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Ten-year incident osteoporosis-related fractures in the population-based Canadian Multicentre Osteoporosis Study — Comparing site and age-specific risks in women and men

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ABSTRACT

Background: Population-based incident fracture data aid fracture prevention and therapy decisions. Our purpose was to describe 10-year site-specific cumulative fracture incidence by sex, age at baseline, and degree of trauma with/without consideration of competing mortality in the Canadian Multicentre Osteoporosis Study adult cohort.
Methods: Incident fractures and mortality were identified by annual postal questionnaires to the participant or proxy respondent. Date, site and circumstance of fracture were gathered from structured interviews and medical records. Fracture analyses were stratified by sex and age at baseline and used both Kaplan–Meier and competing mortality methods.
Results: The baseline (1995–97) cohort included 6314 women and 2789 men (aged 25–84 years; mean ± SD 62 ± 12 and 59 ± 14, respectively), with 4322 (68%) women and 1732 (62%) men followed to year-10. At least one incident fracture occurred for 930 women (14%) and 247 men (9%). Competing mortality exceeded fracture risk for men aged 65+ years at baseline. Age was a strong predictor of incident fractures especially fragility fractures, with higher age gradients for women vs. men. Major osteoporotic fracture (MOF) (hip, clinical spine, forearm, humerus) accounted for 41–74% of fracture risk by sex/age strata; in women all MOF sites showed age-related increases but in men only hip was clearly age-related. The most common fractures were the forearm for women and the ribs for men. Hip fracture incidence was the highest for the 75–84 year baseline age-group with no significant difference between women 7.0% (95% CI 5.3, 8.9) and men 7.0% (95% CI 4.4, 10.3).
Interpretation: There are sex differences in the predominant sites and age-gradients of fracture. In older men, competing mortality exceeds cumulative fracture risk.

Introduction

Fractures are the primary health risk of osteoporosis [1,2]. The costs of acute and chronic care following fractures, especially those at the hip, comprise a major portion of national health-care budgets. In 2005, fractures in the USA were associated with an estimated $17 billion dollars in direct costs [3]. A portion of the post-fracture economic burden includes rehabilitation [4,5], the cost for the increased risks of long-term disability with resulting required increased support [5,6], decreased health-related quality of life [7] including the development of depression in older women [8] and increased mortality [9]. Thus considerable resources might be allocated toward fracture prevention without exceeding those incurred following a fracture [10].

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The FRAX tool, developed to predict the 10-year risk of hip fracture and "major osteoporotic fracture" (MOF, defined as fractures at the hip, distal forearm, clinical vertebral, and proximal humerus) [11,12], was based on combined data from several international cohorts [12]. Calibration of the Canadian FRAX tool used Canadian national hospital hip fracture data [13] with estimated major osteoporotic fracture rates [14].

The FRAX assessment of major osteoporotic fracture has been established as a standard outcome and measure of burden of disease. Implicit to the FRAX algorithm deriving 10-year fracture probability estimates is an adjustment for the competing risk of death. Furthermore, the FRAX tool considered risk of major osteoporotic fracture as a summary measure, but other fracture sites contributing to the overall burden of osteoporosis include the pelvis, rib and leg [15]. Rib fractures are common in both men and women, are associated with classic osteoporosis risk factors, and are a risk factor for future fracture [16–20]. The high-frequency of fractures at sites other than the hip and spine is associated with high health care utilization [21]. In short, the population health burden of osteoporotic fractures includes more skeletal sites than major osteoporotic fracture sites and is also potentially modified by competing mortality.

Our purpose was to describe the site-specific 10-year risk of fracture by sex, age at baseline, fracture site and degree of trauma with and without consideration of competing mortality risk in a national population-based cohort.

Methods

Study population

The Canadian Multicentre Osteoporosis Study (CaMos) is an ongoing national population-based cohort study initiated in 1995. CaMos design, questionnaires and baseline data acquisition have previously been described [22]. Briefly, recruited community dwelling participants lived within a 50-kilometer radius of one of the nine Canadian cities (St John's, Halifax, Quebec City, Toronto, Hamilton, Kingston, Saskatoon, Calgary and Vancouver) and were able to converse in English, French or Chinese (in Vancouver and Toronto only). Households were randomly selected from residential phone numbers; participants were then randomly selected within households by a sex and age-stratified protocol weighted to older adults targeting two-thirds women. Of those randomly selected, 42% agreed to full participation including clinical measurements, BMD and spine radiographs. Ethics approval was granted through McGill University and centre ethics review boards. All participants gave written informed consent and the study is conducted in accordance with the Helsinki Declaration. The population for the present study included all CaMos participants with follow-up data who were aged 25 to 84 years at baseline.

