Clin Orthop Relat Res (2011) 469:1900–1905
DOI 10.1007/s11999-011-1780-7

SYMPOSIUM: AAOS/ORS/ABJS MUSCULOSKELETAL HEALTHCARE DISPARITIES RESEARCH SYMPOSIUM

Gender Differences in Osteoporosis and Fractures

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Published online: 25 January 2011

Abstract

Background Osteoporosis is generally thought of as a "woman's disease" because the prevalence of osteoporosis and the rate of fractures are much higher in postmenopausal women than in older men. However, the absolute number of men affected by osteoporosis and fractures is large, as at least 2.8 million men in the United States are thought to have osteoporosis.

Questions/purposes The purposes of this review are to (1) highlight gender differences in osteoporosis and fracture risk, (2) describe disparities in treatment and outcomes after fractures between men and women, and (3) propose solutions to reducing disparities in treatment and prevention.

Methods A literature survey was conducted using MEDLINE with a variety of search terms and using references from the author's personal collection of articles. A formal search strategy and exclusion criteria were not employed and the review is therefore selective.

Where are we now? Postmenopausal women have a higher prevalence of osteoporosis and greater incidence of fracture than older men. Despite the higher fracture risk in postmenopausal women, older men tend to have worse outcomes after fracture and poorer treatment rates, although less is known about the disease course in men. Multifaceted interventions to improve the screening and treatment for osteoporosis were recently developed.

Where do we need to go? Improvement in treatment rates of those at risk, regardless of gender, is an important goal in osteoporosis management.

How do we get there? Further development and evaluation of cost-effective, multifaceted interventions for screening and treatment of osteoporosis and fractures are needed; such interventions will likely improve the primary prevention of fractures.

Introduction

Osteoporosis is generally thought of as a "woman's disease" because the prevalence of osteoporosis and the rate of fractures are much higher in postmenopausal women than in older men. For example, the National Osteoporosis Foundation (NOF) estimates there are 9.1 million women with osteoporosis and an additional 26 million with low bone mass, which far exceeds the estimated 2.8 million men with osteoporosis and 14.4 million men with low bone mass [26].

Although osteoporosis is more common in postmenopausal women, older men still suffer poor health outcomes related to osteoporosis and fractures. Additionally, a lower proportion of men at high risk of fracture are treated than women at high risk [19]. Men also tend to have worse outcomes after fracture than women; they are twice as likely to die after hip fracture than women [13].

This review will (1) outline the differences in osteoporosis and fracture risk between the genders, (2) describe disparities in treatment and outcomes after fractures between the genders, and (3) propose solutions that might reduce such disparities between men and women.

The author certifies that she has no commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.

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Search Strategy and Criteria

A literature survey was conducted using MEDLINE with a variety of search terms and using references from the author's personal collection of articles. A formal search strategy and exclusion criteria were not employed and the review is therefore selective.

Where Are We Now?

What are the differences in the rates of fracture and prevalence of osteoporosis between older men and postmenopausal women? Are there differences in bone size, geometry, and strength between men and women? What are the differences in outcomes after fracture between men and women? Are there differences in the treatment of osteoporosis between men and women? Are there differences in the awareness and knowledge of osteoporosis between men and women?

Bone mineral density (BMD) from dual-energy xray absorptiometry (DXA) scans is used to screen for and diagnose osteoporosis in both men and women. Women have lower levels of BMD and a higher prevalence of osteoporosis than men. A t score is used to diagnose osteoporosis and is calculated from an individual's areal BMD level and a reference value. The t score is the number of SDs an individual's BMD is from a young reference value [1]. A negative t score indicates the individual's BMD is lower than the reference. A person is said to have osteoporosis if the t score is −2.5 or less, representing a BMD that is at least 2.5 SDs less than the young reference value. Low bone mass, sometimes referred to as osteopenia, is present if the t score is between −2.5 and −1.0, and normal bone mass is −1.0 or more. The World Health Organization recommends the femoral neck as the anatomic region of interest, while the International Society of Clinical Densitometry (ISCD) and the NOF guidelines diagnose osteoporosis at the femoral neck, total hip, or lumbar spine. There is some controversy about whether a young female reference value or a gender-specific reference value should be used to calculate the t score in men and women [10]. Some professional societies, such as the ISCD, recommend a young female reference be used to calculate t scores [1, 20]. This means the same absolute BMD level is used to diagnose osteoporosis in men and women. However, other groups, such as the NOF, suggest a young reference value of the same gender be used to diagnose osteoporosis [27]. If gender-specific young reference values were used to calculate t scores, men would be diagnosed with osteoporosis at a higher absolute BMD level than women, since men have a higher peak BMD than women. Therefore, use of gender-specific reference values would result in a larger number of men being diagnosed with osteoporosis than if using a female reference value.

