Is there an increased risk of falls and fractures in people with early diagnosed hip and knee osteoarthritis? Data from the Osteoarthritis Initiative

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Falls are a serious threat to the wellbeing of older people. They are a significant cause of morbidity and mortality.1 It has been estimated that approximately 30% of community-dwelling individuals aged 65 years and older, and 50% aged 85 years and older, will experience a fall annually.2 This can have a number of consequences, including fall-related injury with associated fractures, reduced confidence and functional independence and ultimately a greater need for long-term care.2 Falls-related fracture is considered the most serious of sequaelle.3 Kannegaard et al.4 estimated that the cumulative mortality among hip fracture patients is 37.1% in men and 26.4% in women 12 months post-fracture. A number of factors have been associated with increased risk of falls. These have included demographic, socio- economic, medical and morbidity-related, poly- pharmacy, environmental and physical, including impaired mobility, balance and gait problems.5

Osteoarthritis is one of the most common musculoskeletal disorders in the elderly.6 The incidence of osteoarthritis is increasing with the increasing global ageing population; it is projected that the prevalence of osteoarthritis will increase from approximately 10% of people aged 60 years or older to 40% over the next 20 years.7,8 Osteoarthritis is associated with joint pain and stiffness, reduced balance, impeded mobility and loss of functional independence.9 These factors have all been previously demonstrated to be risk factors for falls in cohorts of older people.10,11

Previous studies have demonstrated a link between osteoarthritis of the knee and falls. Dore et al.11 recently reported the association between the number of lower limb joints affected and falls risk, reporting an increased likelihood of falling in symptomatic osteoarthritis cohorts. However, previous literature has not examined the risk of subsequent fracture specifically as a falls- related injury in a large cohort such as the Osteoarthritis Initiative dataset. This is important given that fracture is the most serious consequence of falls associated with mortality in older people. It also remains unclear whether falls risk is different for people newly diagnosed with hip or knee osteoarthritis, rather than people diagnosed per se, irrespective of the duration since diagnosis.

The purpose of this analysis was first to determine if there was a difference in the occurrence of falls, with or without consequential fractures, between people newly diagnosed with unilateral hip or knee osteoarthritis within the preceding 12 months, compared to those who had not. Second, we aimed to explore the risk factors associated with falls and subsequent fractures for people with unilateral hip or knee osteoarthritis. Using these findings, it will be possible to better identify when people may be at a greater risk of a fall and falls-related fracture and therefore lead to a greater understanding of the relationship between hip and knee osteoarthritis and these risks.

MATERIALS AND METHODS

Data used in the preparation of this article were obtained from the Osteoarthritis Initiative (OAI) data- base, which is available for public access at http:// www.oai.ucsf.edu/. The OAI is a large-scale, multi-centre (four sites across the USA: the Ohio State University; the University of Maryland School of Medicine; the University of Pittsburgh and the Memorial Hospital of Rhode Island in Pawtucket, Rhode Island), longitudinal cohort study aimed to investigate the role of biomarkers in the development and progression of lower limb osteoarthritis. Through this, ethics approval was granted from the Committee on Human Research, University of California, San Francisco (IRB approval number 10– 00532 approved 10 March, 2015).

Baseline data collected from volunteers to the study commenced between February 2004 and May 2006, with data longitudinally collected at 12, 24, 30, 36, 48, 60, 72 and 84 months follow-up intervals. Data collected has included: individual’s demographic characteristics, previous and current medical history including medical morbidities, lifestyle and physical activity behaviours (assessed using the Physical Activity Scale for the Elderly [PASE]).12 The minimally clinically important difference for the total PASE score is 87 points.13 For this analysis, we collated data on: the number of participants who reported a fall within the first 12 months of a diagnosis of osteoarthritis; the frequency of falls in this period; and whether a fracture was sustained during this period.

To answer this research question, from the OAI data- set, we included all community-dwelling people who were diagnosed with unilateral hip or knee osteoarthritis by a medical practitioner (clinical with or without radiological evidence) within 12 months of the corresponding data collection period. We excluded people who had bilateral hip or knee osteoarthritis, although people with unilateral hip and knee osteoarthritis were potentially eligible. A matched cohort was identified of community-dwelling individuals who had not been diagnosed with hip or knee osteoarthritis (i.e., had not presented to a physician with joint pain diagnosed as osteoarthritis) from the OAI dataset. The cohorts were matched for: age, ethnicity and PASE score to account for the potential confounder of level of participating physical activity.5 There was no overlap of patients between these two groups.

