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Would Screening and Early Treatment Recommendations Decrease the Prevalence of Osteoporosis in Men?

Angie Wallace, Family Nurse Practitioner Student

University of North Dakota

Family Nurse Practitioner Master’s Program
Abstract

Background

Osteoporotic-related fractures in men present a public health concern due to the lack of guidelines available for screening men in older age. Gender inequalities exist in the screening and treatment guidelines for osteoporosis despite the increasing prevalence of fractures in elderly men. Efforts to screen and treat postmenopausal women with a decrease in bone mineral density (BMD) are clearly defined by the experts; however, recommendations for screening men are unclear to this day. Fractures in elderly men related to undiagnosed osteoporosis are important factors to consider in morbidity and mortality rates not to mention the increase in health care costs related to a preventable fracture.

Case Description

A 72-year-old man with a history of chronic tobacco use, intermittent steroid use related to COPD, and hypertension presented to the clinic for a 6-week follow-up for a left total hip replacement due to a recent fall at home. No previous BMD screenings were performed or offered to the patient prior to his fall. Given the patient’s significant risk factors for osteoporosis, he has been scheduled for a dual-energy X-ray absorptiometry (DXA) scan to determine his risk or presence of osteoporosis.

Conclusions

Early diagnosis and treatment options for men should be recognized and initiated, respectively, despite insufficient evidence for screening and treatment recommendations of osteoporosis in men. The MORES is an effective screening tool in identifying men at risk for osteoporosis, and the FRAX may be more beneficial in guiding treatment recommendations. The optimal screening
schedule for osteoporosis in men is unknown; further research is needed to inform screening intervals.
Would Screening and Early Treatment Recommendations Decrease the Prevalence of Osteoporosis in Men?

Despite the large varying rates of osteoporosis screening and treatment between men and women who experience fragility fractures, men are still far less likely to be screened or treated for osteoporosis. According to Gourlay et al. (2016), “one in four elderly men will sustain a fragility fracture during their lifetime, with a heightened increase in fracture incidence after the age of 75” (p. 728). Interestingly, the 1-year mortality rate for men who sustained a hip fracture compared with women is twice as high, with mortality rates reaching as high as 30-48% in men compared to 18-25% in women (Salamanna, Giardino, & Fini, 2017).

The United States Preventative Services Task Force (USPSTF) currently states that the evidence to screen for osteoporosis in men is insufficient to assess the balance of benefits and harms; however, men with a history of traumatic fracture or secondary risk factors could be considered for screening (USPSTF, 2015). The National Osteoporosis Foundation and the Endocrine Society recommend BMD screening in men at age 70 or older with or without risk factors (Cass & Shepard, 2017). Because of the inconsistency in screening and treatment recommendations in men and the lack of data, there is considerable uncertainty regarding which men to recommend for BMD testing.

Although the prevalence for osteoporosis is significantly higher in postmenopausal women compared to elderly men, the strong need for BMD screening and treatment recommendations is necessary to standardize care and prevent osteoporotic fractures in men. Preventable osteoporotic fractures are associated with increased risk for disability, long term care placement, healthcare costs, and mortality. The risk for osteoporosis increases with age as BMD decreases, and the impact it will have on elderly men especially as the U.S. population
Case Report

Mr. J, a 72-year old Caucasian man presented to the clinic for a follow-up after hospital discharge. He spent three days in the hospital for an open reduction and internal fixation (ORIF) of the right hip. Mr. J sustained a fall in his home while ambulating down his stairs resulting in an acute right hip fracture. Past medical history for Mr. J includes chronic obstructive pulmonary disease (COPD), anemia, hypertension, hypercholesterolemia, bipolar disorder, and current tobacco use. He has a 30 plus pack-a-year smoking history and is not interested in quitting at this time. He lives alone in a 2-story home and does not require any assistive devices for activities of daily living.

