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A Single Recent Injury is a Potent Risk Factor for the Development of Accelerated Knee Osteoarthritis: Data from the Osteoarthritis Initiative

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Abstract

We examined the association between previously reported modifiable risk factors for accelerated knee osteoarthritis (AKOA) at the Osteoarthritis Initiative's (OAI) baseline and 48-month visits among adults who develop AKOA between the 48- and 96-month visits . We conducted a case-control study using data from the OAI baseline to the 96 month visit. Participants had no radiographic knee osteoarthritis (KOA) in the index knee at OAI baseline and 48-month visits (Kellgren-Lawrence [KL] <2). We classified 2 groups: 1) AKOA: ≥1 knee developed advance-stage KOA (KL=3 or 4) between 48-and 96-month visits and 2) No KOA: no KOA and no change in radiographic severity bilaterally over 96 months. We used logistic regression models to evaluate the association between the outcome of AKOA (versus no KOA) and several modifiable risk factors collected at OAI baseline and 48-month visits (body mass index (BMI), systolic blood pressure, comorbidity score, and NSAID use). We also explored a new injury from baseline to 48-months and from 48- to 96-months. Adults with greater baseline and 48-month BMI were more

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likely to develop AKOA. Injury was only associated with AKOA onset when it occurred within 4 years of developing AKOA (prior 2 years: odds ratio=6.21; 95% confidence interval [CI]=3.40, 11.35; 2–4 years prior: odds ratio=4.42, 95% CI=2.06, 9.50)). BMI may consistently predispose an adult to AKOA, but certain injuries are likely a catalyst for AKOA.

Keywords

knee; osteoarthritis; injury

INTRODUCTION

Knee osteoarthritis (KOA) is commonly perceived as a slowly progressive disorder. However, approximately 22% of incident cases of KOA within the first 4 years of the Osteoarthritis Initiative (OAI) are an accelerated form of KOA (AKOA) [1,2]. Additionally, within the OAI we found an annual incidence rate of 6 AKOA cases per 1000 people. The incidence of AKOA is characterized by a knee that progresses from normal appearance to advance-stage disease within four years and often in less than 12 months [3,2,4–6,1,7]. We previously found that risk factors such as greater age, greater body mass index (BMI), and prior injury are associated with the development of AKOA [8,3,1] using the data from the first four years of the OAI compared to adults with a gradual onset of KOA or no KOA. In recent years, the OAI has released clinical data and radiographic readings from the 48-, 72- and 96-months visits. This offers a unique opportunity to gain a more nuanced understanding of AKOA-related risk factors among adults who did not initially develop AKOA during the first 48 months but then developed AKOA between 48- and 96-month visits of the OAI. For example, we can now explore how the number of injuries and proximity of injury to the onset of AKOA influence the chances of developing AKOA. Hence, we examined the association between previously reported modifiable risk factors for AKOA at baseline and 48-months later among adults who developed AKOA between the 48- and 96-month visits of the OAI. We hypothesized that probable modifiable risk factors for AKOA (BMI, systolic blood pressure, comorbidity score, NSAID use) at OAI baseline would not be statistically related to 48–96 month onset of AKOA but at 48-months these risk factors would be related to AKOA. Furthermore, we believed that a new injury during the first four years of the OAI would not be related to 48–96 month onset of AKOA but a new injury between these visits would be related to AKOA. These probable risk factors were selected because they were likely to change over 48 months in people without KOA and univariate analyses in an earlier study suggested these factors may be related to incident AKOA (with a p value < 0.10) [1].

METHODS

We identified individuals using data from baseline and the 96-months follow-up of the OAI. The OAI is a multicenter cohort study of 4,796 adults with or at risk for symptomatic KOA. Four clinical sites (Memorial Hospital of Rhode Island, The Ohio State University, University of Maryland and Johns Hopkins University, and the University of Pittsburgh) recruited participants between 2004 and 2006. OAI data are available for public access [9].

Institutional review boards at each OAI clinical site and the OAI coordinating center (University of California, San Francisco) approved the OAI study. All participants provided informed consent prior to participation.

