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Adults with Incident Accelerated Knee Osteoarthritis are More Likely to Receive a Knee Replacement: Data from the Osteoarthritis Initiative

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Abstract

We aimed to determine if knees with incident accelerated knee osteoarthritis (AKOA) were more likely to receive a knee replacement (KR) than those with common knee osteoarthritis (KOA) or no KOA. We conducted a nested cohort study using data from baseline and the first 9 years of the Osteoarthritis Initiative (OAI). Eligible knees had no radiographic KOA at baseline (Kellgren-Lawrence [KL]< 2). We classified 3 groups using KL grades from the first 8 years of the OAI: 1)

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CONFLICT OF INTEREST

The authors declare they have no conflicts of interest with regard to this work.

AKOA: knee progressed to advance-stage KOA (KL 3/4) in ≤4 years, 2) common KOA: knee increased in KL grade (excluding AKOA), and 3) No KOA: no change in KL grade by 8 years. The outcome was a KR (partial or total) at or before the 9-year OAI visit. We conducted a logistic regression with generalized linear mixed model and adjusted for age, body mass index, and sex. Overall, 14% of knees with AKOA received a KR by the 9th year compared with 1% and <1% of those with common or no KOA, respectively. Knees that developed AKOA were >80x and ~25x more likely to receive a KR than knees with no KOA or incident common KOA (adjusted odds ratio=25.08; 95% confidence interval=9.63–65.34). In conclusion, approximately 1 in 7 knees that develop AKOA received a KR; however, KRs were rare in the OAI among other knees with no radiographic KOA at baseline. Urgent steps are needed to identify adults at high-risk for AKOA and develop prevention strategies regarding the modifiable risk factors.

Keywords

knee; osteoarthritis; knee replacement; knee arthroplasty; phenotype

INTRODUCTION

Knee osteoarthritis (KOA) is normally a slowly progressive disorder, but accelerated KOA is a subset of KOA that is characterized by a rapid onset of advanced-stage radiographic disease, often within 12 months [1–3]. Adults with accelerated KOA report greater pain and functional impairments than those with a more gradual onset form of KOA (common KOA) [2, 4].

Despite the rapid onset and significant disease burden, it remains unknown if adults who develop accelerated KOA are more likely to receive a knee replacement than those who develop a more gradual onset of KOA (common KOA) or no KOA. We aimed to determine if knees with incident accelerated KOA were more likely to receive a knee replacement than those with incident common KOA or no KOA. To achieve our goal we assessed radiographic readings from the first 8 years of the OAI and knee replacements during the first 9 years of the OAI.

MATERIALS AND METHODS

We conducted a nested cohort study using data from baseline and the first 9 years of the Osteoarthritis Initiative (OAI). The OAI is a multicenter cohort study of 4,796 adults with or at risk for symptomatic KOA. Staff at 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, images, and protocols are publicly available [5]. Institutional review boards at all OAI clinical sites and coordinating center (University of California, San Francisco) approved the study. 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. Participants provided informed consent prior to participation.

Eligible knees had no radiographic KOA at baseline (Kellgren-Lawrence [KL] < 2) and no knee replacement at baseline. We classified 3 groups using KL grades from the first 8 years of the OAI: 1) accelerated KOA: a knee progressed to advance-stage KOA (KL 3 or 4) in 4 years or less, 2) common KOA: a knee with any increase in KL grade (excluding those with accelerated KOA), and 3) No KOA: no change in KL grade by 8 years. For individuals with accelerated KOA or common KOA, the index visit was defined as the visit when a person met the definition for accelerated KOA or common KOA (12-, 24-, 36-, 48-, 72-, or 96-month OAI visit).

Knee Radiographs

Bilateral weight-bearing, fixed-flexion posteroanterior knee radiographs were obtained at baseline and the first 4 annual follow-up visits as well as at the 6- and 8-year follow-up visits. Blinded central readers recorded KL grades (0 to 4). The intrarater agreement for the KL grades was good (weighted kappa=0.70–0.80; files: kXR_SQ_BU##_SAS [versions 0.8, 1.8, 3.7, 5.7, 6.5, 8.2, and 10.2]) [5]. For baseline and the first 4 annual readings we primarily used KL readings in the OAI read project 15; however, we used 20 criteria to harmonize KL readings from baseline and 4-year follow-up with readings in OAI read projects 37/42 (read project for 6- and 8-year follow-up images).