Physical examination of Mr. J revealed an approximated right hip incision without erythema, edema, or drainage present. Review of systems are within normal limits. Vital signs included a heart rate of 72 beats per minute, blood pressure 138/70, respiratory rate 18 with an oxygen saturation of 92%, and an oral temperature of 98.6. His BMI is 20.4 which is consistent with his previous BMI 6 months ago. He reports having no pain in his hip and states he is recovering well. Labs are unremarkable and medication list was reviewed and updated. He just finished a prednisone taper yesterday for an exacerbation of his COPD. He is also prescribed quetiapine 200 mg bid for his bipolar disorder which increases his risk for falls due to the sedation side effect of the medication.

Mr. J was counseled regarding his risk factors for osteoporosis which include his age, smoking history, intermittent steroid use for COPD flares, low body weight, polypharmacy, and physical inactivity. He was advised to undergo a DEXA scan in order to establish a baseline T-
score measurement to assess his risk of bone fractures in the future. He was also highly encouraged to quit smoking. Smoking cessation information was offered to the patient, but he reluctantly declined. Mr. J agreed to undergo a DEXA scan and follow-up in the clinic 1-week after the procedure. The DEXA scan results revealed a T-score of -2.6 which equates to a diagnosis of osteoporosis for Mr. J.

The results of Mr. J’s DEXA scan were given to him in addition to education regarding oral bisphosphonates as a treatment recommendation to prevent future bone fractures and increase his bone mineral density. Medication options were discussed in detail with regard to frequency and side effects, and Mr. J decided to start alendronate (Fosamax) as a daily regimen. Important administration instructions were discussed with Mr. J as well as adverse side effects. Labs were drawn at this appointment to establish a creatinine and calcium baseline. It was recommended that he start on a vitamin D and calcium supplement in addition to the Fosamax. Follow-up for Mr. J is recommended in one month to assess medication response. A DEXA scan is scheduled for 6 months to assess his BMD and determine medication efficacy.

Mr. J revealed his frustration regarding the lack of information he received relating to osteoporosis screening at previous clinic visits. He was never informed of screening options for osteoporosis and was unaware he had significant risk factors for osteoporosis and related fractures. The insufficient guidelines for screening and treatment options were elaborately explained to Mr. J, and his treatment plan was extensively reviewed. He was reassured that his BMD will likely improve with the medication and lifestyle recommendations in place given his compliance with the treatment regimen.
Search Strategies

A literature search was performed using the Harley French Library Website at the University of North Dakota. Three databases were utilized to search for research articles: CINAHL Complete, PubMed, and Clinical Key. A total of 22 articles resulted from the overall search, and 12 articles were chosen based on relevance. The following keywords were used as search terms and derived from the PICO question: osteoporosis, men, treatment, screening, screening tools, and recommendations. CINAHL was the first database used because of its emphasis in nursing and allied health professions. Next, PubMed was searched for comprehensive medical literature. Finally, Clinical Key was searched for high quality, scientific evidence in hopes to find relevant articles related to the PICO question. Inclusion criteria included in all three databases were English articles, articles within the last five years, and human subjects only.

Literature Review

Screening recommendations and treatment strategies for osteoporosis in men is lacking specific guidelines due to the limited number of research studies conducted in men. This results in considerable difficulty when trying to determine which men should be screened and treated for osteoporosis. BMD testing alone is limited in predicting a future osteoporotic-related fracture in men; thus, requiring other screening approaches to assist in determining the risk for osteoporotic-related fractures. Several screening tools have been developed to assess risk factors for fracture including the fracture risk assessment tool (FRAX), the male osteoporosis risk estimation score (MORES), the male osteoporosis screening tool (MOST), and the osteoporosis self-assessment tool (OST).
The World Health’s Organization (WHO) FRAX was developed to predict the 10-year risk of a hip fracture or major osteoporotic fracture using clinical risk factors with and without femoral neck BMD (Diem et al., 2017). The FRAX fracture risk calculator incorporates a white female database combined with a concise set of risk factors to predict a 10-year fracture risk. Several studies have been conducted comparing the effectiveness of various screening tools used in primary care to screen an individual for osteoporosis. The MORES includes age and weight, history of chronic obstructive pulmonary disorder (COPD), and 2 major risk factors to predict men at risk for osteoporosis. Salamanna, Giardino, and Fini (2017) express concern regarding the limitations of the FRAX in that it does not take into account other chronic disease states, dietary factors, and other risk factors that can affect bone mass. Cass, Shepard, Asirot, Mahajan, and Nizami (2016) conducted a study comparing the validity and effectiveness of the MORES and FRAX with a purpose to determine which men should be referred for a DXA scan. The study was done using a cross-sectional sample of men from the United States who participated in the National Health and Nutrition Examination Survey III (NHANES III). The WHO developed their definition of osteoporosis based on BMD of the femoral neck by using the same reference cohort as the NHANES III. Likewise, the MORES was developed from the NHANES III same sample population as the FRAX; therefore, this study was able to directly compare the MORES with the FRAX to determine which screening tool is more efficacious in screening for osteoporosis in men. The researchers found the MORES screening tool to be more effective than FRAX due to the remarkably higher sensitivity (Cass, Shepard, Asirot, Mahajan, & Nizami, 2016).

