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Associations between baseline and longitudinal semi-automated quantitative joint space width at the hip and incident hip osteoarthritis: Data from a community-based cohort

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Abstract

Objective: To evaluate quantitative joint space width (qJSW, at 10-, 30-, and 50-degree locations) in relation to incident radiographic and symptomatic hip osteoarthritis (rHOA and sxHOA, respectively) in a community-based cohort.

Methods: Data were from Johnston County OA Project (JoCoOA) participants with supine hip radiographs at each of 4 timepoints; all had Kellgren-Lawrence grades (KLG) and qJSW. We assessed covariates (age, race, height, weight, body mass index [BMI]) associated with qJSW, and

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Disclosure of Interest

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hip-level associations between qJSW and HOA, over time using sex-stratified and multivariableadjusted linear mixed models. A cluster analysis with logistic regression estimated associations between qJSW trajectory groups and incident rHOA and sxHOA.

Results: At baseline, 397 participants (784 hips, 41% men, 24% Black, mean age=57 years) had a mean BMI=29 kilograms/meter². Over a mean of 18 years, 20% and 12% developed incident KLG-defined rHOA or sxHOA, respectively. QJSW was more sensitive to changes over time at 50 degrees. Values were stable among men but declined over time in women. Heavier women lost more qJSW; changes in qJSW were not significantly associated with race, education, or injury in women or men. In women only, loss of qJSW over time was associated with 2–3 times higher odds of rHOA and sxHOA; among women and men, narrower baseline qJSW was associated with these outcomes.

Conclusion: Hip qJSW demonstrates marked sex differences, with significant loss over time only in women. Loss of qJSW over time in women, and narrower baseline qJSW in men and women, was associated with incident rHOA and sxHOA.

Hip osteoarthritis (HOA) is an important source of pain, limited mobility, and disability particularly in older patients (1, 2). The lifetime risk of developing symptomatic HOA has been estimated at 25%, meaning that one in four people will be affected by age 85 (3). The estimates of the prevalence of radiographic HOA (rHOA) vary widely, from 1–27% (4), with around 10% reporting symptomatic HOA (sxHOA) (5). In end stage osteoarthritis (OA), total hip arthroplasty (THA) is often pursued to improve pain and function. The most recent data available for the National Inpatient Survey indicate a steady rise in the number of discharges for THA and partial hip arthroplasty from 2009 (421,447) to 2014 (522,820); OA was the diagnosis with the 2nd most inpatient stays in 2017 (over 1.2 million, excluding maternal/neonatal admissions (6)). HOA, and particularly THA, is a large and growing financial burden in the US and around the world (7–9).

Using baseline data from the Johnston County OA Project (JoCoOA), we reported the prevalence of rHOA and sxHOA as 28% and 10%, respectively (5). Despite similar HOA prevalence among Blacks and Whites, incidence rates (IRs) were significantly lower among Blacks for both rHOA and sxHOA compared to Whites (10). Other significant risk factors for incident disease were older age, low socioeconomic status (annual income <\$15K), obesity, and prior hip injury.

These estimates, as with most other cohort studies, were based on radiographic Kellgren-Lawrence grades (KLG), a method for defining OA presence and severity, developed over 6 decades ago (11). The KLG uses a 0–4 scale, with 0 meaning no features of OA are present and higher grades reflecting increasing damage, osteophytosis, sclerosis, and deformity. To date, KLG is the most widely used grading scheme for radiographic OA, especially for the knees and hips (12). However, there is inherent subjectivity in this grading scale which leads to variability between interpretations, which has been well documented for the knee (13). Additionally, KLG has been criticized for placing less emphasis on joint space narrowing (JSN) and more on osteophyte formation when determining severity and grade (4, 14). Composite ordinal measures such as the KLG provide a useful cutoff for defining the presence or absence of OA in epidemiologic cohorts (15). However, assessments of joint space width (JSW) are more responsive than KLG for assessing change in OA over time or in relation to potential therapies (standardized response mean [SRM, the mean change divided by the standard deviation of the change] for JSW=0.6–0.7(16)). In particular, computer assisted quantitative JSW (qJSW (17)) measurements are more responsive (SRM=1) and may help to identify other risk factors or interventions for HOA.

The purpose of the current analysis was to determine the association between qJSW and incidence of KLG-defined rHOA and sxHOA and evaluate key sociodemographic and anthropometric characteristics and their association with changes in qJSW over time in this cohort.

Participants and Methods

The JoCoOA is a longitudinal study of civilian, non-institutionalized Black and White men and women who were: 45 or older at baseline, residents of one of six designated townships in Johnston County for at least one year, and physically and mentally capable of study completion at baseline (5). All participants completed written informed consent, and the study has been continuously approved by the IRBs of the Centers for Disease Control and Prevention and University of North Carolina (#92–0583) since its inception. For this analysis, we selected individuals with a complete set of 4 standardized, longitudinal, supine anteroposterior pelvis radiographs (with the feet in 15 degrees internal rotation) at baseline (1991–1997) and 3 subsequent time points (T1: 1999–2003; T2: 2006–2011; T3: 2013– 2015), with visits approximately 6 years apart. Per protocol, women under 50 years old did not undergo pelvis radiography. All hips were assigned a KLG by an expert musculoskeletal radiologist (JBR) as previously described and with excellent reliability (κ =0.86 and 0.89 for inter- and intra-rater reliability, respectively (18)).

At all timepoints, participants were asked about the presence of hip symptoms (On most days, do you have pain, aching, or stiffness in your (right, left) hip?"). Incident rHOA was defined as KLG 2 at follow-up in a hip with KLG < 2 at baseline. Incident sxHOA required the presence of both rHOA and symptoms in the same hip at follow-up in a hip without both rHOA and symptoms at baseline. QJSW measurements were performed at 3 predefined fixed locations per hip, at 10, 30 and 50 degrees with respect to a polar coordinate system, by an independent assessor blinded to other radiographic or clinical information, with high reliability (intra-class correlations >0.8) as previously described (17). The 0-degree location on the coordinate system was defined by a point placed manually marking the acetabular roof; the center point was the center of a circle determined by three manually placed seed points on the femoral head. To maximize longitudinal consistency, a second anatomical landmark was placed on the images at a location that was clearly visible on all images longitudinally. The point was also chosen so that it was less sensitive to changes due to HOA progression (e.g., avoiding osteophytes). The polar coordinate system was adjusted so that this second point was at the same angle for all images, thus ensuring longitudinal consistency.

