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The epidemiology of wrist fractures in older men: The Osteoporotic Fractures in Men (MrOS) study

Nicole C. Wright¹, Elizabeth R. Hooker², Carrie M. Nielson², Kristine E. Ensrud³, Stephanie L. Harrison⁴, Eric S. Orwoll⁵, Elizabeth Barrett-Connor⁶, and for The Osteoporotic Fractures in Men (MrOS) Study Research Group

¹Department of Epidemiology, University of Alabama at Birmingham

²OHSU-PSU School of Public Health, Oregon Health & Science University

³Division of Epidemiology & Community Health, University of Minnesota

⁴San Francisco Coordinating Center, University of California, San Francisco

⁵Division of Endocrinology, Oregon Health & Science University

⁶Division of Epidemiology, Department of Family Medicine and Public Health, University of San Diego School of Medicine

Abstract

Purpose—To calculate the incidence of wrist fractures and their risk factors in older community-dwelling men from the U.S. Osteoporotic Fractures in Men (MrOS) Study.

Methods—Using triannual postcards, we identified incident wrist fractures (centrally confirmed by radiology) in men aged ≥65. Potential risk factors included: demographics, lifestyle, bone mineral density (BMD), selected medications, biomarkers, and physical function and performance measures. Both baseline and time-varying models were adjusted for age, race/ethnicity, MrOS geographic location, and competing mortality risks.

Corresponding Author: Elizabeth Barrett-Connor, MD, 9500 Gilman Dr. #0607, La Jolla, CA 92093-0607, (858) 543-0511, ebarrettconnor@ucsd.edu.

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CMN: analysis plan creation, analysis interpretation, manuscript editing, manuscript approval

KEE: data acquisition, analysis plan creation, analysis interpretation, manuscript approval

SLH: data analysis, analysis interpretation, manuscript approval

ESO: data acquisition, analysis plan creation, analysis interpretation, manuscript approval

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Results—We observed 97 incident wrist fractures among 5,875 men followed for an average of 10.8 years. The incidence of wrist fracture was 1.6 per 1,000 person-years overall and ranged from 1.0 among men aged 65-69 to 2.4 among men age 80. Significant predictors included: fracture history after age 50 [hazard ratio (95% CI): 2.48 (1.65, 3.73)], high serum phosphate [1.25 (1.02, 1.53)], use of selective serotonin receptor inhibitor (SSRI) [3.60 (1.96, 6.63), decreased right arm BMD [0.49 (0.37, 0.65) per SD increase], and inability to perform the grip strength test [3.38 (1.24, 9.25)]. We did not find associations with factors commonly associated with wrist and other osteoporosis fractures like falls, diabetes, calcium and vitamin D intake, and alcohol intake.

Conclusions—Among these older, community-dwelling men, we confirmed that fracture history is a strong predictor of wrist fractures in men. Medications such as SSRIs and corticosteroids also play a role in wrist fracture risk. We identified novel risk factors including kidney function and the inability to perform the grip strength test.

Keywords

wrist fracture; men; risk factors; epidemiology

Introduction

Fracture of the distal radius or wrist is one of the most common injuries, accounting for 14% of all fragility fractures.[1] Most wrist fractures occur in women, with the highest incidence between ages 40 and 60 years.[2, 3] Studies have shown that a wrist fracture history increases the risk for subsequent fragility fractures. For example, the Women's Health Initiative reported that a wrist fracture history increased the risk for a subsequent fracture by 37% for any fracture and as much as 80% for any non-wrist upper extremity fracture.[4] In the Study of Osteoporotic Fractures (SOF), a study of community-dwelling women aged 65 and older at baseline, having a confirmed distal radius fracture after minor trauma significantly increased the odds of another fracture, and predicted functional decline in instrumental activities of daily living (IADLs) independent of age, BMI, health status, baseline functional status, lifestyle factors, and co-morbidities.[5]

Although women represent the majority of osteoporotic fractures, a worldwide study reported 39% of nine million reported fragility fractures occurred in men.[6] Forearm fractures represented 10% of fractures in men. We know that wrist fractures are less common and occur at a later age in men than in women, but we do not know if the risk factors are the same or have similar magnitude in both sexes.

Estimates show that about 35% of American men 50 years of age have low bone mineral density (BMD) (T-score between -1 and -2.5), and another 4.3% have osteoporosis (T-score -2.5) based on femoral neck or lumbar spine BMD.[7] It has been suggested that measurement at skeletal sites where osteoarthritis is uncommon, such as the lower 1/3 of the radius, is potentially more sensitive for detecting bone loss than other sites in older men, and could provide a more reliable measure of male skeletal status.[8, 9] However, no trials have shown that men with osteoporosis only at the wrist respond to current therapy.[10] The FDA currently does not accept radial BMD or wrist fracture prevention as an indication for bone medication.[11] Given the large number of men at risk for fractures and the growing

population of older men, it is important to increase information on the causes and consequences of wrist fractures in men. The goal of this paper was to calculate the incidence of wrist fractures in men over time and to identify independent risk factors for wrist fracture.

