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Self-perception of fracture risk: what can it tell us?

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Conflict of interest:

Anna Litwic, Juliet Compston, Allison Wyman, Ethel Siris, Stephen Gehlbah, Jonathan Adachi, Roland Chapurlat, Adolfo Diez Perez, Andrea LaCroix, Jeri Nieves, Coen Netelenbos, Johannes Pfeilschifter, Maurizio Rossini, Christian Roux, Kenneth Saag, Stuart Silverman, Nelson Watts, Susan Greenspan, Lyn March, Celia Gregson,Cyrus Cooper and Elaine Dennison declare that they have no conflict of interest.

Mini abstract

In this study we report that self-perception of fracture risk captures some aspect of fracture risk not currently measured using conventional fracture prediction tools and is associated with improved medication uptake. It suggests that adequate appreciation of fracture risk may be beneficial and lead to greater healthcare engagement and treatment.

Abstract

Purpose: This study aimed to assess how well self-perception of fracture risk, and fracture risk as estimated by the fracture prediction tool FRAX, related to fracture incidence and uptake and persistence of anti-osteoporosis medication among women participating in the Global Longitudinal study of Osteoporosis in Women (GLOW).

Methods: GLOW is an international cohort study involving 723 physician practices across 10 countries in Europe, North America and Australia. 60393 women aged ≥55 years completed baseline questionnaires detailing medical history, including co-morbidities, fractures and self-perceived fracture risk (SPR). Annual follow-up included self-reported incident fractures and anti-osteoporosis medication (AOM) use. We calculated FRAX risk without bone mineral density measurement.

Results: Of the 39241 women with at least one year of follow-up data, 2132 (5.4%) sustained an incident major osteoporotic fracture over 5 years of follow-up. Within each SPR category, risk of fracture increased as the FRAX categorisation of risk increased. In GLOW only 11% of women with a lower baseline SPR were taking AOM at baseline, compared with 46% of women with a higher SPR. AOM use tended to increase in the years after a reported fracture. However, women with lower SPR who fractured still reported lower AOM rates than women with or without a fracture but a higher SPR.

Conclusions: These results suggest that SPR captures some aspect of fracture risk not currently measured using conventional fracture prediction tools and is also associated with improved medication uptake.

Keywords: Fracture risk, FRAX, Osteoporosis, Treatment, Adherence

Introduction

Osteoporosis-related fractures confer a significant healthcare burden. Approximately one in two women and one in four men over age 50 will have an osteoporosis-related fracture in their lifetime [1]. In addition to the personal impact on millions of people around the world, fractures caused by osteoporosis represent a major and growing socioeconomic burden. In 2005 in the United States alone, there were 297,000 hip fractures, 547,000 vertebral fractures, 397,000 wrist fractures, 135,000 pelvic fractures, and 675,000 fractures at other sites costing nearly $17 billion [2]. The cost of osteoporotic fracture in the UK approaches £3 billion annually and, across the EU, the estimated total economic cost of the approximately 3.5 million fragility fractures in 2010 was €37 billion [3]. As the population ages, costs are expected to escalate.

Therapeutic options can significantly reduce the risk of osteoporosis-related fractures. However, suboptimal use of anti–osteoporosis medications (AOM) and low adherence among women who have started AOM are recognised problems, similar to adherence problems reported for many non-communicable diseases such as ischaemic heart disease, chronic obstructive pulmonary disease and osteoporosis [4-6]. More than one third of people do not comply with prescribed treatment regimens [7]. A more recent study of patients, who received AOM within 1 year after fracture, reported that persistence with AOM was 75% and 45.3% after 1 and 5 years respectively [8].

It is possible that empowering patients through improved understanding of their disease and adequate appreciation of fracture risk may be beneficial, as increased self-awareness might lead to greater healthcare engagement and treatment. Although, it has been demonstrated that a person's perception of osteoporosis is associated with improved medication adherence [9], it has been reported that people with an increased fracture risk commonly underestimate their actual risk, suggesting that there might be a disconnect between self-perception of fracture risk and actual fracture risk [10].

In a study to consider self-perception of fracture risk further, we aimed to determine how well a person's fracture risk perception aligned with fracture probability as assessed by FRAX in a large, multinational cohort study, and also assess whether incident fracture was associated with altered (i) use of AOM (ii) self-reported adherence to AOM.

