THE GERONTOLOGICAL SOCIETY OF AMERICA®

Journals of Gerontology: Medical Sciences
cite as: *J Gerontol A Biol Sci Med Sci*, 2023, Vol. 78, No. 1, 97–103
https://doi.org/10.1093/gerona/glac050
Advance Access publication February 20, 2022

OXFORD

Research Article

The Association Between Severity of Radiographic Knee OA and Recurrent Falls in Middle and Older Aged Adults: The Osteoarthritis Initiative

Rebekah Harris, PhD, PT, DPT,[1,2,*] Elsa S. Strotmeyer, PhD, MPH,[1] Leena Sharma, MD,[3] C. Kent Kwoh, MD,[4] Jennifer S. Brach, PhD, PT,[5] Robert Boudreau, PhD,[1] and Jane A. Cauley, DrPH[1]

[1]Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania, USA. [2]VA Boston Healthcare System, Boston, MA, USA. [3]Department of Medicine, Northwestern University, Chicago, Illinois, USA. [4]Department of Medicine, University of Arizona, Tucson, Arizona, USA. [5]Department of Physical Therapy, University of Pittsburgh, Pittsburgh, Pennsylvania, USA.

*Address correspondence to: Rebekah Harris, PhD, PT, DPT, New England GRECC, VA Boston, 150 South Huntington Ave, Boston, MA 02130, USA. E-mail: rebekah.harris@va.gov

Received: December 6, 2021; Editorial Decision Date: February 15, 2022

Decision Editor: Lewis A. Lipsitz, MD, FGSA

Abstract

Background: Knee osteoarthritis (KOA) is the most prevalent type of OA and a leading cause of disability in the United States. Falls are a major public health concern in older adults. Our aim was to examine how the severity of radiographic KOA affects recurrent falls in a cohort of middle-aged and older individuals enrolled in the Osteoarthritis Initiative.

Methods: About 3 972 participants, mean age of 63 years, 58% female were included. Participants were divided into 5 mutually exclusive groups based on their worst Kellgren–Lawrence grade of radiographic KOA from annual x-rays from baseline to 36 months. Generalized estimating equations for repeated logistic regression were used to model the association between KOA severity and the likelihood of recurrent falls (≥2 falls/year) over 5 years of follow-up (>36 to 96 months).

Results: Older adults (≥age 65) with KOA were at higher odds of recurrent falls in comparison to individuals without KOA in multivariate models (possible OA odds ratio [OR] = 2.22, 95% CI = 1.09–4.52; mild OA OR = 2.48, 95% CI = 1.34–4.62; unilateral moderate–severe OA OR = 2.84, 95% CI = 1.47–5.50; bilateral moderate–severe OA OR = 2.52, 95% CI = 1.13–5.62). Middle-aged adults (aged 45–64) with KOA did not have increased odds of recurrent falls in comparison to those without KOA except for possible KOA (OR = 1.86, 95% CI = 1.01–2.78; KOA severity × Age interaction = 0.025).

Conclusion: Older adults with radiographic evidence of KOA have an increased likelihood of experiencing recurrent falls in comparison to those without KOA independent of established risk factors. Our results suggest that fall prevention efforts should include older adults with all stages of KOA.

Keywords: Falls, Osteoarthritis, Physical function

Falls are a leading cause of morbidity and mortality in older adults and have a major public health impact (1,2). Approximately 30% of adults aged 65 years and older in the United States fall at least once per year, and this number rises to 50% in adults aged 85 years and older (3,4). The cost for care after a fall contributes significantly to health care expenditure, over $31 billion dollars in 2015 (5,6). Beyond the health care expense, falls can pose a variety of consequences, such as injury, functional decline, increased need for long-term care, and death (7–9). While a fall may not always result in physical injury, there is often subsequent fear of falling and decreased confidence that may result in activity modifications (10,11). With the rising rates of falls, which increased 31% from 2007 to 2016 among those aged 65 years and older, and fall-related injuries and deaths, which have increased 3% per year among those aged

65 years and older from 2007 to 2016, a more in-depth understanding of risk factors contributing to falls is warranted (12,13).

Knee osteoarthritis (KOA) is the most prevalent type of OA and a leading cause of disability and lost work days in the United States (9). In the United States, the prevalence of radiographic KOA in adults aged at least 60 years of age was estimated to be 37% (14). The presence of KOA contributes significantly to functional limitations in participation and performance of weight-bearing activities, such as walking, stair climbing, and household chores, which may lead to negative health outcomes and declines in quality of life (15,16).

Cross-sectional studies have shown mixed associations between falls and KOA (17–19). Doré et al. (20) have shown that adults with symptomatic OA of the lower extremities, defined as radiographic evidence plus corresponding joint symptoms, have an increased risk of a fall event that trends up with the number of joints involved. This longitudinal study suggested an association between OA and subsequent falls but was limited by a single follow-up. Another longitudinal study reported a null association with clinician-diagnosed KOA and falls over a 3-year follow-up period (21). Severity of KOA may also affect falls, with higher fall risk associated with greater severity of KOA (22). Aspects of disease progression including knee instability, reduction in knee range of motion, increased pain and other symptoms of KOA, and muscle weakness may be important factors to consider when assessing the association between KOA and falls (3,15,20,23). However, previous studies have not considered whether these factors influence the associations between severity of KOA and fall risk.