Patients

All eligible participants had no radiographic KOA (Kellgren-Lawrence [KL] grade < 2) in the index knee at the OAI baseline and 48-month visits. We defined AKOA as someone who developed AKOA (at least one knee reached KL 3 or 4, development of a definite osteophyte and joint space narrowing) between the 48- and 96-month OAI visits. Adults with no KOA had no KOA in either knee at baseline and no change in KL grade from OAI baseline to 96 months.

Knee Radiographs

Participants had bilateral weight-bearing, fixed-flexion posteroanterior knee radiographs at baseline, each annual visit up to 48 months, the 72-month visit, and the 96-month visit. Central readers, who were blinded to the order of follow-up radiographs, scored the images for KL grades. The read-reread agreement for these readings was good (weighted κ [intrarater reliability] = 0.70–0.80). These KL grades are publicly accessible (files: kXR_SQ_BU##_SAS [versions 0.6, 1.6, 3.5, 5.5, 6.3, 8.2, and 10.2]) [9].

Clinical Data

At OAI baseline and 48 months, age, sex, and BMI, systolic blood pressure, comorbidity score (Charlson Comorbidity Index), over-the-counter NSAID use and injury were acquired based on a standard protocol. The data and protocol are publicly available [9].

Injury Reporting

At each annual visit participants were asked “Since your last annual visit to the OAI clinic about 12 months ago, have you injured your right knee badly enough to limit your ability to walk for at least two days?”. A similar question was asked for the left knee. We defined injury during the first 48-months as an affirmative response at 12-, 24-, 36- or, 48-month visits. We defined an injury during the second 48-months as an affirmative response at 60-, 72-, 84-, or 96-months contacts (60- and 84-month contacts were not in-person). We also summed the number of years with a reported injury between OAI baseline and when the person met the definition of AKOA (72- or 96-month visit) or no KOA (96-month visit; possible range: 0 to 8 years with reported injury). For people who developed AKOA we focused on the first knee that developed AKOA (index knee) and for individuals with no KOA we considered an injury to either knee.

Pain Medication

Participants were asked “During the past 30 days, have you used any of the following medications for joint pain or arthritis on most days? By most days, we mean more than half the days of the month: Non-steroidal anti-inflammatory drugs, or NSAIDS, you get with a prescription such as Ibuprofen (Motrin), Diclofenac (Voltaren), Naproxen (Naprosyn), or others?” [9]

Ethical Standards

The OAI has been approved and meets all criteria for ethical standards regarding human and animal studies defined in the 1964 Declaration of Helsinki and all amendments made after. Institutional review boards at each OAI clinical site and the OAI coordinating center (University of California, San Francisco) approved the OAI study. All participants provided informed consent prior to participation.

Statistical analysis

To assess the association between probable modifiable risk factors (exposures) and AKOA (versus no KOA as a reference) we performed univariate logistic regression models. Two sets of analyses were performed. The first examined risk factors collected at the OAI baseline visit and a new injury between OAI baseline and 48-month follow-up visit. The second set examined risk factors collected at the 48-month OAI visit and a new injury between the 48-month and 96-month OAI visit. Additionally, we ran sensitivity analyses among those with no KOA in either knee at baseline. Finally, we conducted secondary analyses to further explore the association between knee injury and AKOA. Specifically, we examined injuries after 48-months but before the person met the definition of AKOA (72- or 96-month visit) or no KOA (96-month visit). We also evaluated the number of years when a participant reported an injury and the timing of the most recent injury (within 2 years of meeting definition, 2 to 4 years before meeting definition, and no injury within 4 years (reference)). All analyses were performed with SAS Enterprise 7.13 (Cary, NC) and statistical significance was defined as $p < 0.05$.