Methods

Study design

GLOW is an observational cohort study conducted in physicians' practices at 17 sites in 10 countries (Austria, Belgium, Canada, France, Germany, Italy, Netherlands, Spain, UK and USA). Details of the study design have been previously described [11]. In brief, typical practices of each region were recruited through primary care networks. Each practice provided a list of women aged 55 years or older, who within the past 24 months had consulted their primary care physician. Sampling was age-stratified to ensure that two thirds of women were 65 years of age or older, excluding those who were unable to complete the study survey due to cognitive impairment, language barriers, institutionalisation or illness. Each study site obtained ethics committee approval to conduct the study in the specific location.

Questionnaires

Self-administered questionnaires covered domains that included: demographic characteristics and risk factors, perception about fracture risk relative to women of the same age (ranked as much lower', 'little lower', 'about the same', 'little higher' and 'much higher', on a 5 point scale), medication use, medical diagnosis, healthcare use and access, physical activity and physical and emotional health status including self - rated health. Self-reports of personal risk factors included: current weight and height, parental hip fracture, falls in the past 12 months, current use of cortisone or prednisolone, diagnosis of rheumatoid arthritis, personal history of fracture (clavicle, arm, wrist, spine, rib, hip, pelvis, upper leg, lower leg, and ankle) since age 45 years, current cigarette smoking and consumption of three or more units of alcohol daily.. Follow up questionnaires were sent annually for 5 years. These asked about any incident fractures and requested information about site of fracture and any hospital treatment received.

FRAX

FRAX scores were calculated for women from responses on their baseline survey, without inclusion of bone mineral density measurement. The FRAX tool with or without the use of BMD is a well-validated instrument and enhances fracture risk prediction [12]. Women were classified as 'high risk', 'medium risk' and 'low risk' if their FRAX 10 year probability of

major osteoporotic fracture and hip fracture was both ≥20% and ≥3%, either ≥20% or ≥3%, or both ≤20% and ≥3% respectively.

Medication

Women were considered to be taking anti-osteoporosis medications (AOM) if they reported current use of alendronate, etidronate, ibandronate, risedronate, pamidronate, zoledronate, strontium ranelate, calcitonin, PTH [1-84], teriparatide, raloxifene, or tibolone.

Analysis

Data from women who completed a baseline questionnaire and at least one year of follow-up were included in the analysis. Women who reported any incident major fracture (hip, spine, upper arm, shoulder, or wrist) that occurred between baseline and their last year of consecutive follow-up-- between 1 and 5 years after baseline-- were classified as incident fracture positive. If a woman reported more than one incident fracture, the date of her earliest fracture was used. For this analysis SPR was defined as 'higher' when women rated their SPR, using a five point scale as 'little higher' and 'much higher'; and as 'lower' when rated as 'much lower' or 'little lower', compared with women of the same age. A Cox proportional hazards model predicting 5-year incident fracture based on SPR category, FRAX risk category, and an interaction term of SPR with FRAX was used to calculate unadjusted hazard ratios (HRs) and 95% confidence intervals (CI) for each SPR and FRAX risk category combination. A separate Cox proportional hazards model predicting 5-year incident fracture based on SPR and FRAX was used to determine if the two were independently significant predictors of fracture. Finally, as a sensitivity analysis, two additional Cox proportional hazards model predicting 5-year incident fracture were run. The first added number of falls reported in the past 12 months on the baseline GLOW survey to a model with SPR and FRAX, and was used to determine if the relationship between SPR, FRAX, and incident fracture would remain after adjusting for history of falls. The second added a variable for the country of the GLOW respondent to a model with SPR and FRAX, to determine if the relationship between SPR, FRAX, and incident fracture would remain after adjusting for geographic region. Associations were considered significant if the p-value was <0.05. All calculations were done using SAS version 9.4.