The objective of this analysis was to examine whether the severity of radiographic tibiofemoral KOA is associated with recurrent falls in a cohort of middle-aged and older adults, while being able to adjust for the important confounding variables. We also aimed to test whether these associations differed by age. We hypothesized that adults with increasing severity of tibiofemoral KOA, taking into account radiographic severity in both knees, will have higher likelihood of recurrent falls compared to adults without evidence of radiographic tibiofemoral OA in either knee and that the associations will be more pronounced in older individuals. Improving our understanding of fall risk in adults with knee OA can aid in tailoring intervention and public health programs to groups that would benefit most.

Method

The participants were enrolled in the Osteoarthritis Initiative (OAI) cohort, a prospective study investigating risk factors and biomarkers associated with the development and progression of KOA. Briefly, OAI recruited 4 796 adults aged 45–79 years with or at high risk to develop KOA at 5 clinical sites (John Hopkins Bayview Medical Center and the University of Maryland, Baltimore, Maryland; Ohio State University, Columbus, Ohio; University of Pittsburgh, Pittsburgh, Pennsylvania; and Memorial Hospital, Pawtucket, Rhode Island) between years 2004 and 2006. Approval was obtained from the Institutional Review Board at each participating OAI site.

Each participant provided written informed consent. Participants enrolled in OAI either had symptomatic KOA in at least one knee or risk factors for developing KOA, including being overweight or obese, knee symptoms, history of knee injury, knee surgery, or repetitive knee bending, family history of knee replacement, or the presence of Heberden's nodes. Persons with rheumatoid or inflammatory arthritis were excluded. Additional reasons for study exclusion included findings of severe joint space narrowing in both knees on baseline knee radiographs, unilateral total knee arthroplasty and severe joint space narrowing in the other knee, bilateral total knee arthroplasties, plans to have bilateral knee arthroplasties in the next 3 years, inability to undergo a 3.0 T magnetic resonance imaging of the knee due to contraindications, positive pregnancy test, inability to provide a blood sample, use of ambulatory aids other than a single straight cane for 50% of the time during ambulation, comorbid conditions that may interfere with the ability to participate in a 4-year study, or current participation in a double-blind randomized trial. The data and additional details are publicly available at https://nda.nih.gov/oai/.

Data Collection and Management

Participants were assessed annually at clinic visits, and detailed self-reported questionnaires (eg, demographics, health status/behaviors), clinical and physiological measurements, and measures of progression of KOA were collected.

Primary Independent Variable: Radiographic Severity of OA in Both Knees

All OAI participants underwent knee radiography at baseline and subsequent assessment visits, following the posteroanterior fixed flexion weight-bearing protocol with a SynaFlexer frame.

The presence and stage of OA in the tibiofemoral joint was based on the Kellgren–Lawrence (KL) grading system using annual radiographs from baseline to the 36-month visit to allow time for potential disease progression in adults at high risk for knee OA who were also enrolled into the OAI study. Serial radiographs were graded on an ordinal scale of 0 (normal) to 4 (most advanced). Participants were divided into mutually exclusive groups based on their worst radiograph disease status from baseline through the 36-month visit. The groups included those with no radiographic knee OA (0/0), possible knee OA (0/1, 1/1), mild radiographic knee OA unilaterally or bilaterally (0/2, 1/2, 2/2), unilateral moderate to severe radiographic knee OA (0/3, 0/4, 1/3, 1/4, 2/3, 2/4), or bilateral moderate to severe radiographic knee OA (3/3,3/4, 4/4). For those with a total knee arthroplasty prior to the baseline visit, the KL grade was given a zero (24). In centralized readings, experts (weighted kappa inter-reader agreement 0.79), blinded to others' reading, hypothesis, and all other data, assessed KL grade. Adjudication for KL 0–1 versus 2 included a third reader.

Primary Outcome: Recurrent Falls

The number of falls in which the participant had landed on the floor or ground in the past 12 months was self-reported by participants and assessed annually for 5 years from the 48-month visit through the 96-month visit (25). Our primary outcome was repeated recurrent falls, defined as having 2 or more falls in a 12-month period.

Covariates

Demographic and lifestyle variables were collected at in-person clinic assessments through self-report and included age, sex, race, education, self-reported physical activity (Physical Activity Scale for the Elderly [PASE]) (26), smoking status, alcohol intake, depressive symptoms (Center for Epidemiologic Studies—Depression scale) (27), number of persons living in household, comorbidities (Katz modification of the Charlson Comorbidity Index) (28), Knee Injury and Osteoarthritis Outcome Score symptom subscale (KOOS), knee

confidence rating, and medication usage via "brown bag" collection (29). Higher scores on the KOOS indicate less symptomology. Knee confidence was rated based on patient self-report to the question from the KOOS "how much are you troubled with lack of confidence in your knees?" (23). Lifestyle activity modification was also assessed using self-report to the question from the KOOS "have you modified your lifestyle to avoid potentially damaging activities to your knees." Age, sex, race, education, smoking status, average alcohol consumption, and comorbidity score were assessed at the baseline visit. Standardized physical examination assessments were used to collect information on body mass index (BMI), knee range of motion, medial–lateral knee joint laxity, knee joint effusion, knee alignment (varus, valgus, neutral), and physical performance (chair stand pace). BMI was categorized into groups based on the Centers for Disease Control cutpoints (30). The clinical examination variables of knee range of motion, laxity, alignment, and effusion were categorized into person-level variables due to their high correlation between the right and left sides and worse score was used (25). Knee range of motion was categorized into a yes and no variable based on the presence of a flexion contracture. Knee joint laxity was categorized as yes for any level of laxity: mild and moderate/severe. Knee alignment was categorized as neither, varus, or valgus. BMI, knee alignment, self-reported knee confidence, KOOS pain, PASE, chair stand pace, and medication usage were collected annually from baseline through the 36-month visit and used as time-varying covariates in our models.