METHODS

Participants

Participants were community-dwelling men participating in the Osteoporotic Fractures in Men (MrOS) Study, a prospective study of community-dwelling men in the United States. Between March 2000 and April 2002, 5,994 men ages 65 and older were enrolled at six clinical centers: Birmingham, AL; Minneapolis, MN; the Monongahela Valley near Pittsburgh, PA; Palo Alto, CA; Portland, OR; and San Diego, CA. Details of the MrOS study design, recruitment, and baseline cohort characteristics have been reported previously.[12, 13] Participants were recruited from driver's license lists, voter-registration lists, and Medicare data, as well as convenience samples from advertisements and mailers to age-specific populations. Minority recruitment was enhanced through the use of the Centers for Medicare and Medicaid Services and other databases that allowed targeted recruitment. Response to mass mailings surpassed 10-15%, and appointment rates averaged above 85%.

Eligibility criteria were 1) the ability to walk without the assistance of another person, 2) no bilateral hip replacement, and 3) the ability to provide written informed consent. The Institutional Review Board at each center approved the study protocols, and participants provided written informed consent.

All consenting participants completed a baseline clinic visit between March 2000 and April 2002. The current analysis also used follow-up data from clinic visits 2 and 3. Visit 2 took place between March 2005 and May 2006 (97.7% of men completed some part of Visit 2). Visit 3 took place between March 2007 and March 2009; 97.8% of active participants completed some part of Visit 3.

Identification of Incident Wrist Fractures

Using tri-annually mailed one-page questionnaires, participants reported whether or not they had sustained a wrist fracture in the previous four months. Participants who did not return or adequately complete the mailed questionnaire received a telephone call. All participants who reported a fracture were interviewed to determine the date, trauma level, and other circumstances preceding the fracture. Study physicians centrally adjudicated fractures using medical records and radiology reports; all confirmed wrist fractures were included in this analysis. Because exclusion of traumatic fractures has been reported to underestimate the contribution of osteoporosis to fractures in both sexes [14, 15] such fractures were not excluded.

Identification of Potential Risk Factors

MrOS used self-administered questionnaires to ascertain demographic and lifestyle information and personal and family medical history at baseline and at follow-up visits. Interviews and examinations were conducted by trained study staff.

Our variables of interest included: age, race/ethnicity, weight, height, BMI, self-reported overall health, alcohol use, tobacco use, measured BMD, fall and fracture history, serum phosphate, serum calcium, estimated glomerular filtration rate (eGFR), comorbidities, physical activity, functional status, prescription medication use, calcium and vitamin D intake, and physical performance tests (including chair stands, narrow walk, grip strength, leg power, and walking speed). Details for each of these measures are provided below.

Height (cm) was measured on Harpenden stadiometers, and weight (kg) was measured on calibrated standard balance beams or digital scales at every study visit. BMI was calculated as kg/m^2 .

Areal bone mineral density was obtained for total hip, right arm, and left arm using fan-beam DXA (QDR 4500W, Hologic, Inc, Bedford, MA) at all study sites. Participants were scanned by licensed densitometrists using standardized procedures. Scanners were calibrated at baseline, and quality control scans showed no shift in scanner performance at any site during enrollment.

At each visit, participants reported whether they had fallen in the previous 12 months. Baseline fracture history included questions about personal and parental history of osteoporosis and fractures, location of fractures, and whether the fractures occurred between age 50 and baseline.

Blood samples were drawn by trained study nurses for serum phosphate and calcium. All assays were conducted at Oregon Veterans Administration Clinical Laboratory. One serum control was included in each assay run. All samples were measured using a Roche COBAS Integra 800 automated analyzer (Roche Diagnostics Corp., Indianapolis, IN). The analyzer was calibrated daily in the clinical laboratory. eGFR was calculated using the Cockcroft Gault formula using serum creatinine.[16, 17]

Participants were asked if a doctor or other health care provider has ever told them they have or had selected medical conditions, including: osteoporosis, Parkinson's disease, rheumatoid arthritis, any type of cancer, diabetes, hypothyroidism, stroke, and myocardial infarction.

We assessed physical activity using functional status and the Physical Activity Scale for the Elderly (PASE) score. The PASE score included self-reported occupational, household and leisure activities over a recent one-week period. Functional status was assessed by summing the level of difficulty, on a 0-3 scale, with five instrumental activities of daily living (IADLs): walking on level ground, climbing steps, preparing meals, doing housework, and shopping.[18] Functional status and physical activity were assessed at every study visit.

The following measures were used to assess physical performance: repeated chair stand, usual walking pace over 6 meters, 6-m narrow walk time, leg power, and grip strength.[19] For the repeated chair stand test, seated participants were asked to stand from a chair without using their arms. All men who were able to complete the single chair stand were asked to complete a repeated chair stand test; the ability and time required to complete five stands without using their arms were recorded. Men who were unable to do a single chair stand,

those who had missing ability to complete all five stands, and those who refused to do the test were classified as “unable.”

For the narrow walk test, participants were asked to complete a narrow walk trial over a 20cm wide, 6m long course. Each participant was asked to attempt two trials, and if they deviated from the course at least twice during either trial, a third trial was requested. Participants were considered able to complete the narrow walk trial if they had no more than two deviations from the marked lane. Time to complete the narrow walk course was used as an indirect measure of dynamic balance. Men who attempted but were not able to complete the test or those who did not attempt the test were classified to the “unable” category.