Self-reported sex, race/ethnicity, education level (<high school or high school or greater), and prior hip injury were collected at enrollment. Age was calculated from date of birth.

Body mass index (BMI) was calculated from weight (kilogram [kg]) and height (centimeter [cm]) measured by trained staff at a research clinic visit. Weight gain was defined as a greater than 5% relative increase in BMI between baseline and third follow-up for these analyses.

Statistical analysis:

Descriptive statistics were calculated for participant demographic characteristics, including means and standard deviations for continuous variables, and frequencies and percentage for categorical variables. Analyses were stratified by sex a priori due to known sex differences in JSW, hip shape, and OA risk (19–21).

Three sets of analyses were employed. First, we determined the association of relevant covariates to continuous qJSW over time. The outcome modeled was qJSW (millimeters [mm]). Separate multivariable-adjusted linear mixed models (LMM) for each fixed location (i.e., 10, 30, and 50 degrees) were stratified by sex. The full models included fixed effects for baseline age, BMI, weight gain, education, race, and hip injury to estimate model-based fixed effects. LMM were fit using PROC MIXED (SAS/STAT[®], SAS Institute Inc.) with two RANDOM statements: one including random intercept and time (in years from baseline) at the participant level (option SUBJECT=participant) and the other including random intercept at the hip, or side (i.e., right or left), level (option SUBJECT=side(participant) for hips nested at the participant level). Unstructured covariance matrices were indicated in each RANDOM statement. We used the between-within denominator degrees of freedom and restricted maximum likelihood estimation methods. Covariates in these models were reduced using backwards elimination at the alpha = 0.05 level.

Second, the LMMs specified above included only fixed effects for time, with additional strata by incidence status (no incidence, incidence, and presence at baseline) of rHOA or sxHOA. These six strata were included in each model of qJSW (by location) if the stratum was large enough (at least 5% of hips). Each qJSW location was modeled for a total of 3 (sites) \times 2 (rHOA or sxHOA) = 6 models with up to six strata each.

The third set of analysis involved a two-part approach. First, group-based modeling (PROC TRAJ in SAS/STAT[®] software, SAS Institute Inc.) was used to identify distinct clusters of individuals that followed a similar qJSW trajectory over time (22), separately among women and men. The outcome of interest was qJSW change from baseline and left and right hips were modeled together. Consideration of the correlation of qJSW change between hips was not included to avoid modeling complexities given that correlations were low (r=0.2). The number of groups and the shapes of trajectories were determined following prior recommendations (23). Second, population-averaged models using logistic regression, with generalized estimating equations (PROC GENMOD, SAS/STAT[®], SAS Institute Inc.) to estimate a working correlation between hips, were used to model each of incident rHOA and sxHOA. These models estimated adjusted odds ratios and 95% confidence intervals (aOR, 95% CI) for the independent relationship of baseline qJSW and identified trajectory group membership (as defined above) for each hip OA incidence outcome definition. These multivariable-adjusted models were sex-specific and adjusted for: baseline age, race, <hiph

school education, height, BMI, weight gain, and any report of hip injury during follow-up. Height and BMI were not correlated (Pearson correlation –0.1 for men and women) and were not collinear (Condition indices including the intercept term ranged from 5.3 to 6.6 for separate models by side, sex, and incident rHOA or sxHOA outcome) so both were included. As this third set of analysis was to model odds of incidence, those with baseline rHOA or sxHOA, respectively, were excluded from both parts of this final analysis.

Results

There were 577 participants with 1154 hip x-rays available at the third follow-up visit (T3); after exclusion of those missing hip films (at one or more time points) and respondents with hip replacement, 397 participants and 784 hips were analyzed (Figure 1). Of these, 59% were women. The average age \pm standard deviation was 57.5 \pm 5.6 years among women and 55.2 \pm 7.2 years among men (Table 1). A higher percentage of women (28%) than men (18%) identified as Black, and a higher percentage of women reported having <hips chool education (19%) than men (10%). Baseline BMI was 28.6 \pm 5.1 kg/m² and 52% experienced weight gain of >5% BMI from baseline, over the follow-up period (similar by sex). A prior injury was reported among 6.6% of hips. In this sample, the overall cumulative incidence of rHOA and sxHOA was about 20% and 12%, respectively, during an average follow-up time of 18.4 \pm 1.5 years. By location, qJSW was widest at 10 degrees, followed by 30 degrees, and narrowest at 50 degrees, and was consistently smaller among women (Table 1).

Longitudinal associations of demographic and anthropometric characteristics with hip qJSW

Baseline age, height, BMI, and weight gain were significantly associated with qJSW (at 50 degrees) among women. As shown in Figure 2.A and 2.B for representative values (selected to represent ± 1 SD of the sample) of each of these variables among women, qJSW generally declined over time, with baseline qJSW narrower in women who were older at baseline. Taller women had wider qJSW compared with shorter women. Taller women with higher BMI at baseline had more significant narrowing over time if they gained weight compared with those that maintained weight. Taller women with normal BMI (i.e., 24 kg/m^2) had a similar decrease in qJSW regardless of gaining or maintaining weight. Shorter, heavier women had a decline in qJSW regardless of change in weight, while shorter women with normal BMI had a greater decrease in qJSW if they maintained, compared with gained, weight. In stark contrast, among men (Figure 2.C and 2.D), the baseline qJSW was generally larger and stable over time compared with women. Taller men with normal BMI had the largest baseline qJSW, but no changes were noted related to weight gain. Race, education level, and hip injury were not significantly associated with qJSW over time in either women or men. Results using qJSW at 30 and 10 degrees showed less change over time and similar associations between age, BMI, and height with qJSW (data not shown).