Analysis

Participants were classified based on their worst radiographic evidence of OA in both knees from baseline to the 36-month follow-up visit. Those with no radiographic evidence of knee OA in either knee formed the referent group. Participant characteristics at baseline were summarized by worse OA status with appropriate descriptive statistics (mean, standard deviation [SD], frequency, and percentage). We used multiple pairwise comparison methods to compare characteristics across OA groups.

We used generalized estimating equations, with an independent correlation matrix, for repeated logistic regression to model the association between OA groups and the likelihood of experiencing recurrent falls. Base and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were estimated controlling for risk factors age, sex, race, and clinic site. To account for the time between the baseline assessment and our follow-up period which began 4 years after baseline, we created time-varying covariates in the model to account for changes in age, BMI, knee alignment, self-reported knee confidence, KOOS pain, PASE, chair stand pace, use of narcotics, and use of antidepressants from baseline to the 36-month visit.

Models were also adjusted for baseline CES-D score, smoking status, average alcohol consumed per week, comorbidity score, 30-month KOOS lifestyle modification, and education level. We conducted a sensitivity analysis where we excluded participants if they had a total knee arthroplasty. Analysis was completed using SAS version 9.4 software (SAS Institute, Cary, NC).

Results

Overall, 3 972 OAI participants were included in our analysis. About 1 118 (28%) participants had no radiographic evidence of KOA and formed the referent group; 601 (15%) participants have possible KOA; 1 212 (30%) had unilateral or bilateral mild radiographic KOA group; 733 (18%) participants had unilateral moderate to severe radiographic evidence of KOA; and 308 (8%) had bilateral moderate to severe radiographic KOA. Baseline characteristics are summarized in Table 1. Participants in the referent group were more likely to be younger, White race, and have higher level of education in comparison to those with KOA. Participants in the referent group were also less likely to have positive clinical signs of knee joint laxity or effusion, were more likely to report more confidence of no knee buckling, and were less likely to report symptoms based on the KOOS in comparison to the other KOA groups. Self-reported physical activity was highest in those with no KOA and decreased with greater severity of radiographic KOA. Participants in the referent group had higher physical function, measured by the rate of chair stands per second. This measure also demonstrated worse performance with higher levels of radiographic KOA. Participants in the unilateral moderate to severe OA and in the bilateral moderate to severe OA were similar across most study characteristics presented, except those in the bilateral moderate to severe OA group had a greater comorbidities score (0.76 vs 0.61), higher percentage of African Americans (26.6% vs 17.3%), and had a greater BMI on average (31.3 vs 30.1). Participants in the bilateral moderate to severe OA group were more likely to use strong pain medication in comparison to those with no or possible OA. A self-reported history of falls differed minimally between those with possible KOA (227, 37.8%) and those with mild KOA (416, 34.3%), unilateral moderate–severe (240, 32.7%), and bilateral moderate–severe (91, 29.4%). There was no difference in the depression scale and number of medications.

We found a significant interaction between age and KL severity in both knees $p = .025$. To account for this, all the models were stratified by age (≥65 and <65 years). In base models adjusted for sex, race, and clinic site, adults aged at least 65 years of age, with unilateral or bilateral moderate to severe radiographic evidence of knee OA, had an increased likelihood of experiencing recurrent falls in comparison to those with no radiographic evidence of knee OA in either knee (unilateral KOA OR = 1.85, 95% CI 1.28–2.67; bilateral KOA OR = 1.88, 95% CI 1.23–2.87, respectively, and referenced in Table 2). In models additionally adjusting for BMI, knee symptoms and clinical factors (KOOS, knee confidence, lifestyle modification, range of motion, joint alignment, and effusion), physical activity and performance, medication usage, depression, and lifestyle factors, adults at least 65 years old, all groups with radiographic KOA had increased odds of recurrent falls in comparison to the referent group. Adults aged at least 65 years with possible KOA in one or both knees had 2.23 times higher odds (95% CI = 1.10–4.54), with mild OA in one or both knees had 2.48 times higher odds (95% CI = 1.34–4.61), with unilateral moderate to severe radiographic KOA had 2.93 times higher odds (95% CI = 1.52–5.63), and adults with bilateral moderate to severe KOA had 2.52 times higher odds (95% CI = 1.16–5.46) of recurrent falls in comparison to adults with no evidence of radiographic KOA in either knee.