Results

A total of 60,393 patients from 723 physicians' practices enrolled in the study between October 2006 and February 2008. Approximately 25000 participants were recruited in Europe, 28000 in USA, and almost 7000 in Canada and Australia. There were 39,241 (65%) women with at least one year of follow-up data. The mean age was 68 years and mean weight 70kg. History of maternal hip fracture was reported by 14% participants and personal history of a fracture of the wrist, spine, or hip was 11% at baseline. The reported prevalence of common comorbid conditions was: 11% asthma, 0.8% rheumatoid arthritis, 50% hypercholesterolaemia and 49% hypertension; 19% of women said their health status was "fair" or "poor". Fifty six percent of women expressed "some" concern about osteoporosis and 21% said they were "very concerned" about the condition. When women rated their SPR (their own risk of fracture compared with women their own age), 36% rated their risk as lower and 17% as higher. The remaining 46% considered their risk "the same." Women who rated their SPR as higher also reported more falls than women who rated their SPR as lower; among women with lower SPR only 11% reported two or more falls in the prior year, compared to 23% of women with higher SPR ($p<0.0001$). The number of reported comorbidities was also significantly associated with SPR ($p<0.0001$). Similar to falls, women who rated their SPR higher reported more comorbidities than women rating their SPR as lower with figures of 20% and 17% for 3 comorbidities, 11% and 6.6% for 4 comorbidities, and 7.5% and 3.1% for ≥ 5 comorbidities respectively.

Incident major fracture (hip, wrist, spine, shoulder, arm) was reported by 2132 (5.4%) women over 5-years of follow-up. Table 1 shows the associations between SPR and FRAX-derived fracture risk. Within each SPR category, risk of incident fracture increased as FRAX categorisation of risk increased. The highest risk of fracture was seen in women with both a high SPR and high FRAX risk. In a Cox model containing both FRAX risk and SPR both variables were highly significant ($p<0.0001$), suggesting that a woman's own perception of fracture risk is an additional predictor of fracture beyond that calculated by FRAX. In the model, compared to women with lower SPR, women with SPR of "about the same" as other women their age had a slightly increased fracture hazard ratio (95% CI) of 1.15 (1.04 – 1.27). Women with SPR "much or a little higher" as other women their age had almost twice the rate of fracture, with a hazard ratio (95% CI) of 1.88 (1.68 – 2.11). In the same model, compared to women with low FRAX risk, women with medium FRAX risk had a fracture hazard ratio (95% CI) of 1.53 (1.37 – 1.70), and women with high FRAX risk had a fracture hazard ratio (95% CI) of 2.81 (2.52 – 3.12). FRAX was a stronger predictor of a fracture than

SPR (Type 3 Wald chi-square values of 366.34 and 134.40 respectively) but both variables had a highly significant, independent association with fracture.

Woman who have fallen consider themselves at higher risk for fracture ($p < 0.0001$). It is possible that women reporting a high SPR may do so because they perceive their risk of falls to be higher than women of the same age. We attempted to investigate this issue In a separate Cox model that included SPR, FRAX, and the number of falls in the year prior to the survey's baseline, the falls variable was a significant predictor of a subsequent fracture with a hazard ratio (95% CI) of 1.24 (1.12-1.37) for one fall and 1.66 (1.48-1.85) for ≥ 2 falls, but the results for SPR and FRAX both remained highly significant. Moreover, the Type 3 Wald chi-square values for SPR (107.13) and FRAX (345.58) were higher than that of the falls variable (81.68) and the HRs for SPR and FRAX did not change appreciably. This indicates that both have a significant, independent contribution towards predicting fracture, but that SPR was stronger.

At baseline, 7579 (20%) of the cohort reported taking an AOM. There were 565 incident fractures reported at year 1, 531 at year 2, 494 at year 3, and 534 at year 5. Of 14238 women in GLOW with a lower baseline SPR, 1527 (11%) were taking an AOM at baseline, while of 6829 women with a higher SPR 3042 (46%) were taking an AOM at baseline. AOM use tended to increase in the year following an incident fracture in women with lower or higher SPR. For example, among women with a lower baseline SPR 11% were taking AOM at baseline and 23% at year 1 if the woman reported an incident fracture, while the corresponding figures for those with higher baseline SPR were 46% and 55% respectively. However, among women with lower SPR who reported an incident fracture, use of AOM was consistently lower than that of women with higher SPR regardless of their fracture status ($p<0.0001$) (Figure 1).

Results presented throughout did not include country of origin. Although we repeated analyses and in a Cox model that included SPR, FRAX, and the country of the GLOW survey respondent, the country variable was significant ($p<0.0001$), but again without substantial change in effect size or direction.