Women also have a higher fracture risk than men. The lifetime risk of fracture for a 60-year-old woman is approximately 44%, nearly double the risk of 25% for a man of the same age [28]. In 2005, there were approximately 1.45 million fractures in women older than 50 years in the United States, compared with 594,000 fractures in men of the same age [4]. Even though men account for only 29% of fractures, the medical costs associated with fractures in older men are still sizeable, totaling $4.15 billion of $16.9 billion in costs for both genders in 2005 [4]. Even after accounting for age and body size, women have a two times higher risk of nonspine fracture than men [6]. Although this difference between men and women may be lower in nonwhites and different geographic regions, studies show women have no increased fracture risk compared to men in parts of Asia [21, 39]. Vertebral fractures are not as well studied as nonspine fractures, partially because not all of these fractures come to clinical attention. Despite limited data, it appears older men and women have a similar prevalence of vertebral fracture at age 65 years, but the incidence of new vertebral fracture in older women is almost double compared to older men [16, 28].

There are few reports regarding the potentially differential relationship between BMD and fracture risk in men and women. Three studies suggest the relationship between hip BMD and nonspine fracture risk is similar in men and women [18, 29, 34]. The association between hip areal BMD and fracture risk may be stronger in men, although this gender difference becomes less pronounced with advancing age [6]. Regardless of whether men and women fracture at the same areal BMD level, areal BMD is strongly predictive of nonspine fracture in both genders.

Differences in fracture risk between men and women are due not only to differences in areal BMD but also to differences in bone size, bone geometry, and bone strength. However, few studies have explicitly described these differences. Two cross-sectional studies, one [35] in older Icelandic men and women and one [32] in older residents of the Rochester, MN, area, described age-related changes in bone strength. Both studies demonstrated men have a greater cross-sectional area of bone than women, as assessed by quantitative CT [32, 35]. They also showed older women have lower levels of volumetric bone density than men, and both genders' bone size increases with age, resulting in bone strength that worsens more in women than in men as age increases. Such changes in bone strength may, in part, explain the differences between men and women in fracture risk.

While fractures are more common in women, men tend to have worse outcomes after fracture. A meta-analysis of

24 studies, including data from 578,436 women and 154,276 men, estimated the excess mortality risk after hip fracture for both men and women [13]. The 1-year excess mortality in men after hip fracture at age 80 years is 18%, more than twice the excess mortality in women (8%) of the same age at fracture. While most of this excess mortality risk occurs in the first few months after fracture, a small but statistically significant increased risk of mortality persists 10 years after the fracture event in both genders. Data from the prospective Baltimore Hip Fracture study [15] confirmed men are more likely to die after hip fracture than women; however, among survivors, no difference is seen in functional recovery after fracture.

Since fractures are less common in men, all major pharmaceutical interventions for primary prevention of fractures were exclusively tested in postmenopausal women, with more than 40,000 women included in these studies [2, 5, 7, 8, 14, 24, 25]. A smaller study involving men established the effectiveness of these therapies on surrogate markers, such as increased BMD and bone turnover. This study's results are in line with the large trials for fracture outcomes in women. The small study ($n = 241$) designed to evaluate the effect of alendronate on BMD changes in men demonstrated treatment improved BMD compared to placebo [30]. The study also demonstrated men receiving alendronate had a reduced incidence of vertebral fractures, even though the study was not initially designed to detect such an effect.

The cost-effectiveness of osteoporosis screening with DXA assessment and subsequent treatment is established in women. Universal screening of women aged 65 years and older is well under the quality-adjusted life year (QALY) threshold of $50,000 [32]. This indicates such universal screening is cost-effective, and the cost per QALY gained decreases with increasing age in women; universal screening becomes more cost-effective as age increases [33]. In men, screening and treatment are not as cost-effective as in women. However, in certain subgroups of men, screening and treatment are cost-effective. In an analysis that assumed costs of bisphosphonate therapy were $500 a year, the costs per QALY gained were less than $50,000 for men aged 65 years and older with a prior fracture and all men older than 80 years (regardless of fracture status). Lower costs of bisphosphonates, which are now available generically and on which the cost-effectiveness results heavily rely, result in decreased cost per QALY estimates and make screening and subsequent treatment more cost-effective for both genders.