Knee Replacements

The outcome was knee replacement (partial or total) that was reported or observed on radiographs at or before the 9-year OAI visit (>96% adjudicated). Participants were included if they met one of the following three criteria for a partial or total knee replacement: 1) the knee replacement was centrally adjudicated (medical records reviewed by two adjudicators and a physician adjudicator if there was a disagreement between the first two), 2) the knee replacement was observed on a study x-ray, or 3) the knee replacement was self-reported (even if the self-reported replacement had not gone through the adjudication process).

Other Clinical Variables

We extracted potential confounders from the public OAI data files: age, sex, and body mass index (BMI) (Files: enrollees, version 23; allclinical00, version 0.2.2). All variables were collected based on standardized procedures, which are defined in the OAI protocols, which are available on the OAI website [5].

Statistical Analyses

We calculated basic descriptive statistics on the 3 groups. We also determined the median time (and range) from the first visit with radiographic evidence of progression (any increase in KL grade) to knee replacement. To assess the association between group (predictor: accelerated KOA, common KOA, and no KOA) and knee replacement (outcome), we conducted a logistic regression with generalized linear mixed model to adjust for correlations between knees within participants. Analyses were adjusted for baseline age, BMI, and sex. If groups were associated with the knee replacement then we did 3 comparisons: 1) accelerated KOA versus no KOA, 2) accelerated KOA versus common KOA, and 2) common KOA versus no KOA.

As a secondary analysis, we conducted a person-based analysis with people who had no radiographic KOA at baseline in both knees and repeated the analysis. In the secondary analysis we had 3 groups: 1) adults who had accelerated KOA in at least one knee, 2) common KOA (had common KOA in at least one knee without AKOA in either knee), and 3) no KOA in both knees.

We performed all analyses in SAS Enterprise Guide 7.15 (Cary, NC, USA).

RESULTS

We had a total of 213 knees with accelerated KOA (62% female, 61±8 years old, BMI 29.8±4.6 kg/m^2), 798 knees with common KOA (66% female, 59±9 years old, BMI 28.4±4.7 kg/m^2), and 2551 knees with no KOA (52% female, 59±9 years old, BMI 27.1±4.3 kg/m^2). The index visit for adults with AKOA or common KOA were distributed across each follow-up visit: 12-month (AKOA 12.7%, common KOA 24.2%), 24-month (AKOA 10.8%, common KOA 10.5%), 36-month (AKOA 21.1%, common KOA 7.8%), 48-month (AKOA 14.6%, common KOA 6.6%), 72-month (AKOA 16.0%, common KOA 29.5%), and 96-month visit (AKOA 15.5%, common KOA 11.2%). The median time from first radiographic evidence of progression to knee replacement was 2.3 years (range: 0.3 to 7.3 years) compared with common KOA, which was 3.0 (range: 1.7 to 4.2).

Overall, 14% of knees with accelerated KOA received a knee replacement by the 9th year follow-up compared with 1% and <1% of those with common or no KOA, respectively. Knees that developed accelerated KOA are more than 80 times more likely to receive a knee replacement than knees with no KOA (Table 1) and ~25 times more likely than those who develop common KOA (adjusted OR = 25.08; 95% confidence interval = 9.63 to 65.34).

Similar results were observed with a person-based analysis when the sample was limited to people with no KOA in either knee at baseline (Table 2). Accelerated KOA individuals were ~44 times more likely to receive a knee replacement than those with common KOA (adjusted OR = 44.0; 95% confidence interval = 5.3, 362.1).