Longitudinal associations between qJSW and incidence of KLG radiographic and symptomatic HOA

As shown in Table 2, the baseline 50-degree qJSW among women who developed rHOA was about 0.4 mm smaller than among those who did not (4.30, 95% CI [4.12, 4.47] mm

vs 4.74, 95% CI [4.61, 4.87] mm, respectively); women with rHOA at baseline had the narrowest 50-degree qJSW (4.10, 95% CI [3.84, 4.35] mm). Additionally, women who developed rHOA had greater narrowing per year at this location than those who did not (-0.028, 95% CI [-0.018, -0.038] mm vs -0.007, 95% CI [-0.011, -0.0004] mm). Women with baseline rHOA also had significant narrowing at this location over time (-0.014, 95% CI [-0.020, -0.008] mm). Only loss of qJSW (not baseline qJSW) was significant among women with incident rHOA at the 30- and 10-degree locations, though at smaller magnitudes than at the 50-degree location. Similar patterns and magnitude of change were observed among women with incident sxHOA; those with baseline sxHOA were excluded from the models stratifying by sxHOA status due to the small number of hips (n=22, 2.8% or <5%) fitting this criterion at baseline (Table 1).

Similar to women, the baseline 50-degree qJSW among men who developed rHOA was narrower than among men who did not (4.62, 95% CI [4.40, 4.83] mm vs 5.02, 95% CI [4.87, 5.17] mm, respectively); men with rHOA at baseline similarly had the narrowest 50-degree qJSW (4.45, 95% CI [4.13, 4.78] mm). However, men who did not develop rHOA or sxHOA exhibited slight qJSW widening per year at the 50-degree location, while significant loss of qJSW among men was not observed at any location, regardless of rHOA or sxHOA status.

Independent associations of baseline qJSW and patterns of qJSW loss over time with KLG incidence of radiographic and symptomatic HOA

Among women, 80 hips with rHOA (17%) and 10 with sxHOA (2%) at baseline were excluded from the final, two-part incidence analysis. Only hips with readable qJSW at the 50-degree location at baseline and at least one follow-up time point were included (see Table 1). Overall cumulative incidence of rHOA and sxHOA was about 25% out of 360 hips included in the incident rHOA analysis and 13% out of 410 hips included in the incident sxHOA analysis. Here, the clustering procedure identified 3 groups based on differences in qJSW change over time among women: a constant group (Figure 3.A, line=1/red), and two groups (Figure 3.A, line=2/green and 3/blue) with qJSW loss over time, that were combined into one group in the incidence analysis. The non-constant group comprised 6.7% of the 360 hips in the incident rHOA analysis and 6.1% of the 410 hips in the incident sxHOA analysis. As shown in Table 3, narrower baseline qJSW and hips with loss of qJSW over time were independently and significantly associated with 2 to 3 times higher odds of incident rHOA analysis does not a state of the state of

Among men, 32 hips with rHOA (10%) and 12 with sxHOA (3%) at baseline were excluded from the final, two-part incidence analysis. Only hips with readable qJSW at the 50-degree location at baseline and at least one follow-up time point were included (see Table 1). Overall cumulative incidence of rHOA and sxHOA was about 21% out of 261 hips included in the incident rHOA analysis and 10% out of 297 hips included in the incident sxHOA analysis. The clustering procedure did not identify significantly different groups for qJSW change from baseline over time (Figure 3.B). Nevertheless, narrower qJSW at baseline in men was associated with 60% higher odds of incident rHOA and sxHOA (Table 3) among men, adjusted for other covariates.

Discussion

In this subset of data from a community-based cohort with 18 years of complete follow-up, the overall cumulative incidence of rHOA and sxHOA was 20% and 12%, respectively. Older age, greater height, higher BMI at baseline and BMI increase over time, were associated with loss of qJSW over time in women. Among women, the 50-degree location measurement was the most sensitive to change over time. The development of both rHOA and sxHOA was associated with narrower qJSW in women, supporting the validity of changes in qJSW as a sensitive measure of loss of articular cartilage among women. There were marked sex differences in qJSW measurements of the hip, with little change over time seen in men regardless of risk factors or hip OA status. This suggests that qJSW alone is not sufficient to assess hip OA risk among men.

Women who were heavier at baseline tended to lose more qJSW than those who were normal weight, particularly those who were taller and gained weight over time. Although gaining weight was clearly associated with loss of qJSW in taller women, the pattern was not as clear among shorter women. Shorter women with a higher BMI had similar patterns of qJSW loss regardless of weight loss or maintenance, but those with a lower baseline BMI seemed to lose more qJSW if they maintained, rather than gained, weight. This is somewhat counterintuitive but may reflect the lower qJSW at baseline in this group. Additionally, some large cohort studies have found that the impact of BMI on HOA (via THA) is most notable in early life, and weight changes later in life may be less important, particularly among men, but also in women (24, 25). Additionally, and again only in women, the clustering procedure using qJSW change over time identified 3 subgroup patterns – one with constant JSW and two with overall loss in JSW over time. In these models, loss of qJSW was associated with increased odds of development of sxHOA and rHOA. In contrast, among men, subgroups of qJSW loss were not identified, although narrower qJSW at baseline did confer higher odds of incident rHOA and sxHOA.

Importantly, there is not yet an accepted standard for structure modification for clinical trials in OA in general, particularly for HOA (26). Most of these efforts have focused on knee OA for which radiographic loss of JSW has been the most accepted outcome measure to date. Notably, while JSW at the knee is complicated by other factors such as meniscal damage and extrusion, as well as knee positioning (27), JSW from hip x-rays more directly reflects the cartilage thickness, such that this measure may actually be more reliable in the hip. The x-rays in the JoCoOA were obtained in a standardized manner with the participants supine to maximize reproducibility and quality (28, 29); some studies have used weight-bearing films, including the Osteoarthritis Initiative (OAI) with which this software method was initially validated (17). No qualitative differences in the images (i.e., the weight-bearing images from the OAI used in initial method development vs the supine images in the current analysis) were noted during these analyses.

