The Association between Severity of Radiographic Knee OA and Recurrent Falls in middle aged and older adults: The Osteoarthritis Initiative

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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 impacts recurrent falls in a cohort of middle and older aged individuals enrolled in the Osteoarthritis Initiative (OAI).

Methods: 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 follow-up (>36-96 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 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 (age 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).

Conclusions: 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 fall prevention efforts should include older adults with all stages of KOA.

Key Words: Falls, Osteoarthritis, Physical function
INTRODUCTION

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 65 years and older in the US fall at least once per year and this number rises to 50% in adults 85 years and older [3, 4]. The cost for care after a fall contributes significantly to healthcare expenditure, over $31 billion dollars in 2015 [5, 6]. Beyond the healthcare 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 2007-2016 amongst those 65 years and older, and fall related injuries and deaths, which have increased 3% per year amongst those 65 years and older from 2007-2016, 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 US, the prevalence of radiographic KOA in adults ≥ 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]. Dore et al 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 [20]. 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 impact 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 knees 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 knee OA (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 who would benefit most.
METHODS

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 2004-2006. 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 3.0T 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, co-morbid 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 (e.g., 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 that were also enrolled into the OAI study. Serial radiographs were graded on an ordinal scale 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 other’s reading, hypothesis, and all other data, assessed KL grade. Adjudication for KL 0-1 vs 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. Our primary outcome was repeated recurrent falls, defined as having two 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 (CES-D)) [27], number of persons living in household, co-morbidities (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, co-morbidity score was 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 cut points. [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 was 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 (OR) with 95% confidence intervals (CI) 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 anti-depressants from baseline to the 36-month visit.
Models were also adjusted for baseline CESD score, smoking status, average alcohol consumed per week, co-morbidity score, and 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, North Carolina).

RESULTS

Overall, 3,972 OAI participants were included in our analysis. 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 co-morbidities 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= 0.025. To account for this allthe models were stratified by age (≥ 65 years of age and < 65 years of age). In base models adjusted for sex, race, and clinic site, adults ≥ 65 years of age, with unilateral or bilateral moderate to severe radiographic evidence of knee OA had 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 body mass index, 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 life-style factors, adults ≥ 65 years old, all groups with radiographic KOA had increased odds of recurrent falls in comparison to the referent group. Adults ≥ 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 less than 65 years, those with possible KOA in one or both knees had 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% 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 ≥ 65 years of age with possible or definite radiographic tibiofemoral knee osteoarthritis have higher likelihood of experiencing recurrent falls in comparison to adults ≥ 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 reported that persons with incident radiographic unilateral KOA had 54% greater likelihood of experiencing a fall in the 12 months prior to the diagnosis compared to those without KOA. [31] Barbour and Strotmeyer et al 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. [32] 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 <65 years of age, only those with possible radiographic OA in one or both knees had 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 age 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 ≥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 impact a person’s center of balance and gait and may impact 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 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, radiographically confirmed KOA in a large sample of community dwelling adults across the US. 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. Our table 1 shows 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 under-reported event but we used recurrent falls which 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 ‘pre-clinical’ 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.
Conflict of Interest Statement: The authors declare they have no competing interests.

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Author Contributions:

Acquisition of data, study concept and design, data analysis, data interpretation, and manuscript: RH, JAC, CKK, LS, RB, ESS, JSB

Study concept and design, data analysis, data interpretation, and manuscript preparation: RH, JAC, ESS, LS, CKK

Acquisition of data, study concept and design, data interpretation, and manuscript: RH, JAC, ESS, LS, CKK

Data interpretation, and manuscript preparation: RH, JAC, ESS, LS, CKK

Study concept and design, data interpretation, and manuscript preparation: RH, JAC, ESS, LS, CKK, RB, JSB


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Table 1. Baseline Characteristics of Participants