RESULTS

We identified 832 participants with no KOA at all visits (mean baseline age 58.5 (SD = 8.7) years) and 72 adults who developed AKOA (mean baseline age = 61.0 (SD = 8.4) years; Table 1). At the OAI baseline, which was at least five years prior to the onset of AKOA, individuals who had a greater BMI or comorbidity score >0 were more likely to develop AKOA than remain without KOA (Table 1). Baseline over-the-counter NSAID use (odds ratio [OR] = 1.77; p = 0.053), systolic blood pressure (OR = 1.01; p = 0.074), and injury between 0 and 48 months (OR = 0.85; p = 0.694) were not significantly associated with AKOA, although a trend may be present for NSAID use and systolic blood pressure (Table 1).

When using 48-month data, all the risk factors were associated with the development of AKOA with the exception of over-the-counter NSAID use (OR = 1.81, p = 0.620) and a comorbidity score > 0 (OR = 1.51; p = 0.123; Table 2). In particular, the association of an injury in those four years was significantly associated with the development of AKOA (OR=5.52, 95% CI 3.27, 9.32) (Table 2).

For our sensitivity analyses among people with no KOA in either knee at baseline we had 832 participants with no KOA at all visits and 37 participants who developed AKOA. Using data from the OAI baseline, we found similar statistically significant results as our primary analyses, except a comorbidity score > 0 was associated with AKOA at baseline (OR=2.06,

95% CI 1.01, 4.20). Similarly, with 48-month data we also observed similar statistically significant results as our primary analysis but a comorbidity score > 0 was associated with AKOA (OR=2.15, 95% CI 1.09, 4.22).

The timing as well as the number of injuries prior to disease onset were associated with AKOA. We confirmed that an injury after 48-months but before a person met the definition of AKOA (72- or 96-month visit) or no KOA (96-month visit) was associated with the onset of AKOA (OR = 4.86, Table 3). A single reported injury had the strongest association with AKOA (OR=3.71, 95% CI 2.12, 6.48) when compared to no injuries, followed by the report of injuries at 2 or more visits. A knee injury within 2 years of the endpoint was associated with the development of AKOA (OR=6.21, 95% CI 3.40, 11.35). Knee injuries occurring between 2 and 4 years of endpoint had a lower odds ratio but was still significant (Table 3).

DISCUSSION

While numerous studies have evaluated AKOA with data from the OAI [1,5,6,3,2,4,10,11] they have all focused on the first four years of the cohort. By studying people with AKOA after the 48-month visit of the OAI, we could explore which modifiable risk factors are consistently present and which risk factors are unique to the timing of incident AKOA. We could also gain a better understanding of the timing and number of injuries that precede the onset of AKOA. We found consistent evidence that greater BMI is associated with AKOA, even more than four years prior to disease onset. In contrast, a greater systolic blood pressure and new knee injury were only associated with incident AKOA during the time frame that corresponded to disease incidence. Hence, certain injuries may be catalysts for the onset of AKOA among individuals susceptible to AKOA (e.g., heavier adults, adults with higher systolic blood pressure or another comorbidity).

These results confirm and expand our understanding that adults with greater BMI are more likely to develop AKOA, which has been previously reported to be a significant risk factor during the first four years of the OAI [3,11]. This is the first instance where it is shown that BMI is also associated with the onset of AKOA at least 4 to 8 years later. In fact, we originally estimated a 10% greater chance of AKOA during the first four years of the OAI per kg/m^2 of BMI [1] and now we estimate a 16% greater odds of AKOA. Hence, a novel finding from this study is that BMI may be a potential predictor of incident AKOA over long periods of time (e.g., 8 years). Mechanistically, BMI and gradual progression of KOA may be related to overloading a joint and systemic inflammation [12,13,3]. However, people with AKOA may experience years of no change and then a sudden onset of disease. These findings provide new evidence that greater BMI may play a different role in the etiology of AKOA than in gradual KOA. An elevated BMI could predispose someone to AKOA, but a catalyst may be needed to cause joint failure.