Walking speed was assessed on a standard 6-m walking course. Participants were instructed to walk at their normal pace for two trials; their fastest speed (m/s) of the two trials was used for this analysis. The “unable” to complete category consisted of those men who did not attempt the test, as well as those who attempt the test, but unable to complete.

Leg extension power was measured on the Nottingham Power Rig (University of Nottingham, England) with nine trials for each leg. The maximum value (watts) was analyzed.[20, 21] The “unable” category consisted of men who either: 1) attempted the test but unable to complete, 2) had a missing value because of physical limitation, 3) refused to complete the test, or 4) did not complete the test.

Grip strength (kg) was measured twice by a handheld dynamometer (Jamar Hydraulic Hand Dynamometer, Sammons Preston, Inc.; Bolingbrook, IL) in both the right and left hands; the average of the right and left hands was used in this analysis. Men classified as “unable” were those men who were unable to complete the test or did not attempt the test.

Participants were asked to bring to all clinic study visits all of the prescription medications used within the previous 30 days. At subsequent clinic visits, non-prescription medications were also collected. A computerized dictionary based on the original Established Populations for Epidemiologic Studies of the Elderly coding system [22] was used to classify medications. All recorded prescription medications were stored in an electronic medications inventory database (San Francisco Coordinating Center, San Francisco, CA). Each medication was matched to its ingredient(s) based on the Iowa Drug Information Service Drug Vocabulary (College of Pharmacy, University of Iowa, Iowa City, IA). Medications of interest for this analysis were: alpha blockers, loop diuretics, statins, selective serotonin receptor inhibitors (SSRIs), tricyclic antidepressants, thyroid hormones, and oral and inhaled corticosteroids, each of which were previously associated with BMD and/or fracture risk.[23, 24]

Statistical analysis

For the present analysis, we excluded all men who reported baseline use of bisphosphonates, calcitonin, or fluoride; men who had a history of osteoporosis; and men who were taking testosterone injections (n=115). We also excluded one man who had missing follow-up data. We calculated the incidence of wrist fractures overall (age standardized to the 2010 US Census) and by 5-year age-strata as cases per 1,000 person-years. We also calculated the

incidence of overall mortality and by age-strata per 1,000 person-years as a comparator, and to justify the need to adjust for competing mortality risk. To identify the set of risk factors that were independently associated with wrist fracture, we developed three minimally adjusted multivariable Cox proportional hazards models with competing risk of mortality; models were adjusted for age, race/ethnicity, and MrOS site, reporting the adjusted hazard ratio and 95% confidence intervals [HR (95 CI %)]. Our first model only utilized baseline covariates. Due to the length of follow-up time, our second model utilized time-varying covariates except for those that were static or available only at baseline. Lastly, because BMD has been shown to be a strong predictor of wrist fracture, BMD was included in a separate analysis in the minimally adjusted models to determine whether it influenced the selection of other variables into the model. Men with fractures at locations other than wrist were included in this analysis as non-cases. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA) and Stata 14 (StataCorps, College Station, TX, USA).

Results

Our MrOS sample included 5,875 men. Baseline characteristics of the population are shown in Table 1. During an average 10.8 years follow-up, we observed 97 incident wrist fractures in these men. The age-standardized incidence of wrist fractures was 1.60 per 1,000 person years (Table 2). In age-stratified analyses, we observed an increasing wrist fracture incidence with age: Among men 65-69 years of age, the incidence of wrist fracture was 1.04 (0.68, 1.57) per 1,000 person-years, increasing to 1.36 (0.93, 2.00) per 1,000 in men age 70-74, 1.99 (1.38, 2.86) in men age 75 to 79, and finally 2.37 (1.53, 3.67) in men 80 years and older. Compared to the incidence of wrist fractures, the incidence of mortality was significantly higher (Table 2).

After adjusting for age, race/ethnicity, and MrOS location, and accounting for competing mortality risk, the following variables were independent predictors of wrist fracture at $p < 0.05$ in both the baseline and time-varying models: all BMD variables (total hip, right and left arm), all fracture history variables, serum phosphate, eGFR, history of osteoporosis, and the use of SSRIs (Table 3). Higher BMD was the only protective factor for wrist fracture, with 39-57% decreased wrist fracture risk for every standard deviation increase in BMD when using baseline BMD values and 38-55% decreased wrist fracture risk for every standard deviation increase in BMD when using time-varying BMD variables (Table 3). Although all fracture variables indicated increased risk for wrist fracture in both baseline and time-varying models, sustaining any type of fracture between the age of 50 and MrOS baseline was the strongest reported fracture risk predictor for wrist fractures [baseline: 2.50 (1.66, 3.76); time-varying: 2.48 (1.65, 3.73)] (Table 3). Every standard deviation increase in both serum phosphate and eGFR was associated with 21-25% increased risk of wrist fractures in models using baseline or time-varying values (Table 3). Baseline self-report of osteoporosis was associated with an over four-fold increase in the risk of wrist fractures; however, this effect was attenuated to a little over two-fold increased risk when considered as time-varying. The use of SSRIs was associated with about a 2.6 and 3.6 fold increase in the risk of wrist fractures in both the baseline and time-varying models, respectively (Table 3).

