Identifying kinematic, clinical, and radiographic features associated with hip osteoarthritis progression

Laura Chen[1], Fei Jiang[1], Eric Hammond[1], Johanna Luitjens[1], Eugene Ozhinsky[1], Felix Liu[1], Valentina Pedoia[1], Sharmila Majumdar[1], Richard B. Souza[1]
[1]University of California, San Francisco, San Francisco, CA,
Laura.Chen@ucsf.edu

Disclosures: The authors have nothing to disclose.

INTRODUCTION: Osteoarthritis (OA) is a highly prevalent degenerative joint disease and a leading cause of global disability, affecting more than 240 million people worldwide.[1,2] As one of the largest weight-bearing joints in the body, second only to the knee, the hip joint is commonly affected by OA.[3] Investigating risk factors for OA progression could provide direction on ways to potentially mitigate disease progression, and help identify "high risk" groups in clinical trials for disease modifying drugs for OA in the future. While some studies have explored determinants of hip OA progression, including hip kinematics, radiographic features, and demographic factors, they have been limited to studying disease progression in patients who already have hip OA. In addition, they are mostly limited to a 1-year follow-up window.[4–6] This study aims to understand predictors of radiographic OA incidence and progression over a 5-year follow-up. We also assess differences in kinematic, radiographic, clinical, and functional features between hip joints that exhibit OA progression versus those that exhibit no change.

METHODS: All participants provided written informed consent prior to participation and the institutional review board of our institution approved this research. Participants were recruited from the community as healthy controls or patients with mild-moderate radiographic hip OA. Data was collected for each hip at two timepoints, a baseline visit between 2016-2018 and follow-up visit between 2022-2023, with an average of 5.33 years between visits. At each timepoint, participants had an anterior-posterior pelvic radiograph to assess radiographic evidence of hip OA using the Kellgren-Lawrence scale (KL).[7] A multitask deep learning model was applied to cropped left and right hip images from the radiographs to assess the severity of femoral osteophytes, acetabular osteophytes, joint-space narrowing, subchondral cysts, and subchondral sclerosis.[8] At the baseline visit, participants completed the Hip Disability and Osteoarthritis Outcome Scale (HOOS) to assess hip joint pain, symptoms, function during daily living, function in sport and recreation, and hip-related quality of life for each hip side.[9] Participants underwent three-dimensional motion analysis using a computer-aided video motion analysis system to gather kinematics data during the stance phase of walking, stair ascent, and stair descent. Participants also completed functional tests including a 40-meter walk test, stair climb test, 30-second chair rise test, and side plank test. Hip joints (N=35) from 18 patients were divided into progressor and non-progressor groups, where progression was defined as an increase in KL score between timepoints. All analyses were performed using R Statistical Software (v4.2.3; 2023). An analysis of covariance (ANCOVA) was performed to assess between-group differences in baseline kinematics, HOOS scores, and functional test performance, while adjusting for age, gender, BMI, and time between visits. To identify candidate predictors of OA progression, Lasso regression analysis was performed on 15 select features of interest, including baseline KL, age, gender, BMI, HOOS Pain and Symptom subscale scores, chair rise and stair climb performance, presence of osteophytes on radiographs, and peak hip flexion, adduction, and internal rotation during stair ascent. All features were standardized, and penalty parameter for Lasso regression was selected using k-fold cross-validation. Post-selection inference was performed via the selectiveInference R package (v1.2.5; Taylor and Tibshirani 2016) to correct for bias in Lasso regression coefficients and compute p-values.