In base models for participants younger than 65 years, those with possible KOA in one or both knees had an increased likelihood of falls in comparison to those without KOA in either knee (OR = 1.37, 95% CI = 1.05–1.77). Results were similar after further adjustments (OR = 1.68, 95% CI = 1.01–2.79). Participants with mild, moderate–severe unilateral, and moderate–severe bilateral KOA did not have a statistically significant association with recurrent falls in either model (multivariate model mild KOA OR = 1.22, 95% CI = 0.79–1.88; moderate–severe unilateral OR = 1.03, 95% CI = 0.62–1.72; moderate–severe bilateral OR = 0.92, 95%

Table 1. Baseline Characteristics of Participants

Variables	No OA n = 1 118	Possible OA n = 601	Mild OA n = 1 212	Moderate–Severe Unilateral OA n = 733	Moderate–Severe Bilateral OA n = 308	p ($p < .05$)
Age (years)	59.8 (0.11)	61.1 (0.15)	61.9 (0.10)	64.7 (0.13)	66.0 (0.20)	(0v1), (0v2), (0v3), (0v4), (1v3), (1v4), (2v3), (2v4), (3v4)
Female, n %	656 (58.7)	356 (59.2)	771 (63.6)	382 (52.1)	157 (50.9)	(0v2), (0v3), (0v4), (1v2), (1v3), (1v4), (2v3), (2v4)
White, n %	944 (84.4)	507 (84.4)	920 (75.9)	594 (81.1)	222 (72.1)	(0v2), (0v3), (0v4), (1v2), (1v4), (2v3), (3v4)
Postcollege education, n %	489 (43.7)	235 (39.2)	461 (38.2)	281 (38.3)	88 (28.7)	(0v2), (0v3), (0v4), (1v2), (1v3), (1v4), (2v4), (3v4)
Body mass index (kg/m^2)	27.2 (0.06)	28.37 (0.07)	29.96 (0.06)	30.10 (0.07)	31.29 (0.11)	(0v1), (0v2), (0v3), (0v4), (1v2), (1v3), (1v4), (2v4), (3v4)
Charlson Comorbidity Index	0.50 (0.01)	0.59 (0.02)	0.57 (0.01)	0.61 (0.07)	0.76 (0.03)	(0v1), (0v2), (0v3), (0v4), (1v3), (1v4), (2v4), (3v4)
Number of medications	4.9 (0.04)	4.9 (0.05)	5.2 (0.04)	4.9 (0.05)	4.9 (0.07)	—
Narcotics use, n %	31 (2.8)	11 (1.9)	41 (3.4)	29 (3.9)	22 (7.1)	(0v3), (0v4), (1v2), (1v3), (1v4)
Pain medication use (OTC), n %	395 (35.3)	249 (41.5)	599 (49.4)	453 (61.8)	210 (68.1)	(0v1), (0v2), (0v3), (0v4), (1v2), (1v3), (1v4), (2v3), (2v4), (3v4)
KOOS	88.4 (0.19)	87.2 (0.24)	82.7 (0.22)	78.9 (0.29)	77.5 (0.45)	(0v2), (0v3), (0v4), (1v2), (1v3), (1v4), (2v3), (2v4), (3v4)
Knee confidence, n %	655 (58.6)	326 (54.2)	519 (42.8)	229 (31.2)	94 (30.5)	(0v1), (0v2), (0v3), (0v4), (1v2), (1v3), (1v4), (2v3), (2v4)
(+) Bulge sign, n %	97 (8.7)	83 (13.8)	200 (16.5)	155 (21.1)	64 (20.8)	(0v1), (0v2), (0v3), (0v4), (1v3), (1v4), (2v3), (2v4)
(–) Laxity test, n %	792 (70.8)	418 (69.5)	800 (66.0)	449 (61.2)	164 (53.4)	(0v2), (0v3), (0v4), (1v2), (1v3), (1v4), (2v3), (2v4), (3v4)
Neutral alignment, n %	366 (32.7)	165 (27.5)	345 (28.5)	208 (28.4)	80 (26.1)	(0v2), (0v4), (1v4), (2v3), (2v4)
Alcoholic drinks/week	1.8 (0.02)	1.6 (0.02)	1.5 (0.02)	1.7 (0.02)	1.6 (0.03)	(0v1), (0v2), (0v3), (0v4), (1v2), (2v3), (2v4)
History of smoking, n %	178 (15.9)	87 (14.4)	194 (16.0)	65 (8.9)	37 (11.9)	(0v3), (1v3), (2v3)
CES-D	6.8 (0.09)	7.4 (0.13)	7.7 (0.10)	7.0 (0.10)	7.3 (0.16)	—
Lives alone, n %	216 (19.3)	127 (21.1)	287 (23.7)	167 (22.8)	72 (23.3)	(0v1), (0v2), (0v3), (0v4), (1v2), (1v4)
PASE	159.0 (1.05)	155.7 (1.33)	151.0 (0.98)	148.1 (1.19)	138.9 (1.74)	(0v2), (0v3), (0v4), (1v2), (1v3), (1v4), (2v4), (3v4)
Chair stand pace (stand/second)	0.53 (0.002)	0.52 (0.003)	0.47 (0.002)	0.47 (0.002)	0.45 (0.003)	(0v1), (0v2), (0v3), (0v4), (1v2), (1v3), (1v4), (2v4), (3v4)
Fall past year, n %	350 (31.2)	227 (37.8)	416 (34.3)	240 (32.7)	91 (29.4)	(0v1), (0v2), (1v2), (1v3), (1v4), (2v4)

Notes: CES-D = Center for Epidemiologic Studies-Depression scale; KOOS = Knee Injury and Osteoarthritis Outcome Score; OTC = over the counter; PASE = Physical Activity Scale for the Elderly. Adjustment made for multiple comparisons; presented as mean (standard deviation) unless otherwise notes; 0 = no KOA; 1 = possible KOA; 2 = mild KOA; 3 = moderate–severe unilateral KOA; 4 = moderate–severe bilateral KOA; kg/m2 = kilograms/meter squared; OTC = over the counter.