The use of tricyclic antidepressants was the only observed significant predictor in the baseline covariate model that was not in the time-varying covariate model. In contrast, several predictors were significant in time-varying covariate models but not in baseline models: rheumatoid arthritis, inability to perform the grip strength test, and use of inhaled or oral corticosteroid medications; all were associated with an increase in risk of wrist fracture (Table 3). Although statistically non-significant (based on p-value), the hazard ratio point estimate changed from risk to protective or vice versa between the baseline and time-varying models for age (categorical), worst PASE score, report of heart attack, inability to perform the leg power test, and the use of alpha blockers (Table 3).

After further adjusting these models for total hip BMD, the associations of all factors were attenuated, and in some cases the statistical significance changed. Although point estimates did not change, weight and height became significant predictors of wrist fractures after adjusting for total hip BMD in addition to age, race/ethnicity, and MrOS site location in both the baseline and time-varying models (Figure 1). For example, every kilogram increase in weight increased the risk of wrist fracture by 2% [1.02 (1.00, 1.04)] and every centimeter increase in height increased the risk of wrist fracture by 3% [1.03 (1.00, 1.06)]. Conversely, oral and inhaled corticosteroid use was associated with significantly increased risk for wrist fractures in time-varying models, but after adjusting for total hip BMD, the association was no longer statistically significant [1.74 (1.0, 3.01) vs. 1.58 (0.9, 2.78)] (Figure 1). Surprisingly, although point estimates indicated increased risk, age and falls were not significant predictors in any of our models.

Discussion

In this study of community-dwelling older men, we estimated the incidence of wrist fractures over time and identified wrist fracture risk factors. We confirmed that fracture history was a strong predictor of wrist fractures in men. Medications such as SSRIs and corticosteroids also played a role in wrist fracture risk. We identified potential novel serum risk factors—high eGFR and phosphate, as well as the inability to perform the grip strength test.

Over an average of nearly 11 years follow-up, the overall age-adjusted incidence of wrist fractures in the MrOS population was 1.60 per 1,000 person years. Only a few studies have evaluated the incidence of wrist fractures among men nationally and internationally. A U.S.-based study utilizing Truven's Healthcare MarketScan Administrative Claims Database estimated incidence of wrist fractures among men newly diagnosed with osteoporosis, defined as 1) having a primary or secondary osteoporosis diagnosis code, or 2) having a pharmacy claim for an osteoporosis medication.[25] After 12 months, they observed an incidence of 0.018 (0.015, 0.022) per 1,000 person years for men ≥ 65 without a history of fracture at baseline, the six months preceding the osteoporosis diagnosis date, or first pharmacy claim date. In contrast, they observed an incidence of 0.030 (0.017, 0.049) per 1,000 person-years for men ≥ 65 with a history of fracture at baseline.[25] The follow-up time for fracture ascertainment (1 vs. 11 years) was considerably shorter than our study, which possibly explains the much lower incidence. A Canadian study that evaluated annual trends in wrist fractures among community-dwelling older men wrist fracture incidences of

3.09 (2.77, 3.44) and 2.86 (2.62, 3.08) per 1,000 person-years in 2002 and 2012, respectively.[26] Considerably higher rates among Canadian men than our U.S. men may be due to differences in demographic, lifestyle, and medical management characteristics between the two groups.

In Europe, wrist fractures incidence rates in older men range from 0.96 per 1,000 person years in a study utilizing 1990 to 2012 data from the United Kingdom's Clinical Practice Research Datalink (CPRD) [27] to 2.16 per 1,000 in an eight year examination of administrative data in Stockholm County, Sweden.[28] The population incidence of wrist fractures in the Netherlands [29] showed an overall age-adjusted rate of 1.00 (0.83, 1.31) per 1,000 person-years. The European Prospective Osteoporosis Study (EPOS) reported a distal radius fracture incidence of 1.7 per 1,000 after a 3 year follow-up period.[30] These estimates resemble wrist fracture incidence rates observed in our current study, and several have comparable follow-up time. As with the Canadian study, differences in demographic, lifestyle, and health characteristics may explain other differences between these incidence estimates.

Our second objective was to identify predictors of incident wrist fractures in men. After adjusting for age, race and ethnicity, MrOS location, and accounting for competing risk of mortality, we observed that the following variables were significantly associated with increased wrist fracture risk: Height and weight only after adjustment for BMD. Any prior fracture, fracture between age 50 years and baseline, history of wrist fracture, serum phosphate, serum eGFR, rheumatoid arthritis, inability to perform grip strength test, and use of SSRIs or oral or inhaled corticosteroids. We found that better hip or arm BMD was associated with decreased wrist fracture risk.

In 2012, The Endocrine Society Task Force reported a systematic review of 55 "adequate" published studies designed to identify risk factors for fractures in men.[31] Significant risk factors for White men were: age >70 years, low BMI, daily alcohol intake (>10 drinks per week), current smoking, corticosteroid use, prior fracture, falls in the past year, hypogonadism (natural or drug induced), and diabetes. The strongest risk factors were fractures or falls in the previous year. Our study reaffirms the significant role of prior fracture history with respect to wrist fracture risk. We also confirmed the known importance of wrist fracture association with male osteoporosis, and with the use of SSRIs or corticosteroids, although our association was driven mostly by inhaled corticosteroids.