Data analysis

Descriptive statistics were initially used to analyze the trends and patterns in categorical and continuous data. The normality of the dataset was analyzed using the Shapiro–Wilks test.

The aim of the analysis was to determine whether there was a difference in occurrence of falls, with or without consequential fractures, between people newly (within 12 months) diagnosed with unilateral hip or knee osteoarthritis, within the preceding 12 months, compared to those who had not. To determine this we compared the newly diagnosed unilateral hip or knee osteoarthritis cohorts to non-osteoarthritis cohorts using Student’s t-test to assess mean cumulative falls, and a chi-square test to assess the occurrence of a fall and the occurrence of a fracture in a 12 month period between the groups. We also determined the odds of experiencing a fall and fracture in a 12 month period with odd ratios (OR) and 95% confidence intervals (95% CI) for each cohort.

Second, we aimed to determine which factors may be associated with the occurrence of a fall and/or fracture in people who had been diagnosed with unilateral hip or knee osteoarthritis within the preceding 12 months. To determine this, a univariate analysis was initially undertaken with the dependent variables: the occurrence of a fall in the preceding 12 months and the occurrence of a fracture in the preceding 12 months.

The independent variables identified through previous research as potential explanatory factors included: age, gender, ethnicity, marital status, employment status; previous total hip arthroplasty (THA); previous total knee arthroplasty (TKA); diagnosis of hip osteoarthritis; diagnosis of knee osteoarthritis; and use of bisphosphonates (assessed as a binary ‘yes/no’ response) in a 12 month interval. Based on these, all variables identified as significant at P < 0.1 on univariate analysis were entered into a multivariate logistical regression model. All logistical regression data was expressed as ORs with 95% CIs and P-values. The Wald statistic was used to assess statistical significance in each regression model. All analyses were undertaken using STATA version 12.0 (STATACorp LP, College Station, TX, USA).

RESULTS

As summarized in Figure 1, in total, 552 individual with unilateral hip osteoarthritis were compared to 4244 individuals without hip osteoarthritis. Of these, 321 (58%) people also had unilateral knee osteoarthritis. In the knee osteoarthritis analysis, 1350 individuals with unilateral knee osteoarthritis were compared to 3445 individuals without knee osteoarthritis. Of these, 262 (19%) people also had unilateral hip osteoarthritis.

The demographic characteristics of the four groups are presented in Table 1. This demonstrated these were broadly similar in characteristics between the hip analysis group, although there was a higher percentage of individuals employed at baseline analysis in the hip osteoarthritis compared to the non-hip osteoarthritis cohort (48% vs. 60%), and a higher proportion of individuals diagnosed with knee osteoarthritis in the hip osteoarthritis group compared to non-hip osteoarthritis cohort (12% vs. 58%). The percentage of individuals prescribed bisphosphonate was slightly higher in the non-hip osteoarthritis cohort compared to the hip osteoarthritis cohort (87% vs. 80%). Similarly, there

appeared a slightly greater percentage of individuals employed at baseline in the knee osteoarthritis cohort (49%) compared to the non-knee osteoarthritis cohort (35%), and a higher percentage diagnosed with hip osteoarthritis in the knee osteoarthritis cohort (19%) compared to the non-knee osteoarthritis cohort (1%).

Hip osteoarthritis analysis

People with hip osteoarthritis demonstrated a greater likelihood of experiencing a fall within the first 12 months post-diagnosis compared to those without hip osteoarthritis (OR: 1.52; 95% CI: 1.26–1.84; P < 0.01). The chance of experiencing a fall was 52% greater for people with hip osteoarthritis compared to those without. While there was a difference in the cumulative number of falls within the assessing 12 month period, with significantly greater numbers in the hip osteoarthritis cohort (P < 0.01), this remained relatively low in each group (0.47 vs. 0.66; Table 2).

There was a greater likelihood of experiencing a fracture in people who had hip osteoarthritis compared to those without (OR: 1.84; 95% CI: 1.23–2.75; P < 0.01). Thus, those with hip osteoarthritis demonstrated an 84% greater chance of experiencing a fracture compared to those without hip osteoarthritis.

On univariate analysis, the variable bisphosphonate use (OR: 1.30; 95% CI: 1.08–1.56), physician-diagnosed knee osteoarthritis (OR: 1.20; 95% CI: 1.00– 0.05) and ethnic background (OR: 1.14; 95% CI: 0.96– 1.37) were identified as significant predictors of falls in the first 12 months post-diagnosis of hip osteoarthritis. However, when analyzed on multivariate analysis, none of these variables remains statistically significant predictors of falls (Table S1).