Discussion

We have demonstrated that SPR of fracture does capture some aspect of fracture risk not currently measured using the conventional fracture prediction tool FRAX, and also translates to improved medication uptake.Self-perception of risk of a condition is a difficult concept, as it requires an individual to compare their own health status to others. In previous work, SPR of osteoporosis and osteoporotic fractures has previously been reported to be underestimated in postmenopausal women worldwide. Rothmann et al, observed that women participating in the Risk-Stratified Osteoporosis Strategy Evaluation (ROSE) study underestimated their fracture risk compared to the risk estimated by FRAX, although it demonstrated that women did have some understanding of the importance of some risk factors such as prior fracture, parental history and falls [13]. Women at increased fracture risk generally perceive their risk to be lower or about the same as women of the same age, as has been shown previously in GLOW [10, 14]. Our data suggest that SPR offers a further contribution to fracture prediction, independent of fracture prediction by FRAX.

An increased number of falls present in women with higher SPR in this study; a variable not captured by FRAX, is a possible partial explanation for the independent addition of SPR to fracture prediction algorithms. Falls increase fracture risk among older adults and multiple falls are a marker of physical frailty. However, even in our model including falls, SPR remained a significant independent predictor of fracture. Interestingly, fear of falling, a self-perceived concept, has been found to be predictive of future falls [15]. Polypharmacy may be another explanation for our findings. Due to the age range of our study group, most individuals suffered from at least one chronic condition. Some comorbidities increase falls risk, which could lead to increased fracture risk; for example neurological diseases have been shown to have the highest fracture rates among participants of the GLOW study [14]. In this study higher number of comorbidities was associated with higher SPR. The presence of chronic disease may imply a need to take prescribed drugs that might increase the risk of falling. Several types of drugs are associated with a significant risk of falls. Use of antidepressants has been reported to have the strongest association with falls, but also other classes of medication among other including antihypertensives, nonsteroidal anti-inflammatory drugs and antipsychotics were found to have positive association with falling [16]. Furthermore, drug adherence may be lower in frail patients with cognitive impairment.

SPR was also associated with self-reported AOM uptake. In this large, international observational study women with higher SPR were more likely to report AOM use than women with lower SPR. AOM use was higher in the year after an incident fracture for

women in both groups with lower or higher SPR, but the absolute rate of AOM use was always higher among women with higher SPR. Whether changing the SPR from lower to higher would lead to improve in uptake or adherence to AOM requires further investigation.

It is well documented that prescription rates of AOM following osteoporotic fracture are low and adherence to medication is poor. Previous studies suggest that just 17% of treatment naive women with a new fracture began AOM in the first year of follow-up and between 26 - 70% of women prescribed oral bisphosphonates continued to take them at 1 year [8, 17]. This is consistent with our findings, in which a high proportion of women with incident fracture did not start AOM.

Established predictors of treatment initiation include a diagnosis of osteoporosis and low measured bone density [17]. In the current study, SPR of fracture also predicted osteoporosis treatment. Other studies also found that patient health beliefs predicted treatment. For example, patient beliefs in the benefits of medications, and distrust of medications were reported to differentiate between initiators and non-initiators of osteoporosis medication [18, 19]. It is well recognised that a well-informed, empowered patient should be at the heart of the chronic disease management model. In cases of osteoporosis, it may be that improved understanding of the disease, its management and appreciation of fracture risk among patients would help to tackle under-use of AOM, and we hope to address this in future work, in a randomised controlled trial setting.

Our study has some limitations. Educational and cultural differences may influence SPR of fracture. While we performed a sensitivity analysis for country, in this cohort data regarding ethnicity were not available apart from in women from USA and Canada. Furthermore, although some educational data were collected, it is difficult to draw conclusions due to difference in the educational systems between the participating countries. Finally, information on AOM use was based upon self-reported questionnaire and not verified by pharmacy records. It has been reported, however, that agreement between self-report and pharmacy data is high [20].

In conclusion, our data suggest that self-reported risk of fracture does capture an aspect of fracture risk not currently measured using the conventional fracture predictions tool FRAX, and that greater self-reported risk also translates to improved osteoporosis medication uptake. These observations suggest that education interventions may help to improve medication

uptake and adherence, and that a woman's perception of her own risk of fragility fracture should be considered when counselling her regarding management of osteoporosis.

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