Ours is one of the few studies to report the role of physical performance measures with wrist fractures in men. Ward and colleagues evaluated the association between chair stand ability and injurious falls (fractures, sprains, dislocations, pulled/torn muscles, ligaments, or tendons) and found that the poorest performers on the chair stand test had a 60-96% increased risk of injurious falls after adjustment for other covariates.[32] Cawthon and colleagues found that poor performance on the chair stand test was predictive of hip fracture risk in the MrOS cohort, with the worst performers having a 3.6-fold increased risk, and those men who were not able to perform the test, having over an 8-fold increased risk of hip fracture.[19] Knee extension force, balance, and gait speed were assessed as fracture predictors in a Swedish cohort of older women, but none of the physical performance

measures were found to be significant predictors of wrist fractures in crude or adjusted models.[33] Only the worst performers in narrow walk test and walking speed were found to have significant associations with hip fracture in the MrOS cohort.[19] We also observed no association between gait speed and leg power measures with wrist fracture in men. A study among healthy post-menopausal women found that low grip strength was associated with a 2-fold increase in any osteoporosis fracture.[34] Although no association was found by tertile, we did find a 3-fold increase in the risk of wrist fracture among MrOS participants unable to complete the grip strength test. This result was similar to the hip fracture findings in MrOS; men who were unable to complete the grip strength test had a 4.5 fold increased risk of hip fracture.[19]

We saw that increases in two physiological markers, eGFR and serum phosphate were associated with increased risk of wrist fractures. eGFR is a marker of kidney function, with eGFR <60 being used as the diagnostic indicator for chronic kidney disease.[36–38] Studies have found low eGFR to be associated with fractures, particularly at the hip. For example, among residents of Ontario, the fracture incidence rate ratio increased from 1.2 to 4.4 among women with an eGFR of 45-59 to <15 compared to those women with eGFR ≥ 60.[39] However, other studies have found no association between eGFR and fractures. For example, in the same Ontario study, there was no association by eGFR and fracture in men.[39] Similarly, a population based study found no significant differences in hip fracture rates by eGFR levels by age among women and men in the Alberta Kidney Disease Network.[40]

Even within the MrOS cohort, different relationships between eGFR and bone outcomes have been found. When evaluating eGFR with hip bone loss, Ishani et al. found that men with lower eGFR as defined by the modification of diet in renal disease formula had more annualized hip bone loss, but when they used eGFR defined by the Cockcroft-Gault formula, the formula used in our study, they did not see a significant association between eGFR and bone loss.[41] However, when using eGFR estimated from standardized cystatin C, Ensrud et. al, did see a significant association between low eGFR and increased risk for hip fracture.[42]

Ours is one of the first studies to yield an association with higher eGFR and fracture. The Cockcroft-Gault formula, used in our study, depends on age, sex and body weight, and is more associated with creatinine clearance than GFR.[43] Creatinine based formulas have been shown to be problematic in older adults, as lower serum creatinine (correlated with higher GFR) is a correlate of low muscle mass (associated with higher fracture risk, particularly at the hip) in addition to better kidney function. Thus, cystatin C based GFR formulas are better predictors of kidney function[43]; however, we do not have serum cystatin C available in our entire analytical cohort.

There is also a known association between kidney function and phosphate balance. Decreased kidney function is associated with increased serum phosphate. Increased serum phosphate results in decreased calcium absorption, and could reflect hypoparathyroidism, and liver disease,[35] each of which have known associations with osteoporosis, bone loss, and/or fracture risk. Our mean phosphate level (3.18 mg/dl) was elevated, but not considered “high” based on the assay used (normal: 2.5-4.7 mg/dl); nevertheless, our analysis showed

that every standard deviation increase in serum phosphate was associated with a 25% increased risk in wrist fracture. Although interesting, our eGFR and phosphate findings need further exploration.

We did not find association with other factors commonly associated with wrist fractures such as falls, diabetes, calcium and vitamin D intake. This could be in part to power, as many of these variables had point estimates indicative of risk, but did not reach statistical significance. However, history of falls was not a significant predictor of wrist fractures in the men from the Dubbo Osteoporosis Epidemiology Study. The baseline prevalence of older age was high given the design of the MrOS cohort as well as the self-report of any falls. Age became somewhat protective of wrist fracture in the time varying model as these individuals are less mobile, thus less likely to sustain a fall potentially leading to a fracture. Although other studies have found associations with falls and fractures, in wrist fractures, circumstance of the fall may be the largest contributing factor rather than fall history, which we only captured at baseline. Studies have reported significant associations between SSRI use and falls,[44, 45] and although not explicitly related to the aim of this paper, we did observe a significant relationship between the report of falls and the number of falls and SSRI use in our population. Additional significant factors associated with increased wrist fracture risk among men in the Dubbo study included dietary calcium intake and decreased physical activity. We did not find any association with dietary calcium, with self-reported physical activity based on PASE scores or via our walking outdoors variable.

Strengths and Limitations

Despite the long follow-up, we had very few new wrist fractures, and we were therefore unable to provide stable, reliable multivariate models. This could potentially explain our non-conventional eGFR findings. If we had the ability to place in a multivariate model, it is possible that the association could change. Nevertheless, our study is the first to evaluate wrist fracture and its precursors in a large cohort of community-dwelling, older men in the United States. We were able to build on the traditional fracture risk factors and explore the associations of validated physical performance measures and biological markers.

