

Although multivariable models adjust for known risk factors for osteoporosis and fragility fracture, there may still be bias as a result of both unmeasured potential confounders and confounding by indication, where we have not adequately adjusted for other factors related to both the receipt of screening or treatment and the likelihood of fracture.
The concept of time is another consideration. “Time zero” in this study is the beginning of the observation period, not the day of treatment or fracture. Thus, time points do not correlate to a clinical event and should not be used to make clinical decisions about duration of treatment or risk of fracture over time.

Our results regarding pharmacologic intervention must be interpreted with caution because we did not analyze subgroups of pharmacologic osteoporosis treatments separately by medication class; patients were prescribed bisphosphonates, calcitonin, estrogens, selective estrogen receptor modulators, and other hormone combinations. The use of bisphosphonates became standard for treatment of osteoporosis within KPSC over the past decade; the percentage of patients taking hormone derivatives is low. It is also possible that patients received pharmacologic treatment outside KPSC that would not have been recorded in the pharmacy records. Given the vertically integrated model of health care delivery, the number of patients obtaining medication outside KPSC is low and is unlikely to affect the overall result. Finally, we did not address the monitoring of medication compliance in this study.

Conclusions

Given the sizable economic, physical, and emotional impact of PHFs on patients specifically and the health care system broadly, it is imperative that we establish methods to adequately screen and treat at-risk individuals. This study establishes that risk factors for PHFs include age over 60 years (HR, 1.03 per annum), female gender (HR, 3.13), diabetes status (HR, 1.54), persons diagnosed with osteoporosis (HR, 7.43), and white race (HR, 2.02).

This study’s main findings are that osteoporosis screening and treatment each significantly reduce the risk of PHFs. Coordinated screening and treatment reduce fracture risk even more. It is possible to screen and treat a large population.

We strongly support the establishment of osteoporosis management programs for the systematic screening and treatment of osteoporosis to help prevent PHFs. Further study will be necessary to determine how reducing PHF-related morbidity will improve the value and cost-effectiveness of osteoporosis management programs, which have historically not taken the shoulder into consideration.

Disclaimer

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References