Sex differences in HOA have been recognized for many years. Lanyon, et al reported on a cross-sectional analysis of intravenous urography in 2003 where they noted marked age-related loss of JSW in women but not in men, and suggested that sex-specific definitions for HOA might be needed (30). The average difference between men and women of 0.3 mm

is similar to what we found in this study, which is based on the type of prospective data set with serial measurements those authors recommended for future study (30). Another group also found smaller JSW in women and greater JSW at the superolateral position (consistent with our finding of greater qJSW at the 10-degree location) than other locations, although they saw no change with age (31). There are sex differences in the shape of the hip/proximal femur as well as morphology related to femoroacetabular impingement that may affect risk for HOA differentially among men and women (21, 32–34). However, some of the largest prior studies focused on HOA have been among women only and were not able to assess differences by sex (15, 35–37). Kim, et al., reported that radiographs were frequently discordant with pain and that "hip osteoarthritis might be missed if diagnosticians relied solely on hip radiographs (38)," although that study relied on semi-quantitative grading rather than qJSW, and did not consider differences by sex.

Narrowing in the 50-degree location among women may represent a potential endophenotype, as recently explored in a genetic study, which found differing associations for JSN in different locations, as well as atrophic or hypertrophic patterns (39). Our 10degree location is most similar to superior JSN, while our 50-degree location is similar to axial JSN. The 50-degree JSW was also a generally more responsive location (i.e., demonstrating more change over time) based on a case/control study using data from the OAI (17). We did not find narrowing in the 10-degree location to be more common in men. In our previous work, participants who were Black had more superior and medial narrowing (20), while superior or medial JSN were associated with rHOA progression (40). Regarding phenotypes of hip OA, magnetic resonance imaging (MRI) may be useful in the future, given recent advances in technique and reproducibility as well as development of scoring systems with likely validity based on associations with radiography and pain in early work (41). Deep learning models are under development to simultaneously and automatically extract information about a variety of features (osteophytes, JSN, sclerosis, cysts) on radiographs with good accuracy in preliminary work (42). Exploratory work has even suggested associations between MRI features and biomechanics that may provide additional future directions (43).

Limitations of the current analyses include the complete case analysis which excluded individuals missing radiographs at any of the time points; assessments of qJSW in those with only 2 or 3 time points of data are ongoing. It is likely that individuals who completed all follow-ups are different (e.g., healthier, younger) than those who did not. The strengths of this analysis include the long follow-up time, the inclusion of Black and White individuals as well as men in addition to women, and the community-based nature of this cohort which includes individuals with and without OA, joint pain, or risk factors. Further studies using this promising measure could include assessment of longitudinal qJSW in the full cohort (i.e., those with fewer than 4 follow-up visits), development of a threshold for diagnosis of hip OA using qJSW, determining associations between hip area symptoms and qJSW, and analyses of associations between hip shape and cam or pincer morphology and qJSW over time, including a focus on sex differences.

In conclusion, longitudinally, qJSW at the hip demonstrates marked sex differences, with significant loss over time seen only in women, and associated with greater age, height, and

BMI. Development of rHOA and sxHOA were statistically significantly associated with loss of qJSW in women. Among men, only a narrower qJSW at baseline was associated with development of HOA. Further study is needed to determine the optimal thresholds for qJSW for use in clinical studies and the associations between qJSW and other aspects of HOA, accounting for the clear sex differences confirmed in this work.

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References

- Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. Ann Rheum Dis. 2014;73(7):1323–30. [PubMed: 24553908]
- 2. Pereira D, Peleteiro B, Araujo J, Branco J, Santos RA, Ramos E. The effect of osteoarthritis definition on prevalence and incidence estimates: a systematic review. Osteoarthritis Cartilage. 2011;19(11):1270–85. [PubMed: 21907813]
- Murphy LB, Helmick CG, Schwartz TA, Renner JB, Tudor G, Koch GG, et al. One in four people may develop symptomatic hip osteoarthritis in his or her lifetime. Osteoarthritis Cartilage. 2010;18(11):1372–9. [PubMed: 20713163]
- 4. Dagenais S, Garbedian S, Wai EK. Systematic review of the prevalence of radiographic primary hip osteoarthritis. Clin Orthop Relat Res. 2009;467(3):623–37. [PubMed: 19037710]
- Jordan JM, Helmick CG, Renner JB, Luta G, Dragomir AD, Woodard J, et al. Prevalence of hip symptoms and radiographic and symptomatic hip osteoarthritis in African Americans and Caucasians: the Johnston County Osteoarthritis Project. J Rheumatol. 2009;36(4):809–15. [PubMed: 19286855]
- 6. HCUP Fast Stats. Healthcare Cost and Utilization Project (HCUP). 2020 [cited 2020 10/12/2020]; Available from: https://www.hcup-us.ahrq.gov/faststats/NationalProceduresServlet
- Torio CM, Moore B. National Inpatient Hospital Costs: The Most Expensive Conditions by Payer, 2013. HCUP Statistical Brief. Rockville, MD: Agency for Healthcare Research and Quality; 2016. p. 1–15.
- Leal J, Murphy J, Garriga C, Delmestri A, Rangan A, Price A, et al. Costs of joint replacement in osteoarthritis: a study using the National Joint Registry and Clinical Practice Research Datalink datasets. Arthritis Care Res (Hoboken). 2020, in press, 10.1002/acr.24470.
- Ackerman IN, Bohensky MA, Zomer E, Tacey M, Gorelik A, Brand CA, et al. The projected burden of primary total knee and hip replacement for osteoarthritis in Australia to the year 2030. BMC Musculoskelet Disord. 2019;20(1):90. [PubMed: 30797228]