RESULTS SECTION: Between timepoints, 7 hip joints exhibited an increase in KL score of 1 (progressors) and 28 hip joints exhibited no change in KL score (non-progressors). Of the progressors, 6 hip joints were originally part of the healthy control recruitment group, while 1 hip joint was part of the mild-moderate OA recruitment group at baseline. Of the non-progressors, 11 hip joints were originally part of the mild-moderate OA recruitment group, and 17 hip joints were part of the healthy control recruitment group. Variables age, gender, BMI, and time between visits were not significantly different between our progressor and non-progressor groups. Peak hip flexion during stair ascent was higher in progressors than in non-progressor hip joints (56.59° vs. 50.41°, respectively; $p = 0.03$). Peak hip flexion during stair descent was also higher at baseline in progressors compared to non-progressors (26.26° vs. 17.32°; $p = 0.013$). HOOS Symptoms subscale scores at baseline were lower for progressors than non-progressors when controlling for time between visits (85.71 vs. 93.75; $p = 0.037$). HOOS Sports subscale scores were also lower for progressors than non-progressors when controlling for gender (85.71 vs. 96.76; $p = 0.0086$). Performance in functional tests (40-meter walk, stair climb, 30-second chair rise, and side plank tests) did not differ significantly between groups. After Lasso regression of 15 features (lambda = 0.005, alpha = 0.1), the coefficients for femoral osteophytes and peak internal hip rotation during stair ascent were reduced to 0. After post-selection inference, 4 baseline measurements were found to be significantly associated with radiographic OA progression: HOOS Pain score ($\beta = 0.320$, $p = 0.007$), HOOS Symptoms score ($\beta = -0.305$, $p = 0.007$), number of chair rises performed in 30 seconds ($\beta = -0.226$, $p = 0.009$), and peak hip flexion in degrees during stair ascent ($\beta = 0.184$, $p = 0.048$). The presence of acetabular osteophytes on baseline pelvic radiographs was not found to be significant in predicting OA progression. Joint-space-narrowing and subchondral sclerosis were also not found to be important in prediction when Lasso regression was repeated with these features in place of osteophyte grades.

DISCUSSION: We found that compared to hip joints that exhibited no change in radiographic evidence of OA after 5 years, hip joints that progressed had higher degrees of peak hip flexion at baseline during both stair ascent and descent. In addition, we found peak hip flexion during stair ascent, 30-second chair rise performance, and HOOS Pain and Symptoms scores to be significant predictors of progression in our cohort when performing feature selection on a collection of baseline measurements. Previous literature identifies altered kinematics in patients with hip OA, including high degrees of hip flexion in patients with end-stage hip OA[10] and greater hip internal rotation during stair ascent.[11] However, these were cross-sectional studies, and our study suggests that higher degrees of hip flexion, even in hips with no radiographic evidence of OA, may be a possible indicator of OA development later on. Our research also suggests that lower HOOS Symptoms scores could be related to later worsening of OA; this raises the question of how patients' experience of symptoms may affect their movement and lifestyle, and in turn, OA progression. Radiographic features including osteophytes, joint-space-narrowing, and subchondral cysts and sclerosis were not found to be important in predicting OA progression in our cohort. However, this research is considerably limited by sample size, and features identified by Lasso regression and post-selection inference should be interpreted only as candidate predictors to be explored in a larger study.

SIGNIFICANCE/CLINICAL RELEVANCE: Our study identifies candidate predictors of disease progression in not only patients who already have hip OA, but also in healthy patients who develop radiographic evidence of OA over 5 years. Our findings suggest that degree of hip flexion during stair climbing is a potential area of focus for future interventional studies on OA progression.

Variable	Coefficient	Z-score	*P* value	CI
KL at baseline	-0.011	-0.153	0.870	(-0.084, 1.337)
Age	-0.074	-0.903	0.294	(-0.430, 0.211)
Gender	0.026	0.323	0.665	(-0.702, 0.281)
BMI	-0.100	-1.554	0.091	(-0.445, 0.035)
HOOS Pain	0.320	2.897	**0.008****	(0.123, 0.758)
HOOS Symptoms	-0.305	-2.678	**0.007****	(-0.737, -0.115)
Chair rises in 30 s	-0.226	-2.826	**0.010***	(-0.396, -0.074)
Stair climb time	-0.104	-1.480	0.099	(-0.518, 0.047)
Acetabular osteophytes (superior)	-0.123	-1.764	0.222	(-0.540, 0.194
Acetabular osteophytes (inferior)	0.176	3.141	0.061	(-0.014, 0.266)
Peak hip flexion during stair ascent	0.184	2.929	**0.046***	(0.004, 0.286)
Peak hip adduction during stair ascent	-0.068	-0.812	0.302	(-0.564, 0.267)

Predictor variables after Lasso regression and post-selective inference on 15 features, with lambda penalty parameter = 0.011.

REFERENCES: [1] Osteoarthritis Research Society International. [2] *Lancet Lond Engl.*, 2015 [3] Lespasio MJ et al, 2018 [4] Teirlinck CH et al, 2019 [5] Reijman M et al, 2005 [6] Tateuchi H et al, 2017 [7] Kellgren et al, 1957 [8] von Schacky et al, 2020 [9] Nilsdotter AK et al, 2003 [10] Hara et al, 2015, [11] Popovic et al, 2021

ACKNOWLEDGEMENTS: We would like to thank the patients for their years of participation in research. Research reported in this abstract was supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health under award numbers R01AR069006 and 5K24AR072133-05.