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Leg Length Inequality and Hip Osteoarthritis in the Multicenter Osteoarthritis Study and the Osteoarthritis Initiative

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Abstract

Objective—Studies suggest that persons with a 2 cm shorter limb have an increased risk of knee osteoarthritis (OA) in that limb. We examined whether leg length inequality (LLI) confers an increased risk of hip OA.

Methods—Using long limb radiographs from MOST and the Osteoarthritis Initiative, we measured LLI and scored hip radiographs which were obtained at baseline and 3–5 year follow-up. We examined the association of 1 cm LLI and 2 cm of LLI with radiographic hip OA cross-sectionally and longitudinally, assessing risk in shorter limbs and longer limbs compared with limbs with no LLI. We carried out logistic regression analyses with GEE and adjusted for age, sex, BMI, height and cohort of origin.

Results—In MOST, we studied 1,966 subjects and in OAI 2,617 subjects. 12% of persons had LLI of 1 cm and 1% had LLI of 2 cm. For LLI 1 cm, the adjusted OR for prevalent hip OA in the shorter leg was 1.47 (95% CI 1.07–2.02) and for LLI 2 cm, it was 2.15 (95% CI 0.87–5.34). For LLI 1 cm, the odds of incident hip OA in the shorter leg was 1.39 (95% CI 0.81–2.39) while for LLI 2 cm, the odds in the shorter leg was 4.20 (95% CI 1.26 – 14.03). We found no increased risk of hip OA in longer limbs.

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Conclusion—Our findings suggest that, like knee OA, limbs at least 2 cm shorter are at increased risk of hip OA.

Hip osteoarthritis (OA) is a significant source of morbidity and is a major cause of disability in the United States. The age-standardized prevalence of symptomatic hip OA was 4.2% in the urban and suburban community of Framingham. Not much is known about modifiable risk factors for hip OA that could help identify treatment strategies.

One potential risk factor for hip OA is leg length inequality (LLI). In the Multicenter Osteoarthritis Study (MOST), we found that persons with at least 1 cm shorter limb had an increased incidence, prevalence and progression of knee OA compared to the longer limb (1). The shorter leg is likely to sustain increased impact force of the foot during gait, thus transmitting a greater impulse up the ipsilateral leg. LLI is easily treatable and could be modifiable. However, the longitudinal association of LLI and hip OA has not been well characterized. LLI of at least 1 cm is uncommon (~10–15% of subjects in MOST) and LLI of 2 cm is rare (~1% in MOST). Furthermore, hip OA has a lower prevalence and incidence than knee OA. Therefore, to increase the likelihood that we would have enough persons with LLI to examine its association with hip OA, we combined data from MOST and the Osteoarthritis Initiative (OAI), two large longitudinal cohort studies of OA.

METHODS

Multicenter Osteoarthritis Study

The MOST cohort is a multicenter, longitudinal community-based study of 3026 participants aged 50 to 79 years with or at risk for knee OA. MOST participants were recruited from two US communities: Birmingham, Alabama, and Iowa City, Iowa. Details of the study population have been published elsewhere (2–4). Participants were excluded if they had bilateral total knee replacement, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, reactive arthritis, or a history of cancer (except for non-melanoma skin cancer); needed dialysis; were unable to walk without the help of another person or a walker; or planned to move out of the area in the subsequent three years. Long limb films obtained at baseline and 60 months were used to assess LLI and radiographic hip OA.

Long limb length evaluation—Leg lengths were measured as the distance from the center of the femoral head to the tibial midplafond point (the most distal portion of the tibia directly over the talar dome) and LLI was the difference between legs in these lengths. A detailed description of the leg length measurement in MOST has been published (1).