- Moss AS, Murphy LB, Helmick CG, Schwartz TA, Barbour KE, Renner JB, et al. Annual incidence rates of hip symptoms and three hip OA outcomes from a U.S. population-based cohort study: the Johnston County Osteoarthritis Project. Osteoarthritis Cartilage. 2016;24(9):1518–27. [PubMed: 27109873]
- Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis. 1957;16(4):494–502. [PubMed: 13498604]
- Braun HJ, Gold GE. Diagnosis of osteoarthritis: imaging. Bone. 2012;51(2):278–88. [PubMed: 22155587]
- Schiphof D, Boers M, Bierma-Zeinstra SM. Differences in descriptions of Kellgren and Lawrence grades of knee osteoarthritis. Ann Rheum Dis. 2008;67(7):1034–6. [PubMed: 18198197]
- Reijman M, Hazes JM, Koes BW, Verhagen AP, Bierma-Zeinstra SM. Validity, reliability, and applicability of seven definitions of hip osteoarthritis used in epidemiological studies: a systematic appraisal. Ann Rheum Dis. 2004;63(3):226–32. [PubMed: 14962953]
- Arden NK, Lane NE, Parimi N, Javaid KM, Lui LY, Hochberg MC, et al. Defining incident radiographic hip osteoarthritis for epidemiologic studies in women. Arthritis Rheum. 2009;60(4):1052–9. [PubMed: 19333950]
- 16. Maheu E, Cadet C, Marty M, Dougados M, Ghabri S, Kerloch I, et al. Reproducibility and sensitivity to change of various methods to measure joint space width in osteoarthritis of the hip: a double reading of three different radiographic views taken with a three-year interval. Arthritis Res Ther. 2005;7(6):R1375–85. [PubMed: 16277690]
- Ratzlaff C, Van Wyngaarden C, Duryea J. Location-specific hip joint space width for progression of hip osteoarthritis--data from The Osteoarthritis Initiative. Osteoarthritis Cartilage. 2014;22(10):1481–7. [PubMed: 25278059]
- Jordan JM, Linder GF, Renner JB, Fryer JG. The impact of arthritis in rural populations. Arthritis Care Res. 1995;8(4):242–50. [PubMed: 8605262]
- Lanyon P, Muir K, Doherty S, Doherty M. Influence of radiographic phenotype on risk of hip osteoarthritis within families. Ann Rheum Dis. 2004;63(3):259–63. [PubMed: 14962959]
- Nelson AE, Braga L, Renner JB, Atashili J, Woodard J, Hochberg MC, et al. Characterization of individual radiographic features of hip osteoarthritis in African American and White women and men: the Johnston County Osteoarthritis Project. Arthritis Care Res (Hoboken). 2010;62(2):190–7. [PubMed: 20191517]
- Nelson AE, Liu F, Lynch JA, Renner JB, Schwartz TA, Lane NE, et al. Association of incident symptomatic hip osteoarthritis with differences in hip shape by active shape modeling: the Johnston County Osteoarthritis Project. Arthritis Care Res (Hoboken). 2014;66(1):74–81. [PubMed: 23926053]
- Nagin DS, Odgers CL. Group-based trajectory modeling in clinical research. Annu Rev Clin Psychol. 2010;6:109–38. [PubMed: 20192788]
- Andruff H, Carraro N, Thompson A, Gaudreau P, Louvet B. Latent Class Growth Modelling: A Tutorial. Tutorials in Quantitative Methods for Psychology. 2009;5(1):11–24.
- Apold H, Meyer HE, Espehaug B, Nordsletten L, Havelin LI, Flugsrud GB. Weight gain and the risk of total hip replacement a population-based prospective cohort study of 265,725 individuals. Osteoarthritis Cartilage. 2011;19(7):809–15. [PubMed: 21524707]
- 25. Wang Y, Wluka AE, Simpson JA, Giles GG, Graves SE, de Steiger RN, et al. Body weight at early and middle adulthood, weight gain and persistent overweight from early adulthood are predictors of the risk of total knee and hip replacement for osteoarthritis. Rheumatology (Oxford). 2013;52(6):1033–41. [PubMed: 23362222]
- 26. Food and Drug Administration. Draft Guidance for Industry: Clinical Development Programs for Drugs, Devices, and Biological Products Intended for the Treatment of Osteoarthritis (OA). 1999 [cited 9/12/14]; Available from: http://www.fda.gov/downloads/Drugs/ GuidanceComplianceRegulatoryInformation/Guidances/ucm071577.pdf
- 27. Le Graverand MP, Vignon EP, Brandt KD, Mazzuca SA, Piperno M, Buck R, et al. Head-tohead comparison of the Lyon Schuss and fixed flexion radiographic techniques. Long-term reproducibility in normal knees and sensitivity to change in osteoarthritic knees. Ann Rheum Dis. 2008;67(11):1562–6. [PubMed: 18258709]

