Variations in Hip Shape Are Associated with Radiographic Knee Osteoarthritis: Cross-sectional and Longitudinal Analyses of the Johnston County Osteoarthritis Project

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ABSTRACT. Objective. Hip shape by statistical shape modeling (SSM) is associated with hip radiographic osteoarthritis (rOA). We examined associations between hip shape and knee rOA given the biomechanical interrelationships between these joints.

Methods. Bilateral baseline hip shape assessments [for those with at least 1 hip with a Kellgren-Lawrence arthritis grading scale (KL) 0 or 1] from the Johnston County Osteoarthritis Project were available. Proximal femur shape was defined on baseline pelvis radiographs and evaluated by SSM, producing mean shape and continuous variables representing independent modes of variation (14 modes = 95% of shape variance). Outcomes included prevalent [baseline KL ≥ 2 or total knee replacement (TKR)], incident (baseline KL 0/1 with followup ≥ 2), and progressive knee rOA (KL increase of ≥ 1 or TKR). Limb-based logistic regression models for ipsilateral and contralateral comparisons were adjusted for age, sex, race, body mass index (BMI), and hip rOA, accounting for intraperson correlations.

Results. We evaluated 681 hips and 682 knees from 342 individuals (61% women, 83% white, mean age 62 yrs, BMI 29 kg/m^2). Ninety-nine knees (15%) had prevalent rOA (4 knees with TKR). Lower modes 2 and 3 scores were associated with ipsilateral prevalent knee rOA, and only lower mode 3 scores were associated with contralateral prevalent knee rOA. No statistically significant associations were seen for incident or progressive knee rOA.

Conclusion. Variations in hip shape were associated with prevalent, but not incident or progressive, knee rOA in this cohort, and may reflect biomechanical differences between limbs, genetic influences, or common factors related to both hip shape and knee rOA. (J Rheumatol First Release December 15 2015; doi:10.3899/jrheum.150559)

Key Indexing Terms:
HIP JOINT KNEE OSTEOARTHRITIS RADIOGRAPHY

Statistical shape modeling (SSM) methods have been used by several groups, including ours, to describe the variability in hip shape in populations. Hip shape by SSM has been found to be a radiographic biomarker for the development of osteoarthritis (OA) of the hip, defined as structural disease [radiographic OA (rOA)], clinical/symptomatic OA (rOA

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with OA symptoms), and/or total hip replacement[1,2,3,4,5,6]. Specifically, our group has found associations between variations in modes 2 (reflecting changes in the width of the femoral neck and size of the trochanters) and 3 (variations in femoral neck length and the width of the greater trochanter) and incident symptomatic hip OA[6].

The hip and knee are biomechanically interconnected as part of the kinetic chain, and OA at one of these large joint sites increases risk at the other sites in a nonrandom fashion. As shown by Shakoor, *et al*[7], in patients requiring a knee replacement after an initial hip replacement, this procedure was much more likely to be done at the contralateral knee, and similarly, for those undergoing initial knee replacement, a subsequent hip replacement was more likely on the contralateral side. Individuals with OA in 1 of these 4 large joints (right or left, hip or knee) have 40–80% greater odds of having OA in another joint, although the greatest odds were for OA in the contralateral cognate joint (e.g., if the right knee was affected, the odds of left knee OA were dramatically increased)[8]. In addition, individuals with developmental dysplasia of the hip are more likely to undergo not only hip, but also knee replacement compared with controls[9]. Patients with moderate to severe knee OA, compared with controls, also demonstrate differences in biomechanical assessments, not only at the knee, but also at the hip and ankle, including decreased adduction and extension moments at the hip and dorsiflexion moments at the ankle[10]. Although the specific biomechanical consequences of variations in joint shape are not yet known, given the above evidence for the interrelationship between the hip and knee joints, in our current study, we sought to assess potential structural associations between hip shape, described quantitatively using modes of variation, and prevalent, incident, and progressive knee rOA in the Johnston County OA Project (JoCo OA).