Table 2. Odds Ratio (95% Confidence Intervals) for Severity of Knee Osteoarthritis + and Recurrent Falls Stratified by Age: Base Model (Adjusted for Sex, Race, Clinic Site, Age)

	<65 Years (n = 2 458)		≥65 Years (n = 1 514)	
Knee Osteoarthritis (KOA) Group	OR	95% CI	OR	95% CI
No OA (0/0)	1.0		1.0	
Possible OA (0/1, 1/1)	1.37	1.05–1.77*	1.47	0.97–2.22
Mild OA (0/2, 1/2, 2/2)	1.20	0.96–1.50	1.39	0.96–2.02
Moderate–severe OA unilateral (0/3, 0/4, 1/3, 1/4, 2/3, 2/4)	1.04	0.80–1.35	1.85	1.28–2.67*
Moderate–severe OA bilateral (3/3, 3/4, 4/4)	1.06	0.74–1.50	1.88	1.23–2.87*

Notes: OR = odds ratio; CI = confidence interval. Radiographic knee OA defined as worst disease status between baseline and 36-month assessment, adjusted for clinic site, age, race, sex.

*Indicates statistical significance. KL grade × Age interaction, p = .02.

Table 3. Odds Ratio (95% Confidence Intervals) for Severity of KOA and Recurrent Falls: Multivariable (MV) Model

	<65 Years (n = 2 458)		≥65 Years (n = 1 514)	
Knee Osteoarthritis (KOA) Group	OR	95% CI	OR	95% CI
No OA (0/0)	1.0		1.0	
Possible OA (0/1, 1/1)	1.68	1.01–2.78*	2.22	1.09–4.52*
Mild OA (0/2, 1/2, 2/2)	1.22	0.79–1.88	2.48	1.34–4.62*
Moderate–severe OA unilateral (0/3, 0/4, 1/3, 1/4, 2/3, 2/4)	1.03	0.62–1.72	2.84	1.47–5.50*
Moderate–severe OA bilateral (3/3, 3/4, 4/4)	0.92	0.45–1.95	2.52	1.13–5.62*

Notes: OR = odds ratio; CI = confidence interval; Radiographic knee OA defined as worst disease status between baseline and 36-month assessment; MV model adjusts for clinic site, age, race, sex, age × KL grade, knee confidence, knee ROM, joint alignment, joint effusion, history of fall, knee symptoms (KOOS pain, knee confidence), chair stand pace, BMI, physical activity report (PASE), lifestyle activity modification, medication use (narcotic and antidepressants), alcohol intake, smoking status, depressive symptoms (CES-D), education level, and number of comorbidities.

*Indicates statistical significance. KL grade × Age interaction, p = .01.

CI = 0.45–1.95). Complete results are summarized in Table 3. In sensitivity analyses, removing 223 participants who had a total knee arthroplasty after the baseline visit, the results remained the same.

Discussion

We showed that adults at least 65 years of age with possible or definite radiographic tibiofemoral KOA have higher likelihood of experiencing recurrent falls in comparison to adults at least 65 years of age without radiographic evidence of OA independent of many established covariates, including symptoms of knee OA. Older adults with possible or definite radiographic evidence of knee OA are at risk for recurrent falls and should be targeted for future fall prevention research and development of appropriate interventions.

This work builds on the existing research that adults with radiographic KOA have an increased risk of falls in comparison to adults without KOA. Smith et al. (31) reported that persons with incident radiographic unilateral KOA had a 54% greater likelihood of experiencing a fall in the 12 months prior to the diagnosis compared to those without KOA. Barbour et al. (32) recently reported data from the Health, Aging, and Body Composition study demonstrating that men with symptomatic and radiographic KOA have a 2.6 times greater risk for experiencing an injurious fall in comparison to men without pain or radiographic OA in either knee. Our work extends these findings in that we were able to incorporate the severity of radiographic KOA, including KL grade 1, for each knee joint while controlling for OA-related symptoms, detailed clinical examinations, and physical performance measures that are also associated with our outcome of recurrent falls.

For adults younger than 65 years of age, only those with possible radiographic OA in one or both knees had an increased likelihood of recurrent falls in comparison to those without OA. This finding is plausible given the group of younger adults with possible OA, had higher reports of a positive fall history. Possible explanations for why middle-aged adults with more advanced OA do not show increased likelihood of falls may be related to differences in balance and proprioception compared to older adults, which may reduce their likelihood to fall (33,34). Middle-aged older adults may be able to rely on ankle or hip strategies to maintain balance and prevent a fall from occurring.

For adults aged at least 65 years of age, in base models, those with moderate to severe radiographic OA demonstrated increased odds of recurrent falls. After accounting for other factors of disease progression, including changes in clinical symptoms, physical performance, changes in medication usage, and pain in older adults with any stage of KOA (from possible to moderate–severe), an increased odds of recurrent falls was observed.