While undertreatment of osteoporosis is a problem in both genders, men are much less likely to receive treatment for osteoporosis or after a hip fracture [14]. In a recent large study ($n = 51,346$) of adults admitted to hospitals in North Carolina with a hip fracture, osteoporosis treatment was broadly defined as receipt of calcium plus vitamin D and antiresorptive or bone-forming medications [17]. Men were about 75% less likely to receive osteoporosis treatment during the hospital stay than women; only 2.2% of men received any osteoporosis treatment, compared to 8.9% of women. In another study of treatment in a Texas hospital, only 27% of men with hip fracture reported receiving treatment 1 year after the fracture, compared with more than two-thirds (71%) of women reporting treatment [19]. Of the men who received treatment, two-thirds received calcium and vitamin D (compared to 32% of the treated women), rather than an antiresorptive or bone-forming agent. Unfortunately, treatment rates do not appear to be improving, although very recent data about such trends are not available. Specifically, one study from 2004 examining treatment rates after fracture from 1998 to 2001 in older men enrolled in a health maintenance organization noted treatment after fracture does not improve over time; only 7.1% of men in general and 16% of men with a hip or vertebral fracture receive medication [11]. Only 1% of the population has BMD assessed. Even men who experience two consecutive fractures within a short period of time (less than 1 year) do not receive treatment. A report from Australia noted the treatment rate among this high-risk group is only 24.1% [31]. Finally, a study of nearly 50,000 Canadian adults receiving home care noted, even though men with a history of fracture are less likely to be treated, treatment in the presence of a diagnosis of osteoporosis is similar in men and women [37].

Among older men and postmenopausal women, as well as healthcare providers, there is evidence that both awareness of osteoporosis and knowledge about the disease are lacking [38]. It is unclear whether knowledge of osteoporosis differs between men and women; however, it is clear knowledge of osteoporosis among older men is poor. For example, a study of more than 1500 community-dwelling older men noted, on average, only 39% of six male osteoporosis knowledge questions are answered correctly. These data suggest additional education regarding osteoporosis in men is needed.

Several studies determined the effectiveness of intensive intervention programs to increase treatment and/or screening of older men and women after fracture. A randomized study of 220 Canadian patients with hip fracture allocated individuals to either usual care (receipt of printed educational materials) or assignment of an osteoporosis case manager [22]. The case manager educated patients about osteoporosis, arranged BMD tests, provided prescriptions, and communicated with the patient's primary physician. The primary end point of the study was bisphosphonate use 6 months after the fracture. The intervention group had a much higher treatment rate (51%) than the usual-care group (22%), and BMD tests were

completed in 80% of the intervention group compared to only 29% of the usual-care group. The cost of the intervention averaged $50 per patient, which suggested the relatively low-cost intervention improved screening and treatment rates. Another Canadian study of 272 wrist fracture patients (men and women with a distal forearm fracture, regardless of cause) who were randomly selected for either usual care or a multifaceted intervention (telephone-based education to patients and their physicians) also increased treatment in the invention group [23]. However, treatment rates in the intervention group remained suboptimal; only 30% of the intervention group (compared to 7% of the usual-care group) received bisphosphonate treatment within 6 months of the fracture, and more than half of the intervention group did not receive appropriate care after the wrist fracture.