MATERIALS AND METHODS

Study sample. Data were from the JoCo OA baseline and first followup visit (mean followup time 6 yrs, range 4–11 yrs); details of the parent project have been described elsewhere[11]. The JoCo OA has been continuously approved by the institutional review boards of the University of North Carolina at Chapel Hill and the Centers for Disease Control and Prevention, and all participants gave informed consent. The baseline timepoint hip shapes used in our analysis were obtained as part of a prior analysis of hip shape and incident symptomatic and radiographic hip OA[6]. In brief, of the 1726 individuals with paired radiographic data (anteroposterior supine pelvis films with the feet in 15° of internal rotation, read blinded to clinical status and chronological order) from both baseline and followup timepoints, 193 hips developed incident rOA, defined as a Kellgren-Lawrence arthritis grading scale (KL) of 0 or 1 at baseline and 2 or more at followup. All of these were selected, along with randomly selected control hips (KL 0 or 1 at both timepoints) in about equal numbers from 4 race-by-sex strata (men, women, African American, and white) for a total of 342 individuals.

Unlike the previous analysis, which focused on case/control status at the hip[6], for our current analysis, baseline hip shape from all hips from all participants (both cases and controls) with suitable radiographs (n = 681 hips; Figure 1) were included, such that a small number (77 hips, or 11% of the hips) had evidence of prevalent radiographic hip OA (KL ≥ 2) at baseline (these hips were excluded from the prior study).

Hip shape assessment. A 60-point model of proximal femur shape[2,6] was defined on the baseline anteroposterior pelvis radiographs and evaluated by SSM. Principal components analysis was performed on these 60 points; the first 14 principal components were retained, explaining 95% of the shape variance. These, in turn, corresponded to 14 independent modes of shape variation, which were treated as 14 continuous variables in our analysis. Further details on the derivation of these modes have been published previously[6].

Knee OA assessment. Bilateral weight-bearing anteroposterior extended knee radiographs were obtained for all participants and were read for rOA by a single examiner (JBR; from prior study, weighted κ for interrater reliability 0.9; κ for intrarater reliability 0.9[12]). Knee rOA outcomes were defined as follows: (1) prevalent knee rOA was defined as a KL ≥ 2 or total knee replacement (TKR) for OA at baseline; (2) incident knee rOA was defined as a KL ≥ 2 at followup in a knee having KL = 0 or 1 at baseline; and (3) progressive knee rOA was defined as an increase of at least 1 KL or progression to TKR between baseline and followup, regardless of baseline KL (to avoid conditioning on an intermediate[13]) and excluding knees with baseline TKR because they could not progress further by definition.

Statistical analysis. The 14 baseline hip shape mode scores were simultaneously included in 4 separate limb-based logistic regression models for ipsilateral and contralateral comparisons of knee outcomes [(1) right hip/right knee, (2) left hip/left knee, (3) right hip/left knee, and (4) left hip/right knee], adjusted for age, sex, race, body mass index (BMI), and hip rOA (ipsilateral to the mode score in the model), accounting for intraperson correlations (using the cluster option in Stata[14]).

RESULTS

We evaluated 681 hips and 682 knees from 342 individuals (Figure 1); characteristics are shown in Table 1. A total of 77 hips (11%) had prevalent rOA at baseline, and prevalent knee rOA was present in 99 knees (15%) at baseline, of which 53 and 46 were right and left knees, respectively.

Prevalent knee rOA: ipsilateral associations. The odds of having prevalent rOA in the right knee were increased by 74% for every 1 SD reduction in mode 2 at the right hip in

Table 1. Sample characteristics (n = 342). Values are n (%) unless otherwise specified.

Characteristic	Values
Female sex	210 (61.4)
White	282 (82.5)
Age, yrs, mean (SD)	61.7 (8.9)
BMI, kg/m^2, mean (SD)	29.2 (5.9)
Knees at baseline, n = 682	
KL 0	396 (58.1)
KL 1	187 (27.4)
KL 2	61 (8.9)
KL 3	27 (4.0)
KL 4	7 (1.0)
TKR	4 (0.6)
Hips at baseline, n = 681	
KL 0	121 (17.8)
KL 1	483 (70.9)
KL 2	74 (10.9)
KL 3	2 (0.3)
KL 4	1 (0.2)
THR	0 (0.0)

BMI: body mass index; KL: Kellgren-Lawrence arthritis grading scale; TKR: total knee replacement; THR: total hip replacement.