DISCUSSION

We found that almost 1 in 7 knees that develop accelerated KOA received a knee replacement, compared to only 1% or less of knees with common KOA or no KOA. Furthermore, at least 50% of those with incident accelerated KOA who received a knee replacement received it within 2.3 years of the first radiographic evidence of progression. These data suggest a short time window in which to intervene for those with accelerated KOA. Methods to identify adults at high risk for accelerated KOA and prevention strategies regarding modifiable risk factors for the development of accelerated KOA are desperately needed.

Overall, 11.6% of knees in the OAI received a knee replacement during follow-up, regardless of baseline disease status [5]. Hence, the incidence rate among those with accelerated KOA (14%) was comparable and possibly higher than the overall incidence rate of the OAI. This is in stark contrast our findings that knee replacements were extremely rare

among other knees with no radiographic KOA at baseline. This reinforces prior findings that accelerated KOA is not just a dramatic onset of structural changes but also a clinically important subset of KOA that is associated with knee pain and dysfunction [2, 4], which appears to increase the likelihood of receiving a knee replacement. This may also indicate that adults with accelerated KOA are more likely to use healthcare resources to manage their symptoms than their peers with incident common KOA; however, this needs to be explored further.

While this study is an important step in characterizing the incidence of knee replacements among adults with AKOA, there are some limitations. First, it is unclear why the person received the knee replacement. This limits our ability to conclusively state that symptoms or structural changes associated with accelerated KOA caused the person to receive a knee replacement. While this hinders our ability to infer causation, we believe these findings clearly indicate that people with accelerated KOA are more likely to receive a knee replacement, regardless of cause. Another limitation is that the OAI is not a population based study. Hence, these incidence rates may not be generalizable to the general population. However, the OAI provided us with a unique opportunity to address this study question and further clarify the clinical importance of accelerated KOA.

In conclusion, approximately 1 in 7 knees that develop accelerated KOA received a knee replacement; however, knee replacements were rare in the OAI among knees with no radiographic KOA at baseline. By the time radiographic progression starts there is only a short opportunity to intervene; hence, urgent steps are needed to identify adults at high-risk for accelerated KOA and develop prevention strategies regarding the modifiable risk factors for the development of accelerated KOA.

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Table 1

Knees with Accelerated Knee Osteoarthritis (AKOA) are More Likely to Receive a Knee Replacement by 8-Year Follow-up than Knees with Common Knee Osteoarthritis (KOA) and No KOA

	No Knee Replacement	Knee Replacement	OR (95% CI)	aOR (95% CI)
AKOA	184 (86%)	29 (14%)[a]	**80.3 (30.7, 209.9)**	**82.8 (31.3, 219.4)**
Common KOA	793 (99%)	5 (1%)[b]	3.2 (0.9, 11.1)	3.3 (0.97, 11.3)
No KOA	2546 (99.8%)	5 (0.2%)	REFERENCE	REFERENCE

OR = odds ratios, 95% CI = 95% confidence interval,

[*] aOR: odds ratios adjusted for baseline age, BMI, sex

[a] one knee had a partial knee replacement.

[b] one knee had a self-reported knee replacement that was not adjudicated (type of knee replacement is unreported) and 1 knee had a partial knee replacement.

Table 2

People with Accelerated Knee Osteoarthritis (AKOA) are More Likely to Receive a Knee Replacement by 8-Year Follow-up than Knees with Common Knee Osteoarthritis (KOA) and No KOA: No Knee Osteoarthritis Bilaterally at Baseline

	No Knee Replacement	Knee Replacement	OR (95% CI)	aOR (95% CI)
AKOA[a]	83 (90%)	9 (10%)	**94.8 (11.9, 757.2)**	**104.2 (12.4, 878.6)**
KOA	379 (99.7%)	1 (0.3%)	2.3 (0.1, 37.0)	2.4 (0.2, 38.3)
No KOA	874 (99.9%)	1 (0.1%)	REFERENCE	REFERENCE

OR = odds ratios, 95% CI = 95% confidence interval,

*aOR: odds ratios adjusted for baseline age, BMI, sex

[a]AKOA vs KOA (REF): OR = 41.1 (5.1, 328.8); aOR = 44.0 (5.3, 362.1)

All knee replacements were adjudicated and total knee replacements.