- Pessis E, Chevrot A, Drape JL, Leveque C, Sarazin L, Minoui A, et al. Study of the joint space of the hip on supine and weight-bearing digital radiographs. Clin Radiol. 1999;54(8):528–32. [PubMed: 10484220]
- Auleley GR, Rousselin B, Ayral X, Edouard-Noel R, Dougados M, Ravaud P. Osteoarthritis of the hip: agreement between joint space width measurements on standing and supine conventional radiographs. Ann Rheum Dis. 1998;57(9):519–23. [PubMed: 9849309]
- Lanyon P, Muir K, Doherty S, Doherty M. Age and sex differences in hip joint space among asymptomatic subjects without structural change: implications for epidemiologic studies. Arthritis Rheum. 2003;48(4):1041–6. [PubMed: 12687547]
- Lequesne M, Malghem J, Dion E. The normal hip joint space: variations in width, shape, and architecture on 223 pelvic radiographs. Ann Rheum Dis. 2004;63(9):1145–51. [PubMed: 15308525]
- Nelson AE, Stiller JL, Shi XA, Leyland KM, Renner JB, Schwartz TA, et al. Measures of hip morphology are related to development of worsening radiographic hip osteoarthritis over 6 to 13 year follow-up: the Johnston County Osteoarthritis Project. Osteoarthritis Cartilage. 2016;24(3):443–50. [PubMed: 26497609]
- Edwards K, Leyland KM, Sanchez-Santos MT, Arden CP, Spector TD, Nelson AE, et al. Differences between race and sex in measures of hip morphology: a population-based comparative study. Osteoarthritis Cartilage. 2020;28(2):189–200. [PubMed: 31843571]
- 34. van Buuren MMA, Arden NK, Bierma-Zeinstra SMA, Bramer WM, Casartelli NC, Felson DT, et al. Statistical shape modeling of the hip and the association with hip osteoarthritis: a systematic review. Osteoarthritis Cartilage. 2020, in press, 10.1016/j.joca.2020.12.003.
- 35. Lane NE, Nevitt MC, Hochberg MC, Hung YY, Palermo L. Progression of radiographic hip osteoarthritis over eight years in a community sample of elderly white women. Arthritis Rheum. 2004;50(5):1477–86. [PubMed: 15146417]
- 36. Nicholls AS, Kiran A, Pollard TC, Hart DJ, Arden CP, Spector T, et al. The association between hip morphology parameters and nineteen-year risk of end-stage osteoarthritis of the hip: a nested case-control study. Arthritis Rheum. 2011;63(11):3392–400. [PubMed: 21739424]
- Lynch JA, Parimi N, Chaganti RK, Nevitt MC, Lane NE, Study of Osteoporotic Fractures Research G. The association of proximal femoral shape and incident radiographic hip OA in elderly women. Osteoarthritis Cartilage. 2009;17(10):1313–8. [PubMed: 19427402]
- Kim C, Nevitt MC, Niu J, Clancy MM, Lane NE, Link TM, et al. Association of hip pain with radiographic evidence of hip osteoarthritis: diagnostic test study. BMJ. 2015;351:h5983. [PubMed: 26631296]
- Panoutsopoulou K, Thiagarajah S, Zengini E, Day-Williams AG, Ramos YF, Meessen JM, et al. Radiographic endophenotyping in hip osteoarthritis improves the precision of genetic association analysis. Ann Rheum Dis. 2017;76(7):1199–206. [PubMed: 27974301]
- 40. Foley B, Cleveland RJ, Renner JB, Jordan JM, Nelson AE. Racial differences in associations between baseline patterns of radiographic osteoarthritis and multiple definitions of progression of hip osteoarthritis: the Johnston County Osteoarthritis Project. Arthritis Res Ther. 2015;17:366. [PubMed: 26680278]
- 41. Crema MD, Watts GJ, Guermazi A, Kim YJ, Kijowski R, Roemer FW. A narrative overview of the current status of MRI of the hip and its relevance for osteoarthritis research - what we know, what has changed and where are we going? Osteoarthritis Cartilage. 2017;25(1):1–13. [PubMed: 27621214]
- 42. von Schacky CE, Sohn JH, Liu F, Ozhinsky E, Jungmann PM, Nardo L, et al. Development and Validation of a Multitask Deep Learning Model for Severity Grading of Hip Osteoarthritis Features on Radiographs. Radiology. 2020;295(1):136–45. [PubMed: 32013791]
- Pedoia V, Samaan MA, Inamdar G, Gallo MC, Souza RB, Majumdar S. Study of the interactions between proximal femur 3d bone shape, cartilage health, and biomechanics in patients with hip Osteoarthritis. J Orthop Res. 2018;36(1):330–41. [PubMed: 28688198]

Significance and Innovations

- Although the Kellgren-Lawrence grade is frequently used, it has several limitations (for example, subjectivity and associated interrater variability), and the optimal radiographic measure for hip osteoarthritis has not yet been established.
- Semi-automated quantitative joint space width (qJSW) provides an objective, reproducible, and responsive quantitative measure of hip joint space over time.
- This longitudinal analysis of qJSW over a mean of 18 years of follow-up demonstrates that qJSW at the 50-degree location is sensitive to change and associated with incident hip OA in women, while only baseline qJSW is predictive of hip OA in men.

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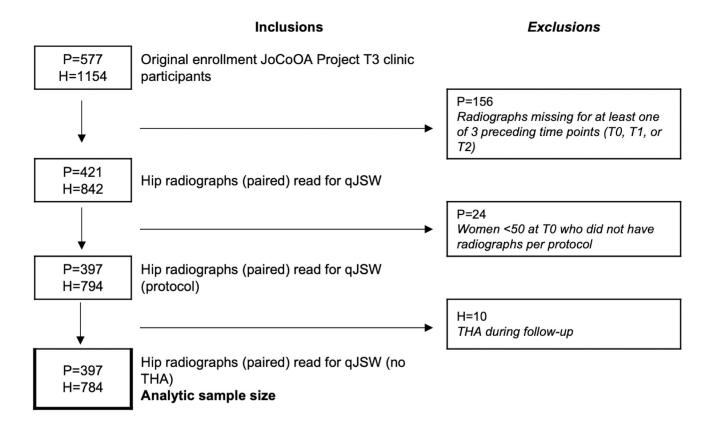
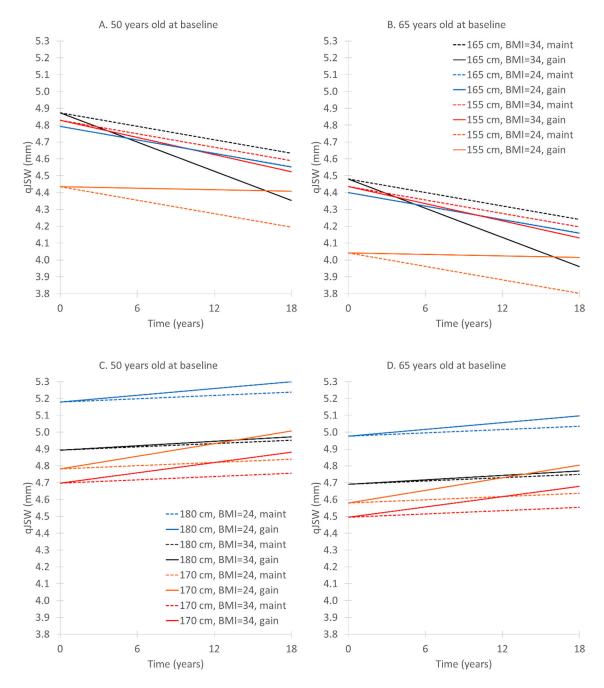


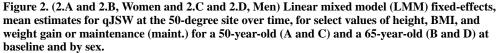
Figure 1. Flowchart detailing final analytic sample size.