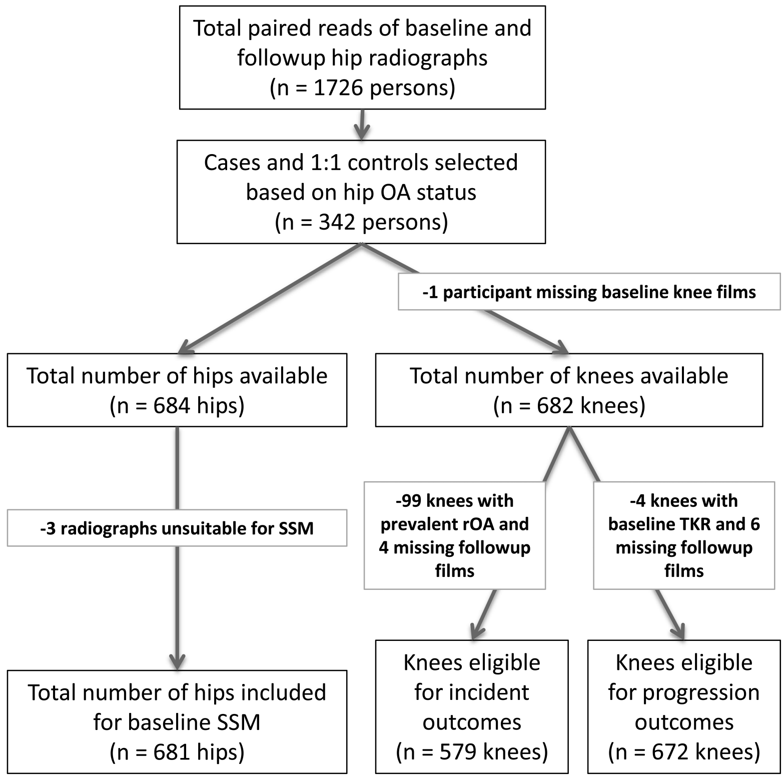

Figure 1. Flowchart of included participants and joints. OA: osteoarthritis; SSM: statistical shape modeling; rOA: radiographic OA; TKR: total knee replacement.

analyses adjusted for age, sex, race, BMI, and right hip rOA (Table 2). The associations between left hip mode 2 score and prevalent left knee rOA were not statistically significant. In adjusted analyses, for every 1 SD lower score for mode 3 at the right hip, the odds of right knee rOA were increased by 46%; for every 1 SD reduction in mode 3 score at the left hip, the odds of left knee rOA were increased by 50%. As shown in Table 2, there were also statistically significant associations for a 1 SD lower score for modes 8 and 14 at the left hip and prevalent left knee OA, although these modes account for only 2.3% and 0.6% of total shape variance, respectively.

Prevalent knee rOA: contralateral associations. For mode 2, none of the contralateral associations between hip shape

Table 2. Association between a 1 SD decrease in baseline hip shape modes and prevalent radiographic knee OA. Values are aOR* (95% CI).

Mode	% Variance in Hip Shape Explained	Ipsilateral		Contralateral	
		Right Hip/Right Knee	Left Hip/Left Knee	Right Hip/Left Knee	Left Hip/Right Knee
1	37.4	0.87 (0.57–1.32)	1.17 (0.75–1.84)	0.78 (0.50–1.21)	1.31 (0.83–2.08)
2	16.0	**1.74 (1.18–2.57)**	1.06 (0.77–1.47)	1.22 (0.86–1.72)	1.35 (0.96–1.91)
3	12.5	**1.46 (1.03–2.05)**	**1.50 (1.07–2.10)**	1.19 (0.83–1.70)	**1.78 (1.23–2.56)**
4	9.9	1.00 (0.65–1.53)	1.08 (0.71–1.65)	1.05 (0.70–1.59)	0.99 (0.63–1.54)
5	5.1	0.96 (0.66–1.41)	0.97 (0.65–1.46)	0.99 (0.70–1.40)	0.77 (0.52–1.14)
6	3.4	1.03 (0.68–1.57)	1.40 (0.92–2.13)	0.92 (0.64–1.33)	1.17 (0.80–1.73)
7	2.6	0.85 (0.61–1.18)	0.76 (0.53–1.08)	0.89 (0.65–1.21)	0.76 (0.53–1.09)
8	2.3	0.97 (0.69–1.35)	**0.65 (0.44–0.96)**	0.97 (0.70–1.34)	0.71 (0.50–1.02)
9	1.7	1.31 (0.96–1.81)	0.80 (0.55–1.17)	1.21 (0.86–1.70)	1.04 (0.74–1.46)
10	1.3	1.02 (0.73–1.42)	0.70 (0.46–1.07)	1.04 (0.75–1.45)	0.73 (0.47–1.14)
11	1.1	1.06 (0.67–1.66)	1.15 (0.81–1.62)	1.01 (0.62–1.63)	1.27 (0.87–1.86)
12	0.9	0.86 (0.58–1.27)	0.74 (0.48–1.13)	0.97 (0.67–1.41)	0.83 (0.56–1.24)
13	0.7	1.03 (0.74–1.45)	0.83 (0.58–1.20)	1.01 (0.69–1.48)	0.96 (0.67–1.39)
14	0.6	1.08 (0.79–1.48)	**0.65 (0.45–0.94)**	0.95 (0.70–1.28)	0.87 (0.61–1.24)