When the data were assessed for predictors of fractures, both the use of bisphosphonates (OR: 2.51; 95% CI: 1.77–3.56) and physician-diagnosed knee osteoarthritis (OR: 1.43; 95% CI: 0.96–2.14) were identified as significant predictors. On multivariate analysis, only bisphosphonate use was identified as statistically significant, with those taking bisphosphonates over twice as likely to have experienced a fracture within the assessing 12 month interval (OR: 2.27; 95% CI: 1.45–3.56).

Knee osteoarthritis analysis

People with knee osteoarthritis demonstrated a greater likelihood of experiencing a fall within the first 12 months post-diagnosis compared to those without knee osteoarthritis (OR: 1.54; 95% CI: 1.35–1.77; P < 0.01). The chances of experiencing a fall were 54% greater for people with knee osteoarthritis compared to those without. While a significantly greater cumulative number of falls occurred in the knee osteoarthritis cohort (P < 0.01; 0.22 to 0.10), this remains small compared to the non-knee osteoarthritis cohort (0.45– 0.61; Table 2). There was also a greater likelihood of experiencing a fracture in people newly diagnosed with knee osteoarthritis compared to those without (OR: 1.81; 95% CI: 1.34–2.43; P < 0.01). Thus, those with knee osteoarthritis were at 81% greater chance of experiencing a fall compared to those without knee osteoarthritis.

On univariate analysis, the use of bisphosphonates (OR: 1.32; 95% CI: 1.07–1.63), previous THA (OR: 2.16; 95% CI: 1.03–4.51), contralateral TKA (OR: 0.39; 95% CI: 0.15–1.01) and hip osteoarthritis (OR: 1.38; 95% CI: 1.07–1.77) were identified as significant predictors of falls in the first 12 months post-diagnosis of knee osteoarthritis. Of note, the presence of a contralateral TKA was associated with a reduction in falls probability by 61%, whereas having undergone a THA demonstrated an increased chance of experiencing a fall (OR: 2.16; Table 3). On multivariate analysis, the variables bisphosphonate use (OR: 1.29; 95% CI: 1.08– 1.55), previous THA (OR: 2.15; 95% CI: 1.03–4.49) and physician-diagnosed hip osteoarthritis (OR: 1.35; 95% CI: 1.05–1.72) remained statistically significant predictors of falls in the assessment period.

The variables of bisphosphonate use (OR: 2.37; 95% CI: 1.60–3.53) and previous THA (OR: 3.83; 95% CI: 1.30–11.21) were identified as significant predictors of fracture within the first 12 months post-osteoarthritis diagnosis on univariate analysis. On multivariate analysis, both bisphosphonate use (OR: 2.12; 95% CI: 1.47–3.04) and previous THA (OR: 3.83; 95% CI: 1.30– 11.28) remained statistically significant predictors. People taking bisphosphonates were over twice as likely and those who had undergone previous THA were nearly four times more likely to experience a fracture during the first 12 months post-diagnosis of knee osteoarthritis.

DISCUSSION

People who are newly diagnosed with osteoarthritis of the hip or knee are at greater risk of experiencing a fall and/or fracture in the initial 12 months post-diagnosis. The chances of experiencing a fall are over 50% greater and the chances of experiencing a fracture are 85% greater than people of a similar age and characteristics who do not have hip or knee osteoarthritis. Significant predictors of falls in people with knee osteoarthritis include hip osteoarthritis, bisphosphonate use and previous THA, with the latter two factors identified as significant predictors of fracture. While no statistically significant predictors were identified for falls risk in people with hip osteoarthritis, bisphosphonate use was identified as a significant predictor of fracture within a 12 month period, although it was unclear whether this was a cause or consequence of fracture in people with physician-diagnosed hip osteoarthritis.

The findings of this study support that of previous literature. Dore et al.11 reported a similar increase in risk for people with osteoarthritis and specifically reported that risk of falling increased with the number of painful joints. They reported an increased odds of a fall for those with one osteoarthritic joint being 53%, by two joints by 74%, while the chances of a fall increased to 85% with three or more osteoarthritic joints.11 De Zwart et al.14 reported that muscle strength was the most significant independent variable associated with falls in people with knee osteoarthritis, with factors such as proprioception and joint laxity less significant. These findings mirror that of Knoop et al.’s15 analysis of 283 participants from the Amsterdam Osteoarthritis cohort. Accordingly the results of Dore et al.11 and those of this analysis may be related to increased physical risk of experiencing a fall due to reduced hip or/and knee strength and proprioception, leading to greater instability and reduced capability to compensate balance when made unstable and curtailing of physical activity and independence.16,17