<table>
<thead>
<tr>
<th>Variables</th>
<th>No OA n= 1118</th>
<th>Possible OA n= 601</th>
<th>Mild OA n= 1212</th>
<th>Moderate- Severe Unilateral OA n=733</th>
<th>Moderate- Severe Bilateral OA n=308</th>
<th>P-value (p&lt;0.05)</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59.8 (0.11)</td>
<td>61.1 (0.15)</td>
<td>61.9 (0.10)</td>
<td>64.7 (0.13)</td>
<td>66.0 (0.20)</td>
<td>(0v1), (0v2), (0v3), (0v4), (1v3), (1v4), (2v3), (2v4), (3v4)</td>
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<tr>
<td>Female, n,%</td>
<td>656 (58.7)</td>
<td>356 (59.2)</td>
<td>771 (63.6)</td>
<td>382 (52.1)</td>
<td>157 (50.9)</td>
<td>(0v2), (0v3), (0v4), (1v2), (1v3), (1v4), (2v3), (2v4)</td>
</tr>
<tr>
<td>White n,%</td>
<td>944 (84.4)</td>
<td>507 (84.4)</td>
<td>920 (75.9)</td>
<td>594 (81.1)</td>
<td>222 (72.1)</td>
<td>(0v2), (0v3), (0v4), (1v2), (1v3), (2v3), (3v4)</td>
</tr>
<tr>
<td>Post College Education, n,%</td>
<td>489 (43.7)</td>
<td>235 (39.2)</td>
<td>461 (38.2)</td>
<td>281 (38.3)</td>
<td>88 (28.7)</td>
<td>(0v2), (0v3), (0v4), (1v2), (1v3), (1v4), (2v4), (3v4)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m^2)</td>
<td>27.2 (0.06)</td>
<td>28.37 (0.07)</td>
<td>29.96 (0.06)</td>
<td>30.10 (0.07)</td>
<td>31.29 (0.11)</td>
<td>(0v1), (0v2), (0v3), (0v4), (1v2), (1v3), (1v4), (2v4), (3v4)</td>
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<tr>
<td>Charlson Comorbidity Index</td>
<td>0.50 (0.01)</td>
<td>0.59 (0.02)</td>
<td>0.57 (0.01)</td>
<td>0.61 (0.07)</td>
<td>0.76 (0.03)</td>
<td>(0v1), (0v2), (0v3), (0v4), (1v3), (1v4), (2v4), (3v4)</td>
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<tr>
<td>Number of Medications</td>
<td>4.9 (0.04)</td>
<td>4.9 (0.05)</td>
<td>5.2 (0.04)</td>
<td>4.9 (0.05)</td>
<td>4.9 (0.07)</td>
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<tr>
<td>Narcotics Use, n,%</td>
<td>31 (2.8)</td>
<td>11 (1.9)</td>
<td>41 (3.4)</td>
<td>29 (3.9)</td>
<td>22 (7.1)</td>
<td>(0v3), (0v4), (1v2), (1v3), (1v4)</td>
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<tr>
<td>Pain Medication Use (OTC) n,%</td>
<td>395 (35.3)</td>
<td>249 (41.5)</td>
<td>599 (49.4)</td>
<td>453 (61.8)</td>
<td>210 (68.1)</td>
<td>(0v1), (0v2), (0v3), (0v4), (1v2), (1v3), (1v4)</td>
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<tr>
<td>KOOS</td>
<td>88.4 (0.19) 87.2 (0.24) 82.7 (0.22) 78.9 (0.29) 77.5 (0.45)</td>
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<tr>
<td>Knee confidence n, %</td>
<td>655 (58.6) 326 (54.2) 519 (42.8) 229 (31.2) 94 (30.5)</td>
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<td>(+) bulge sign n, %</td>
<td>97 (8.7) 83 (13.8) 200 (16.5) 155 (21.1) 64 (20.8)</td>
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<tr>
<td>(-) laxity test n, %</td>
<td>792 (70.8) 418 (69.5) 800 (66.0) 449 (61.2) 164 (53.4)</td>
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<tr>
<td>Neutral alignment n, %</td>
<td>366 (32.7) 165 (27.5) 345 (28.5) 208 (28.4) 80 (26.1)</td>
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<tr>
<td>Alcoholic drinks/week</td>
<td>1.8 (0.02) 1.6 (0.02) 1.5 (0.02) 1.7 (0.02) 1.6 (0.03)</td>
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<tr>
<td>History of Smoking n, %</td>
<td>178 (15.9) 87 (14.4) 194 (16.0) 65 (8.9) 37 (11.9)</td>
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<tr>
<td>CES-D</td>
<td>6.8 (0.09) 7.4 (0.13) 7.7 (0.10) 7.0 (0.10) 7.3 (0.16)</td>
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<tr>
<td>Lives alone n, %</td>
<td>216 (19.3) 127 (21.1) 287 (23.7) 167 (22.8) 72 (23.3)</td>
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<tr>
<td>PASE</td>
<td>159.0 (1.05) 155.7 (1.33) 151.0 (0.98) 148.1 (1.19) 138.9 (1.74)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chair Stand Pace (stand/second)</td>
<td>0.53 (0.002) 0.52 (0.003) 0.47 (0.002) 0.47 (0.002) 0.45 (0.003)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fall past year n,%</td>
<td>350 (31.2)</td>
<td>227 (37.8)</td>
<td>416 (34.3)</td>
<td>240 (32.7)</td>
<td>91 (29.4)</td>
<td>(0v1), (0v2), (1v2), (1v3), (1v4), (2v4)</td>
</tr>
</tbody>
</table>