* Adjusted OR: adjusted for age, sex, race, body mass index, and hip OA ipsilateral to hip mode score. Significant data are in bold face. OA: osteoarthritis.

modes and prevalent knee rOA were statistically significant. However, a 35% increase in the odds of right knee rOA for every 1 SD reduction in mode 2 score at the left hip was noteworthy and approached statistical significance (adjusted OR 1.35, 95% CI 0.96–1.91; Table 2). For every 1 SD reduction in mode 3 score at the left hip, there was a statistically significant 78% increase in the odds of prevalent right knee rOA in adjusted analyses. Associations between mode 3 at the right hip and left knee rOA were not statistically significant.

Incident knee rOA. Of the 579 eligible knees (99 had prevalent rOA, 4 lacked followup films), 94 (16%) developed incident rOA at followup, of which 50 and 44 were right and left knees, respectively. There were no statistically significant associations between modes and incident knee rOA (Table 3). Of potential interest, although not statistically significant, were suggestive associations between right hip shape and incident right knee rOA (34% higher odds for every 1 SD lower score on mode 9), and between right hip shape and incident left knee rOA (38% higher odds for every 1 SD reduction in mode 7 score, and 39% higher odds per 1 SD higher score for mode 8; Table 3).

Progressive knee rOA. Of the 672 eligible knees (4 had baseline TKR, 6 lacked followup films), 219 (33%) met the definition of progressive knee rOA, of which 118 and 101 were right and left knees, respectively. There were no significant associations between modes and progressive knee rOA (Table 4). Associations approaching statistical significance, though not formally so, were seen in adjusted analyses between right hip shape and progressive right knee rOA (28% higher odds for every 1 SD reduction in mode 9 score) and between right hip shape and progressive left knee rOA (23% lower odds for every 1 SD lower mode 11 score; Table 4).

DISCUSSION

Variations in the shape of the hip (particularly modes 2 and 3) were related to the baseline prevalence of knee rOA in this cohort, although the relationships varied among ipsilateral and contralateral joint pairings. Our findings for the ipsilateral hip shape-knee rOA association are supported by a study of the Osteoarthritis Initiative cohort that reported an association between prevalent knee OA (lateral and medial compartments) with ipsilateral proximal femur shapes[15]. In our study, mode 2 reflects differences in the width of the femoral neck and size of the trochanters, while mode 3 is suggestive of variation in the width of the greater trochanter and femoral neck length[6]. Our prior work showed associations between modes 2 and 3 (explaining 16% and 13% of total shape variance, respectively; shown in Figure 2 as mean shape ± 2 SD for illustrative purposes) with incident symptomatic hip OA. There was a likely, yet not statistically significant, relationship between mode 9 at the right hip and both incident and progressive right knee rOA that was not seen with other joint combinations. Associations with modes 7, 8, and 11 were inconsistent, and these modes explained little of the total shape variance. Therefore, our analysis suggests that radiographic hip shape by SSM represents a modest, independent risk factor for prevalent knee rOA.

Our study is unique in that it considers the effect of hip shape on OA at joints other than the hip in a community-based cohort of African American and white men and women. The question then is how to explain this association. Arguably the most obvious mechanism is biomechanical; the shape of the hip, whether assessed using SSM or geometric measures, may influence loading and forces generated at the knee and in the rest of the lower extremity kinetic chain (i.e., lumbar spine, ankle, foot), although a mechanism has yet to be elucidated given the complexity of the needed analyses.

Table 3. Association between a 1 SD decrease in baseline hip shape modes and incident radiographic knee OA. Values are aOR* (95% CI).