The FRAX can be used for both men and women, but only two screening tools have been developed specifically for men, the male osteoporosis screening tool (MOST) and the MORES.
OSTEOPOROSIS IN MEN

The OST was developed for women originally but was validated in the osteoporotic fractures in men (MrOS) study and has since been adapted as a screening tool for men. The OST requires more complex calculations and its clinical value is limited because of unclear cut off scores in predicting osteoporosis risk; however, Diem et al., (2016) found that the OST performed better than FRAX for identifying osteoporosis. The MOST was validated using a sample of Chinese men in Hong Kong by combining body weight with a quantitative ultrasound index of the heel to predict men at risk for osteoporosis. It was further validated in the MrOS study showing superiority to the OST due to a significantly higher area under the curve (AUC). Unfortunately, the MOST is rarely used in clinical practice due to the limitation of heel ultrasound scans done in primary care (Cass & Shepard, 2013).

The MORES is a simple screening tool that can be done quickly during a primary care office visit and can identify men at greatest risk for osteoporosis in which a DXA scan is necessary. Cass and Shepard (2013) conducted a blinded analysis using the MORES in a cross-sectional analysis of men 60 and older. The aim of the study was to assess the validation of the MORES in a primary care clinical setting. The study incorporated a research questionnaire with a DXA scan to measure BMD. The MORES yielded a sensitivity of .80 in identifying osteoporosis of the hip. The results of this study correctly identified 80% of men with osteoporosis, thus confirming the validity and efficiency of the MORES as an effective screening tool for osteoporosis in men (Cass & Shepard, 2013). It appears the MORES is superior in the aforementioned screening tools used for osteoporosis in men, and the FRAX may be a worthy tool to guide treatment decisions.

Despite the fact that men are not being evaluated and screened appropriately for osteoporosis, they are also not being treated adequately for low BMD even when testing does
occur. The data involving the use of bisphosphonates to treat osteoporosis in men with a low BMD is limited; however, the research that has been completed proves to be clear, showing that bisphosphonates have positive effects on BMD in preventing future fragility fractures. Bisphosphonates, such as alendronate, risedronate, and zoledronate, were developed and approved by the Federal Drug Administration (FDA) as an intervention for osteoporosis treatment in men (Adler, 2014). The efficacy of bisphosphonates in postmenopausal women has been researched thoroughly, but unfortunately clinical trials in men are lacking.

A meta-analysis conducted by Chen, Wang, Zheng, Zhao, & Li (2015) found bisphosphonate therapy in men to be similarly effective to that of women. Despite the results of recent studies that alendronate increases bone mass with a resultant decrease in spine, hip, wrist, and other fragility fractures in men, no systemic reviews or meta-analyses had been done to address the efficacy of bisphosphonates on new fractures related to osteoporosis, serum bone turnover markers, and changes in BMD in elderly men prior to this study. The study utilized high-grade randomized controlled trials (RCTs) to roughly calculate or judge the value of bisphosphonates in the treatment of osteoporosis in adult men. The results of this meta-analysis proved a decrease in new fractures, an increase in BMD, and a reduction in bone-turnover biomarkers. The approved bisphosphonates for men with osteoporosis are just as efficacious at increasing BMD in men and improving bone turn over markers as they are in women according to Adler (2014). The main issue in choosing the correct treatment option for men is the lack of evidence based research and guidelines on improvements in fracture risk.