We previously found that a new injury is associated with incident AKOA but not injuries that reportedly occurred prior to the OAI baseline [1]. In our prior analyses, we were unable to determine when these earlier injuries occurred and if participants may misreport a history of injury from long before baseline. The current study provided a unique opportunity to examine annually reported injuries from the four years (0 to 48 months) before the

timeframe when people developed AKOA and during the key timeframe (48 to 96 months). This likely reduced the risk of major injuries being misreported. We found that an injury during the time frame when participants developed AKOA, but not an earlier injury, was associated with incident AKOA. Furthermore, we observed a stronger relationship between injury and AKOA when an injury occurred within two years of developing AKOA than between 2 and 4 years prior, this confirms that a recent injury is more likely to be a catalyst for AKOA. Hence, certain injuries are likely catalysts for the development of AKOA. It remains unclear which injuries may trigger the incidence of AKOA (e.g., which structures are injured, how severe was the injury, how the injury was treated). Furthermore, future studies are needed to rule out the possibility that the sudden onset of AKOA, which is associated with pain and dysfunction [6], may cause a person to experience a new injury [8]. This also raises the concern that there may be a vicious cycle in which an injury triggers the onset of AKOA, which predisposes the person to a new injury, and another wave of accelerated progression.

This study design also enabled us to evaluate the significance of the number of injuries prior to disease onset. This was particularly novel because we had been unable to capture this data among people who developed AKOA during the first 4 years of the OAI. The occurrence of a single injury was more strongly associated with AKOA than two or more injuries. Hence, it may only take one injury to be a catalyst for disease onset.

Baseline systolic blood pressure was not associated with AKOA but 48-month systolic blood pressure was. This new finding supports our hypothesis that risk factors collected closer to the onset of disease would be associated with incident AKOA. However, in our previous study, we only detected a trend that people with higher systolic blood pressure were more likely to develop AKOA [1]. Future studies should further explore the implications of elevated systolic blood pressure to confirm its role as a risk factor for AKOA.

In our prior study, we only detected trends that comorbidity scores or NSAID use were associated with AKOA. In this study, NSAID use was not significantly associated with AKOA. We previously reported that people with AKOA are more likely to report greater knee pain up to 3 years prior to radiographic onset of AKOA. Hence, it is possible that any signals from NSAID use may simply be a proxy for individuals who are developing pre-radiographic AKOA and reporting more severe symptoms [14]. Contrarily, baseline comorbidity score >0 was significantly associated with AKOA but this was not the case at 48-months. The contradictory results may be an artifact of heterogeneity among the various comorbidities that contribute to the score. However, the results of the sensitivity analysis showed that comorbidity was associated with AKOA at either time among those with no KOA in either knee at baseline. Future studies with larger sample size may help identify specific comorbidities that increase the risk of incident AKOA (e.g., hypertension).

While these results contribute to findings that recent injury may be a catalyst in the development of AKOA, particularly among adults with comorbidities (e.g., obesity, high blood pressure), we acknowledge that there are limitations to our study. Despite identifying a new sample of people who develop AKOA this study is still restricted to people who participated in the OAI. However, the OAI offered us a unique opportunity with a rich

dataset to monitor individuals who did not develop AKOA during the first four years but did later. Another limitation was that the 60- and 84-month visits of the OAI were not in-person visits, thus the information was collected through phone call and survey methods. Therefore, it is possible that some cases of AKOA between 48 and 96 months could have been lost to follow up because there were only two opportunities to collect follow-up radiographs (72 and 96-month visits). The timing of the radiographs also limited our ability to determine exactly when an individual developed AKOA between 48- and 96-months. This could have led us to misclassify injuries that occurred after the onset of AKOA as occurring before the onset of disease. Hence, we can confirm that the onset of AKOA is associated with a new injury but it is challenging to definitively state that the injury was the catalyst for AKOA instead of the onset of AKOA leading to a new injury. Based on our prior study [1], these analyses, and prior studies that have evaluated the association between injury and incident disease we believe it is most likely that the injury antedated the onset of AKOA, but further research is needed to confirm this. Despite these limitations, we believe our results are a critical step in understanding risk factors for the development of AKOA.