Osteoarthritis has been associated with declines in physical activity, physical function, and increased reports of pain, which may lead to the increased likelihood of experiencing a fall (35). Adults with OA, mild through severe also demonstrated decreased physical performance on the chair stand test compared to the referent group which may also contribute to their increased risk of falls (36–38). While radiographic features of OA may not always correlate with symptoms of OA, the radiographic changes occurring may result in biomechanical changes that affect a person's center of balance and gait and may affect lower extremity strength in older adults with various stages of KOA, which cannot be compensated for with other strategies to prevent falls (39–42). KOA may also be associated with

changes in the joint range of motion and alignment that alter normal gait biomechanics, which may imply a greater risk for falls (43,44). Additionally, confidence that the knee will not buckle during weight-bearing activities has been associated with poor future physical function and is also a factor to consider when assessing fall risk (45).

Our results suggest that interventions to prevent falls should be implemented at the early stage of radiographic evidence of KOA, given that those with possible (KL grade 1) and mild (KL grade 2) showed an increased risk of recurrent falls in older adults. Interventions should not be postponed until more severe joint symptoms appear. Interventions to manage and address these clinical features may be a target to reduce falls in this population. Rehabilitation to address lower extremity strength, physical function, range of motion, confidence with movement, balance, and pain are targets common in physical therapy treatments. Development of effective fall prevention programs for older adults with KOA is an important future direction of work.

Strengths of this study include the prospective design, detailed assessment of potential confounders, and radiographically confirmed KOA in a large sample of community-dwelling adults across the United States. KOA was assessed at multiple time points which allows for examination of disease and symptoms at multiple time points, by using x-ray grades from baseline through 36-month follow-up and time-varying clinical and self-reported symptoms, as well as extended follow-up time. However, there are a number of limitations. OAI recruited adults at high risk for knee OA or who already have knee OA, limiting the generalizability. Table 1 displays over 200 statistical tests, having the likelihood that some differences were found by chance. There is potential for reverse confounding in this analysis as with any observational study; however, we have controlled for as many covariates as able in our analysis. Self-reported history of falls in the past year has been shown to be an underreported event but we used recurrent falls that are more likely to be recalled (46,47). The knee joint is comprised of more than the tibiofemoral component, which is what we used to categorize knee OA. Future work should consider the role of the patellofemoral joint, use of "preclinical" features that can be detected with other imaging approaches, as well as additional symptoms associated with KOA. The mechanism of the recurrent falls is not documented and the circumstances surrounding the fall events and the severity of the fall in those with mild knee OA and those with moderate to severe bilateral knee OA may be very different. A more in-depth understanding of these associations, the mechanism and severity, would be warranted in future research.

In conclusion, older adults with radiographic evidence of KOA had an increased likelihood of experiencing recurrent falls in comparison to those without radiographic KOA that was independent of known risk factors. The results from this study indicate that fall prevention efforts should focus on older adults with all stages of KOA from possible to moderate–severe.

Funding

The Osteoarthritis Initiative (OAI) is a public–private partnership comprised of 5 contracts (N01-AR-2-2258, N01-AR-2- 2259, N01-AR-2-2260, N01-AR-2-2261, N01-AR-2-2262) funded by the National Institutes of Health (NIH), a branch of the Department of Health and Human Services and conducted by the OAI Study Investigators. Private funding partners include Merck Research Laboratories, Novartis Pharmaceuticals Corporation, GlaxoSmithKline, and Pfizer, Inc. Private sector funding for the OAI is managed by the Foundation for the National Institutes of Health. This manuscript was prepared using an OAI public use data set and does not necessarily reflect the opinions or views of the OAI investigators, the NIH, or the private funding partners. The authors thank the OAI study participants and clinic staff at each participating site.

Conflict of Interest

None declared.

Author Contributions

Acquisition of data, study concept and design, data analysis, data interpretation, and manuscript: R.H., J.A.C., C.K.K., L.S., R.B., E.S.S., and J.S.B. Study concept and design, data analysis, data interpretation, and manuscript preparation: R.H., J.A.C., E.S.S., L.S., and C.K.K. Acquisition of data, study concept and design, data interpretation, and manuscript: R.H., J.A.C., E.S.S., L.S., and C.K.K. Data interpretation and manuscript preparation: R.H., J.A.C., E.S.S., L.S., C.K.K., R.B., and J.S.B. Study concept and design, data interpretation, and manuscript preparation: R.H., J.A.C., E.S.S., L.S., C.K.K., R.B., and J.S.B.