Given the associated risks presented in this analysis, and the high probability that people with newly diagnosed osteoarthritis will experience a fall, it would appear sensible that falls advice; guidance and training to reduce such risks should be incorporated into early management of people with osteoarthritis. While strength and exercise training are advocated in international guidance for osteoarthritis,18–21 little attention has been made specifically focusing on falls management strategies in this population. This may be particularly important for those with greatest pain levels and those with multiple joint pain.11 The results would suggest that this should be questioned and future guidance should include recommendations on examining individual’s falls risk and intervening where appropriate to mitigate these risks in a tailored, individualistic way.22,23

Bisphosphonate use was a consistent predictor of falls and fracture risk in both people with hip or knee osteoarthritis. This finding should be interpreted with caution. Given the longitudinal data collection phases adopted by the OAI program, it was not possible to distinguish the timing of bisphosphonate use in relation to falls or fracture events. Since it is international guidance that people at risk of falls with subsequent insufficiency fractures should be routinely prescribed some form of bisphosphonate,24,25 it could be interpreted that these cohorts were prescribed bisphosphonates following their initial fall within the 12 month follow-up period. Thus, this finding is a measurement artefact rather than indicating a causal relationship between bisphosphonate use and fracture or falls. In this respect, this finding would suggest that guidance, at least in part, is being met where bisphosphonate prescription is being undertaken for this ‘at-risk’ subgroup of the osteoarthritis population. Furthermore, since the assessment of bisphosphate used was a binary outcome (i.e., yes/no), it is unclear how issues related to medication adherence or dosage influenced the outcome of these analyses. This provides further strength to the notion that this particular conclusion should be viewed with caution.

This study has indicated that people living in the community demonstrated a significantly higher risk of falls compared to those with similar characteristics without newly diagnosed hip or knee osteoarthritis. Nonetheless, the data indicates that falls risk, particularly with older people, remains a high problem irrespective of joint pathology. This is in agreement with previous literature, particularly in those aged 70 years and above.26 Accordingly, the encouragement for older people to be more physically active is supported as a blanket recommendation,22,27 not only for the potential risk of falls in osteoarthritic and non-osteoarthritic cohorts, but also for the more general physical and mental health benefits which physical activity confers.28

This analysis is presented with five notable limitations, which relate to the use of a large, non-inception dataset analyzed retrospectively to answer these specific research questions. First, it was not possible to deter- mine if there was a difference between osteoarthritis and non-osteoarthritic cohorts for the type of falls experienced and possible contributing factor to falls. Second, there was limited data available on the location and type of fracture experienced by the cohort, due to a high number of missing data-points. Such an analysis would have provided an indication as to whether the types of fractures experienced by the cohort differed, and may be a useful addition for future research on this post-surgical population. We were unable to analyze the impact of a diagnosis of osteoarthritis on people’s confidence in their mobility. It was not possible to observe whether the process of gaining a diagnosis had a significant impact on perceived mobility and health. Fourth, we did not intend to assess the relationship of falls in this cohort to medical history or co-morbidities. Therefore the contribution of these factors to this analysis has not been established, but may be investigated in future studies. Finally, the OAI database is a cohort of volunteers from North America. While this provides valuable data, this cohort may be considered a self- selecting sample of potentially healthier and more educated or affluent, altruistic individuals compared to the full spectrum of the population in clinical practice. This may therefore affect the generalizability of these findings to the wider population from different economic, social and cultural backgrounds worldwide.

CONCLUSION

People with newly diagnosed osteoarthritis of the hip or knee have a higher chance of experiencing a fall with or without subsequent fracture, compared to those with similar characteristics without osteoarthritis. While international guidance on the management of this population has emphasized the benefits of exercise and physical activity, consideration should now be made to specify recommendations on the identification of those at highest risk of falls and interventions to reduce such a risk, and its associated mortality and morbidity.

AUTHOR CONTRIBUTIONS

Study design: TS, MM. Data collection/gathering: TS. Data analysis: TS, MM. Data interpretation: TS, EH, MP, MM. Preparation of written report: TS, EH, MP, MM.

Editing and approval of written report: TS, EH, MP, MM. Guarantor: TS.

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CONFLICTS OF INTEREST

None.

PATIENT CONSENT OBTAINED

Ethics approval Committee on Human Research, University of California, San Francisco (IRB approval number 10–00532 Approved 10 March, 2015).

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