Footnote: P=number of participants; H=number of hips; JoCoOA=Johnston County Osteoarthritis Project; qJSW=quantitative joint space width; THA=total hip arthroplasty; Baseline (T0), 1991–1997; First follow-up (T1), 1999–2004; Second follow-up (T2), 2006– 2011; Third follow-up (T3), 2013–2015

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Footnote: LMM=linear mixed model; qJSW=quantitative joint space width; BMI=body mass index; maint=maintained weight; gain=gained weight. The values selected for BMI and height were chosen to reflect ± 1 SD in the sample.

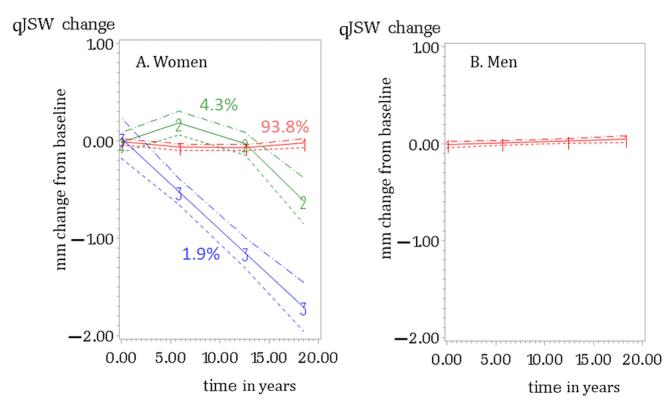


Figure 3. (A, Women and B, Men) Identified groups and patterns of qJSW change over time among women (A) and men (B) using group-based modeling to identify distinct group clusters. Among women, there was a constant group (Figure 3A, line=1/red), and two groups that changed over time (Figure 3A, line=2/green and 3/blue). Only one group (constant) was identified among men (Figure 3B).

Footnote: Dotted or dashed lines are 95% confidence intervals for the mean group trajectory. qJSW=quantitative joint space width

Table 1.

Descriptive statistics of the analytic sample, overall and by sex

Person-level characteristics at baseline $*$	Overall (n=397)		Women (n=233, 59%)		Men (n=164, 41%)		
	n or mean	% or ± SD	n or mean	% or ± SD	n or mean	% or ± SD	
Demographics							
Age, mean \pm SD, years	56.6	± 6.4	57.5	± 5.6	55.2	± 7.2	
% with age 65 years	52	13.1%	30	12.9%	22	13.4%	
Black	95	23.9%	66	28.3%	29	17.79	
<12 years education		15.4%	45	19.3%	16	9.8%	
Anthropometry							
Height, mean \pm SD, cm	167.7	± 9.6	161.8	± 6.1	176.1	± 7.0	
Weight, mean \pm SD, kg	80.6	± 16.2	75.5	± 15.7	87.7	± 14.	
BMI, mean \pm SD, kg/m ²	28.6	± 5.1	28.8	± 5.7	28.3	± 4.1	
Weight gain: >5% BMI increase from baseline to follow-up	205	51.6%	124	53.2%	81	49.4%	
Hip-level characteristics at baseline [*]		Overall (n=784)		Women (n=460, 59%)		Men (n=324, 41%)	
	n or mean	% or ± SD	n or mean	% or ± SD	n or mean	% or ± SD	
Hip injury at any time from baseline to follow-up	52	6.6%	29	6.3%	23	7.1%	
rHOA							
No incidence during follow-up	514	65.6%	229	49.8%	285	88.09	
Incidence during follow-up		20.2%	101	22.0%	57	17.69	
Prevalent at baseline		14.3%	80	17.4%	32	9.9%	
sxHOA							
No incidence during follow-up	671	85.6%	391	85.0%	280	86.49	
Incidence during follow-up	91	11.6%	60	13.0%	31	9.6%	
Prevalent at baseline	22	2.8%	10	2.2%	12	3.4%	
qJSW by degree site at each time-point ${^{\dot{ au}}}$							
JSW at the 10-degree location by time point, mean \pm SD, mm							
T0 (n=460 among women, n=324 among men)	5.27	± 0.93	5.07	± 0.86	5.55	± 0.9	
T1 (n=457 among women, n=324 among men)	5.26	± 0.92	5.06	± 0.85	5.53	± 0.9	
T2 (n=456 among women, n=324 among men)	5.30	± 0.92	5.10	± 0.83	5.57	± 0.9	
T3 (n=455 among women, n=324 among men)		± 0.99	4.99	± 0.87	5.59	± 1.0	
JSW at the 30-degree location by time point, mean \pm SD, mm							
T0 (n=456 among women, n=321 among men)	4.96	± 0.93	4.84	± 0.90	5.14	± 0.9	
T1 (n=447 among women, n=324 among men)	4.95	± 0.97	4.78	± 0.88	5.17	± 1.0	
T2 (n=455 among women, n=320 among men)		± 0.95	4.79	± 0.89	5.18	± 1.0	
T3 (n=459 among women, n=322 among men)	4.89	± 1.05	4.67	± 0.97	5.20	± 1.0	
JSW at the 50-degree location by time point, mean \pm SD, mm							
	4 70	0.04	150	. 0.02	1.00		
T0 (n=420 among women, n=308 among men)	4.70	± 0.94	4.56	± 0.93	4.88	± 0.9	

Person-level characteristics at baseline [*]	Overall		Women		Men	
	(n=397)		(n=233, 59%)		(n=164, 41%)	
	n or	% or	n or	% or	n or	% or
	mean	± SD	mean	± SD	mean	± SD
T2 (n=410 among women, n=303 among men)	4.64	± 1.04	4.40	± 0.98	4.95	± 1.05
T3 (n=436 among women, n=313 among men)	4.57	± 1.07	4.30	± 1.03	4.96	± 1.01

At baseline unless otherwise specified

 † Time points in the JoCo OA: Baseline (T0), 1991–1997; First follow-up (T1), 1999–2004; Second follow-up (T2), 2006–2011; Third follow-up (T3), 2013–2015; missings were due to image quality or obscured joint margins.