Conclusions

Although more common in women, wrist fractures are of concern for aging men, particularly men with prior fracture history, and/or poor physical performance. Our study provides information on the risk factors for wrist fractures in older men. More patient and clinical awareness of these factors can aid in the prevention of future fractures.

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Figure 1. Changes in Predictors of Wrist Fractures after Adjustment for Total Hip BMD
BMD = Bone Mineral Density; CI = Confidence Interval

Table 1**Baseline Descriptive Characteristics of MrOS Study Sample**

Characteristic	Mean $\pm$ SD or N (%)
Age (years)	
65 to 69	1750 (29.8)
70 to 74	1678 (28.6)
75 to 79	1413 (24.1)
80+	1034 (17.6)
Race/ethnicity	
White	5253 (89.4)
Black	242 (4.1)
Asian	188 (3.2)
Hispanic and other race	192 (3.3)
Weight (kg)	174.2 $\pm$ 6.8
Height (cm)	83.3 $\pm$ 13.3
BMI (kg/m ²)	
Underweight + normal (<24.9)	1598 (27.2)
Overweight (25 to 29.9)	3012 (51.3)
Obese I to III ($\geq$ 30)	1265 (21.5)
Fair/poor health	821 (14.0)
No. alcoholic drinks/week	4.3 $\pm$ 6.8
Ever smoked cigarettes	3668 (62.4)
BMD	
Total hip BMD (g/cm ²)	0.96 $\pm$ 0.14
Right arm BMD (g/cm ²)	0.86 $\pm$ 0.09
Left arm BMD (g/cm ²)	0.85 $\pm$ 0.09
Falls	
Any falls in the past year	1226 (20.9)
No. falls in the past year	
0	4649 (79.1)
1	698 (11.9)
2+	528 (9.0)
Fracture history	
Fx after age 50, before baseline	1293 (22.0)
Any fracture before baseline	3222 (54.9)
Wrist fracture before baseline	992 (16.9)
Serum	
Phosphate (mg/dL)	3.18 ($\pm$ 0.44)
Calcium (mg/dL)	9.32 ($\pm$ 0.39)
eGFR (mL/min)	76.69 ($\pm$ 18.05)
Medical history	

Characteristic	Mean $\pm$ SD or N (%)
Osteoporosis	119 (2.0)
Parkinson's disease	48 (0.8)
Rheumatoid arthritis	304 (5.2)
Cancer	1693 (28.8)
Diabetes	637 (10.8)
Low thyroid	403 (6.9)
Stroke	333 (5.7)
Heart attack	822 (14.0)
Functional status	
Difficulty with 1+ IADL	1179 (20.1)
Did not walk outside 7 days	772 (13.1)
PASE score	
Quartile 1 186.7 (best)	1467 (25.0)
Quartile 2 142.4 to <186.7	1473 (25.1)
Quartile 3 100.7 to <142.4	1465 (24.9)
Quartile 4 <100.7 (worst)	1467 (25.0)
Physical performance	
Repeated chair stands (s)	
Tertile 1 <9.5 (best)	1891 (32.3)
Tertile 2 9.5 to <11.85	1910 (32.7)
Tertile 3 11.85 (worst)	1892 (32.3)
Unable	156 (2.7)
Leg power (watts)	
Tertile 1 233.3 (best)	1778 (32.7)
Tertile 2 179.0 to <233.3	1781 (32.7)
Tertile 3 <179.0 (worst)	1782 (32.7)
Unable	102 (1.9)
Narrow walk time (s)	
Tertile 1 <4.73 (best)	1776 (30.8)
Tertile 2 4.73 to <5.74	1759 (30.5)
Tertile 3 5.74 (worst)	1767 (30.6)
Unable	472 (8.2)
Walking speed (m/s)	
Tertile 1 1.35 (best)	1982 (33.8)
Tertile 2 1.17 to <1.35	1851 (31.6)
Tertile 3 <1.17 (worst)	1991 (34.0)
Unable	39 (0.7)
Grip strength (kg)	
Tertile 1 45 (best)	1964 (33.5)
Tertile 2 39 to <45	1674 (28.6)
Tertile 3 <39 (worst)	2128 (36.3)

Characteristic	Mean $\pm$ SD or N (%)
Unable	97 (1.7)
Medication use	
Alpha blocker use	904 (15.4)
Loop diuretic use	291 (5.0)
Statin use	1543 (26.3)
SSRI use	156 (2.7)
Tricyclic antidepressant use	106 (1.8)
Thyroid hormone use	377 (6.4)
Inhaled or oral corticosteroid use	476 (8.1)
Dietary intake	
Calcium (mg)	1128.58 ($\pm$ 585.86)
Vitamin D (IUs)	389.00 ($\pm$ 244.48)

Table 2

Incidence of wrist fracture and mortality by age group

Age at baseline	No. cases	Person-time (person-yrs)	Incidence of wrist fracture (per 1,000 person-yrs)	Incidence of mortality (per 1,000 person-yrs)
All ages	97	63,402	1.60 *	43.41 *
65 to 69 years	22	21,243	1.04 (0.68, 1.57)	17.52 (15.84, 19.39)
70 to 74 years	26	19,134	1.36 (0.93, 2.00)	29.67 (27.34, 32.20)
75 to 79 years	29	14,574	1.99 (1.38, 2.86)	50.33 (46.83, 54.08)
80+ years	20	8,451	2.37 (1.53, 3.67)	89.39 (83.27, 95.96)

* Age standardized incidence, based on US Census (2010)

Table 3

Risk factors for wrist fracture with competing risk of mortality.