In conclusion, BMI is a consistent modifiable risk factor for AKOA that may help predict who is at risk for AKOA within the next 8 years. Furthermore, comorbidity and elevated systolic blood pressure warrant further study as a risk factor for AKOA. Finally, a recent injury is one factor associated with incident AKOA, but only when the injury was during the same time period did the person developed AKOA. Furthermore, a single injury was strongly associated with disease onset, which suggests that certain injuries are likelymay be a catalyst to the onset of AKOA.

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References

1. Driban JB, Eaton CB, Lo GH, Ward RJ, Lu B, McAlindon TE. Association of knee injuries with accelerated knee osteoarthritis progression: data from the Osteoarthritis Initiative. Arthritis Care Res. 2014; 66(11):1673–1679. DOI: 10.1002/acr.22359
2. Driban JB, Stout AC, Lo GH, Eaton CB, Price LL, Lu B, Barbe MF, McAlindon TE. Best performing definition of accelerated knee osteoarthritis: data from the Osteoarthritis Initiative. Ther Adv Musculoskelet Dis. 2016; 8(5):165–171. DOI: 10.1177/1759720X16658032 [PubMed: 27721902]

3. Driban JB, Eaton CB, Lo GH, Price LL, Lu B, Barbe MF, McAlindon TE. Overweight older adults, particularly after an injury, are at high risk for accelerated knee osteoarthritis: data from the Osteoarthritis Initiative. Clin Rheumatol. 2016; 35(4):1071–1076. DOI: 10.1007/s10067-015-3152-2 [PubMed: 26686368]

4. Driban JB, Stout AC, Duryea J, Lo GH, Harvey WF, Price LL, Ward RJ, Eaton CB, Barbe MF, Lu B, McAlindon TE. Coronal tibial slope is associated with accelerated knee osteoarthritis: data from the Osteoarthritis Initiative. BMC Musculoskelet Dis. 2016; 17:299.doi: 10.1186/s12891-016-1158-9

5. Driban JB, Ward RJ, Eaton CB, Lo GH, Price LL, Lu B, McAlindon TE. Meniscal extrusion or subchondral damage characterize incident accelerated osteoarthritis: Data from the Osteoarthritis Initiative. Clin Anat. 2015; 28(6):792–799. DOI: 10.1002/ca.22590 [PubMed: 26149125]

6. Driban JB, Price LL, Eaton CB, Lu B, Lo GH, Lapane KL, McAlindon TE. Individuals with incident accelerated knee osteoarthritis have greater pain than those with common knee osteoarthritis progression: data from the Osteoarthritis Initiative. Clin Rheumatol. 2015; doi: 10.1007/s10067-015-3128-2

7. Wallace, KD. Older Adults with Elevated BMI are at Greater Risk of Accelerated Knee Osteoarthritis: Data from the Osteoarthritis Initiative. Wright State University; Dayton, Ohio: 2016.

8. Driban JB, Lo GH, Eaton CB, Price LL, Lu B, McAlindon TE. Knee Pain and a Prior Injury Are Associated with Increased Risk of a New Knee Injury: Data from the Osteoarthritis Initiative. J Rheumatol. 2015; 42(8):1463–1469. DOI: 10.3899/jrheum.150016 [PubMed: 26034152]

9. The Osteoarthritis Initiative. 2014. http://oai.epi-ucsf.org/

10. Driban JB, Eaton CB, Amin M, Stout AC, Price LL, Lu B, Lo GH, McAlindon TE, Barbe MF. Glucose homeostasis influences the risk of incident knee osteoarthritis: Data from the osteoarthritis initiative. J Orthop Res. 2017; doi: 10.1002/jor.23531

11. Riddle DL, Stratford PW, Perera RA. The incident tibiofemoral osteoarthritis with rapid progression phenotype: development and validation of a prognostic prediction rule. Osteoarthritis Cartilage. 2016; 24(12):2100–2107. DOI: 10.1016/j.joca.2016.06.021 [PubMed: 27390031]

12. Visser M, Bouter LM, McQuillan GM, Wener MH, Harris TB. Elevated C-reactive protein levels in overweight and obese adults. JAMA. 1999; 282(22):2131–2135. [PubMed: 10591334]