Numerous studies have demonstrated the efficacy of alendronate therapy in men with osteoporosis, but there still remains a significant fraction of men in clinical practice experiencing a reduction in BMD during alendronate treatment. Swenson et. al (2013) conducted a small study
in veteran men age 50 and older who received a prescription for alendronate therapy during a particular time frame. Researchers concluded that BMD testing for reevaluation of men being treated with bisphosphonates is paramount given the lack of research in men and their risk for fractures if a desired effect is not achieved. It is apparent that more evidenced based research for osteoporosis in men is needed to determine screening and treatment guidelines, but this highlights the importance of identifying patients who do not respond to bisphosphonate therapy given their increased fracture risk compared to those who do respond (Ebeling, 2013).

Zoledronate is a bisphosphonate that is administered parenterally on a yearly basis and has demonstrated significant improvements in BMD in women; thus, reducing future osteoporotic fractures. Boonen et al. (2012) conducted a placebo-controlled RCT in men diagnosed with osteoporosis and found that at the end of 2 years, the men who had received the zoledronate experienced a 67% relative risk reduction in new vertebral fractures and improved BMD scores. The benefits versus harms of the medication must be considered and vitamin D and calcium supplementation should always be encouraged. Zoledronate increased BMD to a greater level than did risedronate in another study performed on men taking oral glucocorticoids; however, it compared equivalently to alendronate in BMD improvements (Adler, 2014). Risedronate is lacking research data in men with osteoporosis, but one recent RCT of men with osteoporosis found that risedronate actually increased lumbar spine BMD (Ebeling, 2013). More research is needed to predict the anti-fracture efficacy of risedronate in osteoporotic men.

It is clear there remains considerable uncertainty regarding screening tools and treatment recommendations for osteoporosis in men, but when to screen and recommend BMD testing in men also remains controversial. Screening guidelines that have been published vary greatly from one source to the next. “The USPSTF recommends screening all women 65 years and older with
further recommendations for women younger than 65 whose 10-year fracture risk is greater than or equal to that of a 65-year old white woman without additional risk factors” (USPSTF, 2015). The USPSTF incorporates the WHO FRAX screening tool as a method to determine increased future fracture risk for women. Insufficient evidence was found to recommend routine screening for osteoporosis in men. The USPSTF (2015) does state that men with minimal trauma, older than 50 years of age, or those with secondary causes associated with bone loss could be considered for screening, but the ambiguity in these guidelines pose uncertainty for providers regarding appropriate screening strategies.

The Endocrine Society recommends screening men for osteoporosis at age 70 or older by measurement of BMD, and younger men aged 50-69 should undergo testing if additional risk factors are present (Watts et al., 2012). The American College of Physicians (ACP) offers no specific algorithm for osteoporosis screening in men, but instead recommends individualized screening decisions based on risk factors and comorbidities. The National Osteoporosis Foundation (NOF) and the American College of Preventive Medicine (ACPM) recommend universal DXA screening of men 70 years of age or greater without regard to risk factors or previous fracture history (Cass & Shepard, 2017).

In an effort to close this healthcare gap in screening recommendations, a concise, uniform algorithm must be established to delineate the responsibilities of the primary care provider. This is not a simple task but rather a complex process involving responsibilities that include performing a clinical risk assessment and BMD evaluation, interpreting results, and recommending appropriate treatment options. Further research aimed at developing targeted screening of men and additional pharmacologic research trials to identify appropriate candidates
for treatment are crucial in order to standardize screening strategies for men and develop evidence-based research to support universal BMD testing in men.

Learning Points

• Osteoporosis is still frequently unrecognized and untreated in men before a fracture occurs.

• Men are far less likely to be screened and treated for osteoporosis in comparison to women of the same age.

• The 1-year mortality rate for men who sustain a hip fracture compared with women is twice as high.

• The MORES appears to be the best screening tool in predicting men at greatest risk for osteoporosis in which a DXA scan is warranted. The FRAX may be more worthy of predicting treatment decisions.

• Limited research is available regarding treatment recommendations for osteoporosis in men, but oral bisphosphonates are FDA approved and should be recommended to reduce the risk for vertebral fracture in men who have clinically recognized osteoporosis.
References