Adjustment made for multiple comparisons; presented as mean (standard deviation) unless otherwise noted; 0= no KOA; 1=Possible KOA; 2= mild KOA; 3=moderate-severe unilateral KOA; 4=moderate-severe bilateral KOA.
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)

<table>
<thead>
<tr>
<th>Knee Osteoarthritis (KOA) Group</th>
<th>&lt; 65 years OR 95% CI (n=2,458)</th>
<th>≥ 65 years OR 95% CI (n= 1,514)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No OA (0/0)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Possible OA (0/1, 1/1)</td>
<td>1.37 1.05-1.77*</td>
<td>1.47 0.97-2.22</td>
</tr>
<tr>
<td>Mild OA (0/2, 1/2, 2/2)</td>
<td>1.20 0.96-1.50</td>
<td>1.39 0.96-2.02</td>
</tr>
<tr>
<td>Moderate-Severe OA Unilateral (0/3, 0/4, 1/3, 1/4, 2/3, 2/4)</td>
<td>1.04 0.80-1.35</td>
<td>1.85 1.28-2.67*</td>
</tr>
<tr>
<td>Moderate-Severe OA Bilateral (3/3, 3/4, 4/4)</td>
<td>1.06 0.74-1.50</td>
<td>1.88 1.23-2.87*</td>
</tr>
</tbody>
</table>

Note: 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 = 0.02
Table 3: Odds Ratio (95% Confidence Intervals) for Severity of KOA and Recurrent Falls: Multivariable (MV) model

<table>
<thead>
<tr>
<th>Knee Osteoarthritis (KOA) Group</th>
<th>&lt;65 years OR</th>
<th>95% CI (n=2,458)</th>
<th>≥ 65 years OR</th>
<th>95% CI (n=1,514)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No OA (0/0)</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Possible OA (0/1, 1/1)</td>
<td>1.68</td>
<td>1.01-2.78&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.22</td>
<td>1.09-4.52&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mild OA (0/2, 1/2, 2/2)</td>
<td>1.22</td>
<td>0.79-1.88</td>
<td>2.48</td>
<td>1.34-4.62&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Moderate-Severe OA Unilateral (0/3, 0/4, 1/3, 1/4, 2/3, 2/4)</td>
<td>1.03</td>
<td>0.62-1.72</td>
<td>2.84</td>
<td>1.47-5.50&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Moderate-Severe OA Bilateral (3/3, 3/4, 4/4)</td>
<td>0.92</td>
<td>0.45-1.95</td>
<td>2.52</td>
<td>1.13-5.62&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Note: Radiographic knee OA defined as worst disease status between baseline and 36-month assessment; MV model adjust 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 anti-depressants), alcohol intake, smoking status, depressive symptoms (CESD), education level, number of comorbidities.

<sup>a</sup> Indicates statistical significance;

KLgrade*age interaction p = 0.01