References

1. Vennu V, Bindawas SM. Relationship between falls, knee osteoarthritis, and health-related quality of life: data from the Osteoarthritis Initiative study. *Clin Interv Aging*. 2014;9:793–800. doi:10.2147/CIA.S62207
2. Evans D, Pester, J, Vera L, Jeanmonod D, Jeanmonod R. Elderly fall patients triaged to the trauma bay: age, injury patterns, and mortality risk. *Am J Emerg Med*. 2015;33(11):1635–1638. doi:10.1016/j.ajem.2015.07.044
3. Scott D, Blizzard L, Fell J, Jones G. Prospective study of self-reported pain, radiographic osteoarthritis, sarcopenia progression, and falls risk in community-dwelling older adults. *Arthritis Care Res*. 2012;64(1):30–37. doi:10.1002/acr.20545
4. Bergen G, Stevens M, Burns ER. Falls and fall injuries among adults aged ≥65 years—United States, 2014. *MMWR Morb Mortal Wkly Rep*. 2016;65(37):993–998. doi:10.15585/mmwr.mm6927a5
5. Cruz DT, Ribeiro LC, Vieira MdT, Teixeira MT, Bastos RR, Leite IC. Prevalence of falls and associated factors in elderly individuals. *Rev Saude Publica*. 2012;46(1):138–146. doi:10.1590/s0034-89102011005000087
6. Centers for Disease Control and Prevention. *Cost of older adult falls*. July 9, 2020. Cited January 6, 2022. https://www.cdc.gov/falls/index.html.
7. Nevitt MC, Cummings SR, Kidd S, Black D. Risk factors for recurrent nonsyncopal falls. A prospective study. *JAMA*. 1989;261(18):2663–2668. doi:10.1001/jama.1989.03420180087036
8. Rubenstein LZ, Josephson K. Falls and their prevention in elderly people: what does the evidence show? *Med Clin North Am*. 2006;90:807–824. doi:10.1016/j.mcna.2006.05.013
9. Lawrence RC, Felson D, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. *Arthritis Rheum*. 2008;58(1):26–35. doi:10.1002/art.23176
10. Campbell AJ, Borrie M, Spears GF, Jackson SL, Brown JS, Fitzgerald JL. Circumstances and consequences of falls experienced by a community population 70 years and over during a prospective study. *Age Ageing*. 1990;19(2):136–141. doi:10.1093/ageing/19.2.136
11. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. *N Engl J Med*. 1988;319(26):1701–1707. doi:10.1056/NEJM198812293192604
12. Burns E. Deaths from falls among persons aged >65 years—United States, 2007–2016. *MMWR Morb Mortal Wkly Rep*. 2018;67:509–524. doi:10.15585/mmwr.mm6718a1
13. Centers for Disease Control and Prevention. Older Adult Fall Prevention – STEADI. 2020. Accessed June 6, 2021. https://www.cdc.gov/steadi/materials.html.
14. Dillon CF, Rasch EK, Gu Q, Hirsch R. Prevalence of knee osteoarthritis in the United States: arthritis data from the Third National