Thus, although intensive intervention improves treatment and screening, it does not guarantee all individuals at risk of subsequent fracture are screened or treated. Other interventions, such as the development of an osteoporosis exemplary-care program that identified, educated, evaluated, referred, and treated patients at risk of fracture through coordination among orthopaedists, a metabolic bone disease clinic, and nuclear medicine, have had more success; a study of 430 Canadians found nearly 96% receive appropriate attention after a fracture [3]. Another model for osteoporosis disease management is the Healthy Bones program of Kaiser Permanente Southern California (Kaiser SCAL), a health maintenance organization (HMO) [9, 12]. Kaiser SCAL has an electronic medical records (EMR) system that can track DXA scans, fractures, and medication use. The Healthy Bones program makes use of this EMR system, with the orthopaedic surgeon and the nurse practitioner having major roles in identifying and treating those with osteoporosis and a high risk of fracture. Between 2002 and 2007, this program dramatically increased the DXA screening rate (263% increase in women and 914% increase in men) and the number of patients receiving antiosteoporotic medication (a 153% increase). These improvements in screening and treatment resulted in a hip fracture rate between 2002 and 2007 that was 38% lower than what would have been expected had the program not be initiated. Thus, the use of an EMR system of reminders to healthcare providers for screening and treatment of at-risk patients is another model that could improve osteoporosis care.

The role of the orthopaedist in screening and treating patients with hip fracture was evaluated. One study of 171 orthopaedic surgeons in Utah, Idaho, and Wyoming [36] noted, although 63% of the respondents agree or strongly agree that it is appropriate to expand orthopaedic practice to include prescription of pharmacologic agents for treatment of osteoporosis, nearly 50% are concerned about adverse events of these medications and would avoid prescribing such treatments. The study concluded, although most orthopaedists agree with expansion of care, many do not initiate treatment, mainly because they believe it is something that should be covered by the primary care physician. Therefore, one barrier to care is the incomplete integration of treatment and screening of osteoporosis across orthopaedics and primary care. The interventions in the randomized trials described attempt to bridge this gap.

Discussion

The purposes of this review were to (1) highlight gender differences in osteoporosis and fracture risk, (2) describe disparities in treatment and outcomes after fractures between men and women, and (3) propose solutions to reducing disparities in treatment and prevention.

A major limitation in the literature is the lack of studies about osteoporosis that include older men compared to the number of studies that include postmenopausal women, likely because men have a lower fracture rate than women. Therefore, evidence regarding all the topics discussed in this review, from the knowledge of osteoporosis to the effectiveness of medications, is less strong in men than in women. Further and expanded studies of osteoporosis in men across all areas are needed to address this limitation.

Where Are We Now?

The prevalence of osteoporosis and the risk of fracture are higher in women than in men. This is partially due to differences in BMD, bone size, and bone strength between men and women. Even though women fracture more often, men tend to have worse outcomes after fractures. All clinical trials for pharmacologic interventions for the primary prevention of fractures are conducted exclusively in postmenopausal women; smaller trials in men tend to suggest the medications are effective on surrogate markers such as BMD. Since older women have a high risk of fracture, universal screening for osteoporosis with DXA and subsequent treatment are highly cost-effective in women older than 65 years; such screening and treatment are somewhat less cost-effective in older men. Treatment and diagnosis of osteoporosis are poor in both men and women but likely worse in men. Multifaceted interventions, such as the use of an osteoporosis case manager, improve the screening and treatment of fracture patients and may be cost-effective, although these interventions do not necessarily ensure all patients receive appropriate care. Finally, while many orthopaedists support expansion of care to include screening and treatment of osteoporosis,

many do not take such steps, since postfracture osteoporosis care is generally viewed as something that should be covered by the primary care physician.

Where Do We Need to Go?

The evidence suggests universal screening for osteoporosis is cost-effective for women older than 65 years and men older than 80 years. Therefore, one goal is to increase screening for osteoporosis in older women and men. Additionally, while more postmenopausal women have osteoporosis than men, the absolute number of men with osteoporosis is high. However, little research regarding the effectiveness of primary prevention of fractures in older men has been undertaken. Thus, another goal would be to increase the amount of research in osteoporosis for men. After fractures, many older adults do not receive appropriate care; thus, efforts should be focused on improving care after fracture.

How Do We Get There?

Increases in screening and treatment for osteoporosis is achieved through multifaceted interventions in patients after hip and wrist fractures (and perhaps other fracture types such as vertebral fractures). Such interventions can include patient education, EMR-based reporting of patients at risk of fracture, and use of case managers. The rapid expansion of EMRs suggests such programs may be possible outside of large HMO-type networks. Expansion and further evaluation of these potentially cost-effective efforts should improve the rate at which older adults receive appropriate care after fractures. Additional support for research evaluating primary prevention strategies for fractures in older men will provide additional data about the disease in this gender. Novel methods to educate patients about prevention strategies should also be evaluated and employed.

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