	Minimally-adjusted model ^a			
	Baseline ^b		Time-varying ^c	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Demographic & lifestyle characteristics				
Age (years)	1.01 (0.99, 1.04)	0.35	1.02 (0.99, 1.06)	0.12
65 to 69	Reference	-	Reference	-
70 to 74	1.20 (0.68, 2.11)	0.53	1.00 (0.47, 2.11)	0.99
75 to 79	1.60 (0.92, 2.78)	0.10	1.09 (0.52, 2.29)	0.72
80+	1.37 (0.76, 2.47)	0.29	1.58 (0.80, 3.12)	0.80
Race/ethnicity				
White	Reference	-	Reference	-
Black	1.21 (0.45, 3.28)	0.71	1.24 (0.46, 3.36)	0.68
Asian	1.17 (0.41, 3.32)	0.77	1.19 (0.42, 3.39)	0.74
Hispanic and other race	0.55 (0.13, 2.31)	0.41	0.57 (0.14, 2.38)	0.44
Weight (kg)	1.01 (0.99, 1.02)	0.58	1.01 (0.99, 1.03)	0.54
Height (cm)	1.02 (0.99, 1.06)	0.15	1.03 (1.00, 1.06)	0.17
BMI (kg/m ²)				
Underweight + normal (<24.9)	Reference	-	Reference	-
Overweight (25 to 29.9)	0.77 (0.48, 1.22)	0.26	0.71 (0.44, 1.13)	0.14
Obese I to III (30)	0.75 (0.40, 1.39)	0.36	0.86 (0.47, 1.57)	0.62
Fair/poor vs. excellent health	0.99 (0.56, 1.77)	0.98	0.87 (0.63, 1.53)	0.63
No. of alcoholic drinks/week	1.00 (0.98, 1.02)	0.87	1.00 (0.98, 1.03)	0.83
Ever vs. never smoked cigarettes	1.28 (0.84, 1.96)	0.25	1.29 (0.84, 1.98)	0.24
BMD				
Total hip BMD (g/cm ²) ^d	0.61 (0.48, 0.77)	<0.01	0.62 (0.49, 0.78)	<0.01
Right arm BMD (g/cm ²) ^d	0.48 (0.36, 0.64)	<0.01	0.49 (0.37, 0.65)	<0.01
Left arm BMD (g/cm ²) ^d	0.43 (0.32, 1.99)	<0.01	0.45 (0.33, 0.61)	<0.01
Falls				
Any falls in the past year (yes vs. no)	1.30 (0.82, 2.08)	0.27	1.25 (0.81, 1.93)	0.31
No. falls in the past year				
No falls	Reference	-	Reference	-
1 fall	1.39 (0.79, 2.45)	0.26	0.97 (0.53, 1.83)	0.97
2 or more falls	1.19 (0.61, 2.32)	0.60	1.52 (0.90, 2.56)	0.12
Fracture history (yes vs. no)				
Having a Fx after age 50, before baseline	2.50 (1.66, 3.76)	<0.01	2.48 (1.65, 3.73)	<0.01
Any Fx before baseline	1.72 (1.12, 2.63)	0.01	1.72 (1.13, 2.64)	0.01
Wrist Fx before baseline	2.03 (1.30, 3.16)	<0.01	2.04 (1.31, 3.17)	<0.01
Serum				
Phosphate (mg/dL) ^d	1.25 (1.02, 1.53)	0.03	1.25 (1.02, 1.53)	0.03