SD: standard deviation; BMI: body mass index; rHOA: radiographic hip osteoarthritis; sxHOA: symptomatic rHOA; qJSW: quantitative joint space width at fixed locations

Table 2.

Unadjusted linear mixed model estimates (in mm) and 95% confidence intervals (CI) for qJSW at 50, 30, and 10 degrees, stratified by sex and rHOA or sxHOA incidence status.

Radiographic OA (rHOA) Strata	50 degrees30 degreesEstimateEstimate(95% C1), mm(95% C1), mm		10 degrees Estimate (95% CI), mm			
Women	qJSW at	qJSW change	qJSW at	qJSW change	qJSW at	qJSW change
	baseline	per year	baseline	per year	baseline	per year
No rHOA	4.74	-0.007	4.90	-0.002	5.01	0.001
	(4.61, 4.87)	(-0.011, -0.004)	(4.77, 5.03)	(-0.005, 0.001)	(4.90, 5.13)	(-0.003, 0.004)
Incident rHOA	4.30	-0.028	4.88	-0.022	5.22	-0.012
	(4.12, 4.47)	(-0.038, -0.018)	(4.66, 5.10)	(-0.032, -0.012)	(5.01, 5.42)	(-0.021, -0.002)
Baseline rHOA	4.10	-0.014	4.45	-0.005	4.98	-0.003
	(3.84, 4.35)	(-0.020, -0.008)	(4.19, 4.71)	(-0.016, 0.006)	(4.72, 5.23)	(-0.014, 0.009)
Men	qJSW at	qJSW change	qJSW at	qJSW change	qJSW at	qJSW change
	baseline	per year	baseline	per year	baseline	per year
No rHOA	5.02	0.006	5.28	0.003	5.54	0.004
	(4.87, 5.17)	(0.002, 0.010)	(5.11, 5.44)	(-0.001, 0.007)	(5.39, 5.69)	(-0.000, 0.008)
Incident rHOA	4.62	0.006	4.98	0.002	5.44	-0.001
	(4.40, 4.83)	(-0.006, 0.018)	(4.73, 5.23)	(-0.011, 0.014)	(5.17, 5.71)	(-0.014, 0.011)
Baseline rHOA	4.45	0.010	4.85	0.004	5.45	0.002
	(4.13, 4.78)	(-0.014, 0.034)	(4.51, 5.20)	(-0.008, 0.015)	(5.08, 5.83)	(-0.010, 0.015)
Symptomatic	50 degrees		30 degrees		10 degrees	
OA (sxHOA)	Estimate		Estimate		Estimate	
Strata [*]	(95% CI), mm		(95% CI), mm		(95% CI), mm	
Women	qJSW at	qJSW change	qJSW at	qJSW change	qJSW at	qJSW change
	baseline	per year	baseline	per year	baseline	per year
No sxHOA	4.66	-0.012	4.90	-0.006	5.08	-0.001
	(4.55, 4.78)	(-0.016, -0.008)	(4.78, 5.02)	(-0.010, -0.002)	(4.97, 5.19)	(-0.005, 0.003)
Incident sxHOA	4.12	-0.030	4.68	-0.017	5.19	-0.009
	(3.90, 4.34)	(-0.043, -0.018)	(4.37, 4.98)	(-0.030, -0.005)	(4.94, 5.43)	(-0.023, 0.006)
Men	qJSW at	qJSW change	qJSW at	qJSW change	qJSW at	qJSW change
	baseline	per year	baseline	per year	baseline	per year
No sxHOA	4.91	0.007	5.17	0.004	5.49	0.004
	(4.77, 5.05)	(0.001, 0.012)	(5.02, 5.32)	(0.000, 0.009)	(5.35, 5.63)	(-0.000, 0.008)
Incident sxHOA	4.55	-0.013	4.97	-0.008	5.71	-0.015
	(4.25, 4.86)	(-0.030, 0.005)	(4.61, 5.33)	(-0.021, 0.005)	(5.34, 6.08)	(-0.035, 0.004)

JSW change over time that are significant from zero are shown in **bold**. rHOA: radiographic hip osteoarthritis; sxHOA: symptomatic rHOA; qJSW: quantitative joint space width at fixed locations

* Those with baseline sxHOA were excluded from the models stratifying by sxHOA status due to the small number of hips (n=22, 2.8% or <5%) in this group

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Table 3.

Adjusted * odds ratios (aOR) and 95% confidence intervals (CI) for the association of baseline 50-degree qJSW and non-constant change in qJSW over time with incident rHOA or sxHOA, separately among women and men

Sex	Main effect(s) for each model	Incident rHOA	Incident sxHOA
Women	Overall effect	(360 hips)	(410 hips)
	Loss of qJSW over time group †	3.56 (1.67, 7.74)	3.37 (1.10, 10.4)
	1 mm narrower (1SD) at baseline	2.04 (1.43, 2.92)	2.68 (1.67, 4.28)
Men	Overall effect	(261 hips)	(297 hips)
	1 mm narrower (1SD) at baseline	1.63 (1.11, 2.37)	1.62 (1.04, 2.52)

* Adjusted for: baseline age, race, <high school education, height, BMI, weight change defined by more than 5% change in BMI by 3rd follow-up, report of hip injury by 3rd follow-up.

 ${}^{\not\!\!\!\!\!\!\!\!\!\!\!\!\!}^{}Compared with the group that had constant qJSW over time$

rHOA: radiographic hip osteoarthritis; sxHOA: symptomatic rHOA; qJSW: quantitative joint space width at fixed locations