Data collection

Participants completed a standardized interviewer-administered questionnaire (CaMos questionnaire ©1995) at baseline assessing demographics, general health, nutrition, reproduction, medication use and medical history to capture detailed information about risks for fracture.

Fracture assessment

Self-reported incident fractures were identified by yearly postal questionnaire or interviewer-administered questionnaires at scheduled interviews (year 3, [baseline ages 40–60], year 5 and year 10). A structured interview confirmation of postal questionnaires determined the fracture-specific date, site, circumstances, trauma and management. Those with missing fracture questionnaires (including those who died) were identified and secondary contact information was used to complete the fracture questionnaire by proxy. Independent medical records (obtained with consent to contact the treating physician/hospital) were obtained for 78% of all incident fractures and these could be further adjudicated (e.g. hip vs. non-hip leg). We were unable to adjudicate all fractures, therefore to avoid the underestimation of fractures due to failure to obtain relevant records we also included self-reported fractures that were confirmed in the telephone interview.

Fragility fractures were defined to be those involving a force less than or equal to a fall from a standing height. In this osteoporosis-specific description, we excluded incident fractures of the skull, face, hands, ankles, and feet. WHO major osteoporotic fractures (hip, clinical spine, forearm, and humerus) are reported for comparison purposes. Fractures designated "leg" occurred at sites excluding the proximal femur or hip.

Statistical methods

We assessed between-group differences (incident fracture vs. no incident fracture) for continuous variables using a *t*-test and for categorical variables using a chi-squared test. We performed the main analyses separately for women and men and further stratified analysis by baseline age-category (5-year bands). Person-time for this analysis included the period from study enrolment to exit (earliest date of: incident fracture, death, last complete fracture questionnaire, 10-year study anniversary). For specific skeletal sites, we considered person-time up until the fracture at that site, ignoring fractures at other sites. In the first analyses, cumulative fracture incidence or fracture risk was computed without considering competing mortality by Kaplan–Meier method treating deaths as a censored outcome. We tested age–sex interactions and age-gradients with a Cox proportional hazards model. Since the FRAX tool adjusts for competing mortality, we performed further analyses with death as a competing risk [23]. All analyses were performed with Stata (Version 12) (College Station, Texas, USA); we used the package "stcompet" for the competing risks calculations.

Results

The study sample consisted of 6314 women and 2789 men with a follow-up duration from study entry to study exit (first fracture, death, or study discontinuation) of 50,300 person-years in women and 21,800 person-years in men. The study sample excluded 186 women and 62 men who did not meet the initial age eligibility criteria (<85 years) and 39 women and 33 men who did not have at least one year of follow-up. A total of 4322 (68%) women and 1732 (62%) men were still alive and in the cohort at year 10.

Incident fracture risk and competing mortality by age, sex

A total of 930 women (14%) and 247 men (9%) had one or more incident fractures (excluding head, hands, ankles and feet) during the 10-year study period (Table 1). Those who had incident fractures were older, had lower BMD values, lower physical function (SF-36), were more likely to have entered the cohort with diagnoses of osteoporosis or prevalent fractures and were more likely to be white when compared to those without incident fracture. Fig. 1 shows the distribution of fracture sites (for the first incident fracture) by sex. The distribution of skeletal sites differed by sex; forearm fractures were most common among women and rib fractures were most common among men. For some incident fractures these occurred at multiple fracture sites in a single event; this occurred for 48 women and 11 men. Finally, among those who experienced incident fractures during the 10-year follow-up, multiple fractures (stratified as 2, 3, 4, 5+) were observed in 185 women (145, 27, 8, 5, respectively) and 43 men (35, 7, 1, 0, respectively).

For most sex and age groups, the estimates of 10-year fracture risk using Kaplan–Meier methods are very similar to the estimates of 10-year fracture risk taking into account competing mortality (Table 2),