Mode	% Variance in Hip Shape Explained	Ipsilateral		Contralateral	
		Right Hip/Right Knee	Left Hip/Left Knee	Right Hip/Left Knee	Left Hip/Right Knee
1	37.4	1.24 (0.84–1.84)	0.85 (0.56–1.30)	0.94 (0.63–1.38)	0.98 (0.67–1.42)
2	16.0	0.97 (0.68–1.39)	1.17 (0.81–1.69)	1.24 (0.84–1.83)	0.98 (0.70–1.38)
3	12.5	1.05 (0.76–1.45)	1.08 (0.78–1.48)	1.04 (0.74–1.48)	1.12 (0.83–1.51)
4	9.9	0.95 (0.68–1.32)	0.99 (0.67–1.47)	1.03 (0.71–1.52)	0.93 (0.67–1.31)
5	5.1	1.27 (0.86–1.88)	0.98 (0.66–1.46)	0.97 (0.66–1.44)	0.91 (0.63–1.31)
6	3.4	0.95 (0.68–1.33)	1.26 (0.86–1.84)	1.13 (0.83–1.52)	0.90 (0.62–1.32)
7	2.6	1.05 (0.76–1.45)	0.96 (0.64–1.45)	1.38 (0.97–1.97)	0.95 (0.68–1.34)
8	2.3	0.99 (0.72–1.36)	1.07 (0.71–1.61)	1.39 (0.96–2.01)	0.96 (0.67–1.37)
9	1.7	1.34 (0.97–1.87)	1.25 (0.80–1.94)	1.00 (0.66–1.51)	1.30 (0.90–1.86)
10	1.3	1.27 (0.91–1.78)	0.82 (0.55–1.22)	1.01 (0.72–1.41)	1.05 (0.71–1.56)
11	1.1	0.82 (0.58–1.16)	0.86 (0.60–1.22)	0.74 (0.51–1.07)	0.88 (0.61–1.27)
12	0.9	0.81 (0.59–1.10)	0.88 (0.61–1.29)	0.81 (0.60–1.08)	0.83 (0.60–1.15)
13	0.7	0.97 (0.70–1.33)	0.91 (0.62–1.32)	1.26 (0.89–1.79)	1.02 (0.71–1.45)
14	0.6	1.10 (0.83–1.46)	1.23 (0.88–1.71)	1.24 (0.89–1.73)	1.06 (0.78–1.44)

* Adjusted OR: adjusted for age, sex, race, body mass index, and hip OA ipsilateral to hip mode score. OA: osteoarthritis.

Table 4. Association between a 1 SD decrease in baseline hip shape modes and progressive radiographic knee OA. Values are aOR* (95% CI).

Mode	% Variance in Hip Shape Explained	Ipsilateral		Contralateral	
		Right Hip/Right Knee	Left Hip/Left Knee	Right Hip/Left Knee	Left Hip/Right Knee
1	37.4	1.16 (0.88–1.54)	0.98 (0.74–1.29)	1.06 (0.80–1.41)	1.07 (0.81–1.42)
2	16.0	0.98 (0.76–1.26)	1.06 (0.81–1.39)	1.07 (0.82–1.39)	0.99 (0.76–1.28)
3	12.5	0.96 (0.75–1.23)	0.92 (0.72–1.19)	0.97 (0.76–1.24)	0.88 (0.68–1.13)
4	9.9	1.11 (0.83–1.48)	1.03 (0.79–1.35)	0.95 (0.70–1.29)	1.02 (0.78–1.33)
5	5.1	1.16 (0.89–1.51)	0.93 (0.71–1.22)	1.02 (0.79–1.33)	1.13 (0.88–1.45)
6	3.4	0.98 (0.76–1.26)	0.95 (0.73–1.25)	0.91 (0.71–1.17)	1.00 (0.77–1.30)
7	2.6	0.96 (0.75–1.23)	1.07 (0.82–1.41)	1.03 (0.80–1.33)	1.08 (0.83–1.40)
8	2.3	0.86 (0.68–1.09)	0.88 (0.68–1.15)	0.91 (0.71–1.16)	0.94 (0.73–1.20)
9	1.7	1.28 (0.98–1.67)	1.01 (0.77–1.34)	1.06 (0.80–1.40)	1.07 (0.81–1.42)
10	1.3	0.93 (0.74–1.19)	1.01 (0.77–1.32)	1.02 (0.80–1.32)	0.94 (0.73–1.23)
11	1.1	0.80 (0.61–1.05)	1.01 (0.78–1.30)	0.77 (0.59–1.02)	0.87 (0.68–1.12)
12	0.9	0.86 (0.67–1.09)	0.90 (0.69–1.16)	0.86 (0.67–1.10)	0.96 (0.75–1.22)
13	0.7	0.89 (0.71–1.12)	0.85 (0.64–1.13)	1.00 (0.79–1.26)	0.98 (0.75–1.27)
14	0.6	1.18 (0.93–1.49)	0.96 (0.75–1.23)	1.14 (0.90–1.45)	1.15 (0.90–1.47)

* Adjusted OR: adjusted for age, sex, race, body mass index, and hip OA ipsilateral to hip mode score. OA: osteoarthritis.