Health and Nutrition Examination Survey 1991–94. *J Rheumatol*. 2006;33(11):2271–2279.
15. Guccione AA, Felson D, Anderson JJ, et al. The effects of specific medical conditions on the functional limitations of elders in the Framingham study. *Am J Public Health*. 1994;84(3):351–358. doi:10.2105/ajph.84.3.351
16. Salaffi F, Carotti M, Stancati A, Grassi W. Health-related quality of life in older adults with symptomatic hip and knee osteoarthritis: a comparison with matched healthy controls. *Aging Clin Exp Res*. 2005;17(4):255–263. doi:10.1007/BF03324607
17. Foley SJ, Lord S, Srikanth V, Cooley H, Jones G. Falls risk is associated with pain and dysfunction but not radiographic osteoarthritis in older adults: Tasmanian older adult cohort study. *Osteoarthr Cartil*. 2006;14(6):533–539. doi:10.1016/j.joca.2005.12.007
18. Muraki S, Akune T, Oka H, et al. Prevalence of falls and the association with knee osteoarthritis and lumbar spondylosis as well as knee and lower back pain in Japanese men and women. *Arthritis Care Res*. 2011;63(10):1425–1431. doi:10.1002/acr.20562
19. Barbour KE, Stevens J, Helmick CG, et al. Falls and fall injuries among adults with arthritis—United States, 2012. *MMWR Morb Mortal Wkly Rep*. 2014;63:379–383.
20. Doré AL, Golightly YM, Mercer VS, et al. Lower-extremity osteoarthritis and the risk of falls in a community-based longitudinal study of adults with and without osteoarthritis. *Arthritis Care Res*. 2015;67:633–639. doi:10.1002/acr.22499
21. Arden NK, Crozier S, Smith H, et al. Knee pain, knee osteoarthritis, and the risk of fracture. *Arthritis Rheum*. 2006;55(4):610–615. doi:10.1002/art.22088
22. Khalaj N, Abu Osman N, Mokhtar AH, Mehdikhani M, Wan Abas WA. Balance and risk of fall in individuals with bilateral mild and moderate knee osteoarthritis. *PLoS One*. 2014;9(3):e92270. doi:10.1371/journal.pone.0092270
23. Sharma L, Chmiel J, Almagor O, et al. Knee instability and basic and advanced function decline in knee osteoarthritis. *Arthritis Care Res*. 2015;67(8):1095–1102. doi:10.1002/acr.22572
24. Riddle DL, Golladay G. A longitudinal comparative study of falls in persons with knee arthroplasty and persons with or at high risk for knee osteoarthritis. *Age Ageing*. 2016;45(6):794–800. doi:10.1093/ageing/afw126
25. National Institutes of Health. The Osteoarthritis Initiative. 2006. Accessed January 18, 2021. https://nda.nih.gov/oai/
26. Washburn RA, Smith K, Jette AM, Janney CA. The Physical Activity Scale for the Elderly (PASE): development and evaluation. *J Clin Epidemiol*. 1993;46(2):153–162. doi:10.1016/0895-4356(93)90053-4
27. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas*. 1977;1(3):385–401. doi:10.1177/014662167700100306
28. Katz JN, Chang L, Sangha O, Fossel AH, Bates DW. Can comorbidity be measured by questionnaire rather than medical record review? *Med Care*. 1996;34(1):73–84. doi:10.1097/00005650-199601000-00006
29. Marcum ZA, Perera S, Thorpe JM, et al. Antidepressant use and recurrent falls in community-dwelling older adults: findings from the Health ABC Study. *Ann Pharmacother*. 2016;50(7):525–533. doi:10.1177/1060028016644466
30. Centers for Disease Control and Prevention. Accessed June 7, 2021. https://www.cdc.gov/healthyweight/assessing/bmi/index.html
31. Smith TO, Higson E, Pearson M, Mansfield M. Is there an increased risk of falls and fractures in people with early diagnosed hip and knee osteoarthritis? Data from the osteoarthritis initiative. *Int J Rheum Dis*. 2018. 21(6):1193–1201. doi:10.1111/1756-185X.12871
32. Barbour KE, Sagawa N, Boudreau RM, et al. Knee osteoarthritis and the risk of medically treated injurious falls among older adults: a community-based US cohort study. *Arthritis Care Res (Hoboken)*. 2019;71(7):865–874. doi:10.1002/acr.23725
33. Mackey DC, Robinovitch SN. Mechanisms underlying age-related differences in ability to recover balance with the ankle strategy. *Gait Posture*. 2006;23(1):59–68. doi:10.1016/j.gaitpost.2004.11.009
34. King GW, Stylianou AP, Kluding PM, Jernigan SD, Luchies CW. Effects of age and localized muscle fatigue on ankle plantar flexor torque development. *J Geriatr Phys Ther*. 2012;35(1):8–14. doi:10.1519/JPT.0b013e318221f53b
35. Sharma L. Osteoarthritis year in review 2015. *Osteoarthr Cartil*. 2016;24(1):36–48. doi:10.1016/j.joca.2015.07.026
36. Ward RE, Leveille S, Beauchamp MK, et al. Functional performance as a predictor of injurious falls in older adults. *J Am Geriatr Soc*. 2015;63(2):315–320. doi:10.1111/jgs.13203
37. Shea CA, Ward R, Welch SA, Kiely DK, Goldstein R, Bean JF. Inability to perform the repeated chair stand task predicts fall-related injury in older primary care patients. *Am J Phys Med Rehabik*. 2018;97(6):426–432. doi:10.1097/PHM.0000000000000889
38. de Zwart AH, van der Esch M, Pijnappels MA, et al. Falls associated with muscle strength in patients with knee osteoarthritis and self-reported knee instability. *J Rheumatol*. 2015;42(7):1218–1223. doi:10.3899/jrheum.140517
39. Hannan MT, Felson D, Pincus T. Analysis of the discordance between radiographic changes and knee pain in osteoarthritis of the knee. *J Rheumatol*. 2000;27(6):1513–1517.
40. Ro DH, Lee J, Lee J, Park JY, Han HS, Lee MC. Effects of knee osteoarthritis on hip and ankle gait mechanics. *Adv Orthop*. 2019;2019:9757369. doi:10.1155/2019/9757369
41. Astephen Wilson JL, Deluzio KJ, Dunbar MJ, Caldwell GE, Hubley-Kozey CL. The association between knee joint biomechanics and neuromuscular control and moderate knee osteoarthritis radiographic and pain severity. *Osteoarthr Cartil*. 2011;19(2):186–193. doi:10.1016/j.joca.2010.10.020
42. Kim HS, et al. Balance control and knee osteoarthritis severity. *Ann Rehabil Med*. 2011;35(5):701–709. doi:10.5535/arm.2011.35.5.701
43. Astephen JL, Deluzio K, Caldwell GE, Dunbar MJ. Biomechanical changes at the hip, knee, and ankle joints during gait are associated with knee osteoarthritis severity. *J Orthop Res*. 2008;26(3):332–341. doi:10.1002/jor.20496
44. Gustafson JA, Gorman S, Fitzgerald GK, Farrokhi S. Alterations in walking knee joint stiffness in individuals with knee osteoarthritis and self-reported knee instability. *Gait Posture*. 2016;43:210–215. doi:10.1016/j.gaitpost.2015.09.025
45. Colbert CJ, Song J, Dunlop D, et al. Knee Confidence as it relates to physical function outcome in persons with or at high risk of knee osteoarthritis in the osteoarthritis initiative. *Arthritis Rheum*. 2012;64(5):1437–1446. doi:10.1002/art.33505
46. Hoffman GJ, Ha J, Alexander NB, Langa KM, Tinetti M, Min LC. Underreporting of fall injuries of older adults: implications for wellness visit fall risk screening. *J Am Geriatr Soc*. 2018;66(6):1195–1200. doi:10.1111/jgs.15360
47. Lo-Ciganic WH, Floden L, Lee JK, et al. Analgesic use and risk of recurrent falls in participants with or at risk of knee osteoarthritis: data from the Osteoarthritis Initiative. *Osteoarthr Cartil*. 2017;25(9):1390–1398. doi:10.1016/j.joca.2017.03.017