13. Farrokhi S, Voycheck CA, Gustafson JA, Fitzgerald GK, Tashman S. Knee Joint Contact Mechanics during Downhill Gait and its Relationship with Varus/Valgus Motion and Muscle Strength in Patients with Knee Osteoarthritis. Knee. 2016; 23(1):49–56. [PubMed: 27030846]

14. Davis J, Eaton CB, Lo GH, Lu B, Price LL, McAlindon TE, Barbe MF, Driban JB. Knee symptoms among adults at risk for accelerated knee osteoarthritis: data from the Osteoarthritis Initiative. Clin Rheumatol. 2017; :1–7. DOI: 10.1007/s10067-017-3564-2 [PubMed: 27896522]

Table 1

Association between accelerated knee osteoarthritis (AKOA) and risk factors at Osteoarthritis Initiative (OAI) Baseline

Risk Factor at OAI Baseline	No KOA (n = 832)	AKOA (n = 72)	AKOA vs No KOA OR (95% CI)
Body Mass Index (kg/m^2)	26.7 (4.3)	30.1 (4.7)	**1.16 (1.10, 1.22)**
Systolic Blood Pressure (mmHg)	120.2 (15.5)	123.6 (15.4)	1.01 (1.00, 1.03)
Comorbidity Score > 0 (dichotomous)	155 (18.9%)	21 (29.6%)	**1.81 (1.05, 3.09)**
OTC NSAID Use (dichotomous)	124 (14.9%)	17 (23.6%)	1.77 (0.99, 3.14)
Injury in the next 4 years (dichotomous)	93 (11.7%)	7 (10.1%)	0.85 (0.38, 1.91)

KOA = knee osteoarthritis, OR = odds ratio, 95% CI = 95% confidence interval. All analyses are unadjusted. Bold = statistically significant odds ratio.

Table 2

Association between accelerated knee osteoarthritis (AKOA) and risk factors at Osteoarthritis Initiative (OAI) 48-month visit

Risk Factor at 48-months	No KOA (n = 832)	AKOA (n = 72)	AKOA vs No KOA OR (95%CI)
Body Mass Index (kg/m^2)	27.0 (4.4)	30.7 (5.5)	**1.16 (1.11, 1.22)**
Systolic Blood Pressure (mmHg)	121.7 (15.5)	129.9 (19.0)	**1.03 (1.02, 1.04)**
Comorbidity Score > 0 (dichotomous)	198 (24.1%)	23 (32.4%)	1.51 (0.90, 2.54)
OTC NSAID Use (dichotomous)	98 (11.8%)	14 (19.4%)	1.81 (0.97, 3.36)
Injury in the next 4 years (dichotomous)	102 (12.9%)	29 (42.0%)	**4.91 (2.92, 8.27)**

KOA = knee osteoarthritis, OR = odds ratio, 95% CI = 95% confidence interval. All analyses are unadjusted. Bold = statistically significant odds ratio.

Table 3

Association between accelerated knee osteoarthritis (AKOA) and knee injury prior to onset of disease

	No KOA n = 787	AKOA n = 69	Odds Ratio (95% CI)
Injury After 48-months but before endpoint	97 (12%)	28 (41%)	**4.86 (2.87, 8.22)**
Number of Prior Injuries:			
0 injuries	631 (80%)	38 (55%)	REFERENCE
1 injury	103 (13%)	23 (33%)	**3.71 (2.12, 6.48)**
2 injuries	32 (4%)	7 (10%)	**2.51 (1.11, 5.65)**
3 or more injuries	21 (3%)	1 (1%)	combined with 2 injuries for analyses
Most Recent Injury Prior to Endpoint:			
No injury within 4 years	690 (88%)	39 (57%)	REFERENCE
Within 2 years of endpoint	57 (7%)	20 (29%)	**6.21 (3.40, 11.35)**
Between 2 and 4 years of endpoint	40 (5%)	10 (14%)	**4.42 (2.06, 9.50)**

Sample size is limited to those with complete injury data.

For adults with no KOA we considered injury to either knee. Number of prior injuries is based on the number of years a person reported an injury.