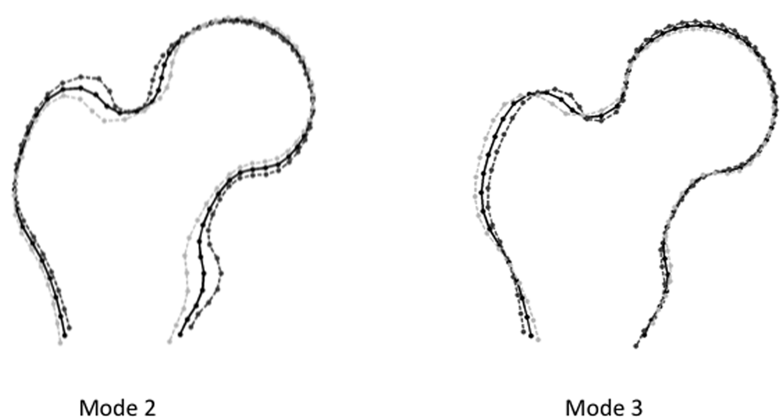

Figure 2. Hip shape modes associated with prevalent radiographic knee OA. Figure based on the same data as Figure 2 in reference 6. A lower mode score (similar to –2 SD line) was associated with incident symptomatic hip OA in reference 6. Mean: black solid lines; +2 SD: dark dashed lines; –2 SD: light dashed lines.

Alternatively, there may be common factors underlying both the shape of the hip and the development of knee OA that may explain their relationship, such as genetics or lifestyle factors. A necessary part of future research will be to examine biomechanics, genetics, and other potentially shared risk factors for these conditions.

The associations between hip shape and knee rOA varied between ipsilateral and contralateral relationships. Consistent with prior research[16,17,18], we found a higher frequency of knee rOA on the right versus the left side. Kopec, *et al* reported moderate associations between prevalent hip and knee rOA, but these did not vary by side[18]. Shakoor, *et al*, in addition to demonstrating nonrandom distribution of joint replacement[7], also found higher joint loads in contralateral knees of patients undergoing unilateral hip replacement, even after surgery[19]. Overall, in our current analysis, ipsilateral associations between hip shape and knee rOA were stronger than contralateral ones; that the strongest associations identified were those between right hip shape variations and right-sided prevalent knee rOA may be consistent with greater right leg dominance in the participants. These findings may reflect biomechanical differences between limbs, but our present study lacked comprehensive biomechanical assessments to test this hypothesis.

Unlike prevalent knee rOA, we did not see any associations reach statistical significance between hip shape and incident and progressive knee rOA. This may be in part because of the older age of our cohort, because variation in hip shape is likely primarily genetically determined, and is present throughout life in the absence of pathologic changes (such as those that occur with OA). Therefore, variation in hip shape may primarily be a risk factor for early onset or rapidly progressive knee rOA, and may not be associated with later incident or progressive disease in this population, though it would still be associated with prevalent disease. Alternatively, 6 years of followup may be insufficient to allow incident and progressive knee outcomes to develop. Additionally, although our study design was longitudinal, we were not able to conclusively evaluate the causal relationship; it is conceivable that hip joint shape may lead to altered knee joint mechanics and therefore to a greater risk of knee OA, or equally reasonably, that knee OA could result in remodeling at the hip, altering its shape, or potentially even a combination of these. A next step in this research is to examine the clinically relevant association of hip shape with symptomatic knee OA.

Our study has several strengths, including the assessment of multiple joints on participants in this well-characterized cohort, the ability to conduct longitudinal analyses, and the standardized radiographs read with high reliability for KL and for hip shape. The limitations of this work include the relatively small sample size, precluding subgroup analyses (such as stratification by sex or race), the use of a single cohort which may limit generalizability, and the lack of long-limb radiographs for assessment of alignment.

Radiographic hip shape is a modest risk factor for prevalent knee rOA independent of age, sex, race, BMI, and baseline hip rOA. Future studies should examine the involvement of biomechanical factors in this relationship, as well as assessment of multiple lower-body joint OA over a longer followup time.

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