Minimally-adjusted model ^a				
	Baseline ^b		Time-varying ^c	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Calcium (mg/dL) ^d	0.99 (0.80, 1.22)	0.92	0.99 (0.81, 1.22)	0.95
eGFR (mL/min) ^d	1.21 (1.04, 1.41)	0.01	1.23 (1.05, 1.43)	<0.01
Medical history (yes vs. no)				
Osteoporosis	4.26 (2.04, 8.90)	<0.01	2.80 (1.47, 5.33)	<0.01
Parkinson's disease	-	-	-	-
Rheumatoid arthritis	1.48 (0.69, 3.20)	0.32	2.11 (1.15, 3.85)	0.02
Cancer	1.28 (0.83, 1.98)	0.26	1.21 (0.80, 2.52)	0.37
Diabetes	1.07 (0.58, 1.96)	0.84	1.09 (0.63, 1.91)	0.76
Low thyroid	0.57 (0.21, 1.56)	0.27	0.62 (0.25, 1.53)	0.30
Stroke	0.34 (0.09, 1.36)	0.13	0.69 (0.28, 1.71)	0.43
Heart attack	0.77 (0.42, 1.44)	0.42	1.14 (0.68, 1.91)	0.62
Functional status				
Difficulty with 1+ IADL (yes vs. no)	1.55 (0.97, 2.48)	0.07	1.55 (0.97, 2.47)	0.07
Did not walk outside 7 days (yes vs. no)	0.79 (0.41, 1.51)	0.47	0.75 (0.40, 1.42)	0.38
PASE score				
Quartile 1 186.7 (best)	Reference	-	Reference	-
Quartile 2 142.4 to <186.7	1.38 (0.79, 2.42)	0.26	1.23 (0.66, 2.29)	0.52
Quartile 3 100.7 to <142.4	1.39 (0.80, 2.44)	0.25	1.61 (0.90, 2.88)	0.11
Quartile 4 <100.7 (worst)	0.73 (0.38, 1.41)	0.35	1.16 (0.63, 2.15)	0.63
Physical performance				
Repeated chair stands (s)				
Tertile 1 <9.5 (best)	Reference	-	Reference	-
Tertile 2 9.5 to <11.85	1.36 (0.80, 2.33)	0.26	1.34 (0.77, 2.31)	0.30
Tertile 3 11.85 (worst)	1.62 (0.96, 2.75)	0.07	1.27 (0.73, 2.21)	0.40
Unable	1.00 (0.23, 4.22)	0.99	1.55 (0.68, 3.54)	0.29
Leg power (watts)				
Tertile 1 233.3 (best)	Reference	-	Reference	-
Tertile 2 179.0 to <233.3	1.01 (0.59, 1.74)	0.97	0.88 (0.48, 1.63)	0.68
Tertile 3 <179.0 (worst)	0.94 (0.51, 1.73)	0.85	0.84 (0.44, 1.62)	0.61
Unable	1.14 (0.27, 4.87)	0.86	0.98 (0.32, 3.00)	0.97
Narrow walk time (s)				
Tertile 1 <4.73 (best)	Reference	-	Reference	-
Tertile 2 4.73 to <5.74	0.84 (0.50, 1.42)	0.53	0.89 (0.50, 1.58)	0.68
Tertile 3 5.74 (worst)	0.85 (0.50, 1.44)	0.54	0.80 (0.44, 1.44)	0.45
Unable	0.80 (0.34, 1.86)	0.60	1.11 (0.55, 2.21)	0.78
Walking speed (m/s)				
Tertile 1 1.35 (best)	Reference	-	Reference	-
Tertile 2 1.17 to <1.35	0.99 (0.59, 1.64)	0.96	0.89 (0.52, 1.53)	0.67
Tertile 3 <1.17 (worst)	0.93 (0.54, 1.61)	0.80	0.93 (0.53, 1.61)	0.79

	Minimally-adjusted model ^a			
	Baseline ^b		Time-varying ^c	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Unable	1.29 (0.17, 9.61)	0.81	1.42 (0.46, 4.36)	0.54
Grip strength (kg)				
Tertile 1 45 (best)	Reference	-	Reference	-
Tertile 2 39 to <45	1.39 (0.83, 2.35)	0.21	1.21 (0.69, 2.10)	0.51
Tertile 3 <39 (worst)	1.07 (0.63, 1.82)	0.79	1.15 (0.67, 1.98)	0.61
Unable	2.31 (0.69, 7.77)	0.18	3.38 (1.24, 9.25)	0.02
Medication use (yes vs. no)				
Alpha blocker	0.98 (0.56, 1.69)	0.94	1.35 (0.85, 2.15)	0.20
Loop diuretic	0.57 (0.17, 1.88)	0.36	1.01 (0.48, 2.10)	0.98
Statin	0.87 (0.54, 1.39)	0.56	0.75 (0.48, 1.18)	0.22
SSRI	2.55 (1.12, 5.83)	0.03	3.60 (1.96, 6.63)	<0.01
Tricyclic antidepressant	0.0	<0.01	1.41 (0.35, 5.79)	0.63
Thyroid hormone	0.45 (0.14, 1.43)	0.18	0.58 (0.23, 1.42)	0.23
Inhaled/Oral corticosteroid	1.54 (0.84, 2.82)	0.17	1.74 (1.00, 3.01)	0.049
Dietary intake				
Calcium (mg)	1.00 (1.00, 1.00)	0.94	1.00 (1.00, 1.00)	0.95
Vitamin D (IUs)	1.00 (1.00, 1.00)	0.78	1.00 (1.00, 1.00)	0.79

HR = Hazard Ratio, BMD = Bone Mineral Density, FX = Fracture, eGFR = estimate Glomerular Filtration Rate, IADL = Instruments of Activities of Daily Living, PASE = Physical Activity Scale for the Elderly, SSRI = Selective Serotonin Reuptake Inhibitor

^a Minimally-adjusted models include age, race/ethnicity, and MrOS site.

^b All characteristics at baseline.

^c Time-varying covariates: All variables are time-varying in this Cox analysis, except for those that are static or available only at baseline: race, alcohol use, any fracture before baseline, any fracture between age 50 and baseline, wrist fracture before baseline, phosphate, calcium, and eGFR.

^d Per SD increase

NOTES

Exclusions: (1) Self-reported currently taking (at baseline) calcitonin (n=20), fluoride (n=0), or 1 or more testosterone injections per month *and* have ever had osteoporosis (n=5), or (2) bisphosphonate use at baseline (n=101), or (3) no follow up time (n=1).

P-value in bold if p<0.05