Hip osteoarthritis evaluation—Long limb radiographs were read independently by two trained investigators, one an experienced musculoskeletal radiologist (AG) and the other a rheumatologist trained in reading hip films (CK), for individual features of radiographic hip OA (RHOA) in accordance with the Osteoarthritis Research Society International (OARSI) atlas (6). Definite femoral and acetabular osteophytes and superolateral and superomedial JSN were defined as OARSI atlas grades 2. Hips were classified as having “definite RHOA” based on the individual radiographic features present using the following criteria (7): a) a Croft grade 2 (presence of two or more of definite osteophytes, definite joint space

narrowing (JSN), sclerosis, cysts or deformity); b) definite JSN plus OARSI grade 1 femoral osteophytes; c) definite femoral osteophytes, regardless of the presence of other radiographic features; d) definite superolateral JSN or OARSI grade 3 superomedial JSN, regardless of other features. CK read the all the radiographs, and AG read a selected number of radiographs including every RHOA read by CK. The intra-observer agreement kappa was 0.80 for the presence/absence of RHOA in a sample of 168 films reread blinded to previous scores. Amongst 90 radiographs that were read as negative OA by CK, AG found 5 of those radiographs had OA. If there was a disagreement between CK and AG, the reading by AG was used.

Osteoarthritis Initiative

The Osteoarthritis Initiative is a multicenter longitudinal cohort study of OA in 4796 people aged 45–79 recruited during 2003–05 at four centers: Columbus, OH; Providence, RI; Baltimore, MD; and Pittsburgh, PA. The researchers recruited participants if they had or were at increased risk for knee OA. A description of the study is available (www.oai.ucsf.edu). Inclusion criteria required participants to be ambulatory (use of assistive devices such as canes and walkers was allowed) with no plans to move away from the area for at least three years. People were excluded if they had a history of bilateral total knee replacement, bilateral bone-on-bone radiographic knee osteoarthritis, rheumatoid arthritis, contraindications to MRI, or comorbidities that might interfere with the ability to participate in a study for four years. The long limb radiographs used to measure leg length were taken at 12 month (26% of subjects), 24 (40%) or 36 (30%) or 48 month (4%) follow up visits. Pelvis radiographs were obtained at baseline and 48 month follow-up and were used to assess radiographic hip OA.

Long limb length evaluation—The long limb measurements were done by the same readers that read MOST films using the same protocol.

Hip osteoarthritis evaluation—In contrast to MOST which used long limb radiographs to assess RHOA, the OAI participants underwent standard, weight-bearing anteroposterior pelvic radiography which were used to assess RHOA. The pelvis radiographs were read by 2 musculoskeletal radiologists (including PMJ) and a rheumatologist (NEL) for individual radiographic features of hip osteoarthritis using the OARSI atlas (5). A detailed radiograph reading protocol has been published (6). RHOA was defined by the same UCSF criteria applied in MOST (7) The test-retest agreement kappa was 0.77 for the presence/absence of RHOA in a sample of 189 radiographs reassessed blindly.

Analyses

Analyses were restricted to subjects with leg length data in both limbs. Subjects with a total knee or hip replacement in either limb at baseline were excluded. If outcome data were missing in one hip (usually unreadable hip joint due to poor film quality), the contralateral limb was still included in the analysis. We performed analyses using 2 different definition of LLI (LLI 1 cm and LLI 2 cm). For analyses evaluating LLI 1 cm, LLI was categorized as either < 1 cm (reference) or 1 cm. For analyses of LLI 2 cm, LLI was categorized as < 1 cm (reference), 1 to < 2 cm, and 2 cm. For each LLI category we examined the risk of

hip OA in the shorter limb separately from the risk in the longer limb. First, we examined the cross-sectional association of LLI with the prevalence of RHOA using logistic regression models with generalized estimating equations. Then, we examined the longitudinal relationship of baseline LLI with incident hip OA. Incident hip OA was defined as a hip without RHOA at baseline that developed RHOA at the follow up. Although total hip replacements were excluded from baseline, total hip replacements were not excluded from the follow up period, and a total hip replacement was included as a case of incident hip OA. Analyses adjusted for age, sex, race (white/nonwhite), BMI, height (sex-specific quartiles) and cohort of origin.

RESULTS

Subject characteristics for both cohorts are shown in Table 1. In MOST, 1,966 subjects and in OAI 2,617 subjects had complete data and were included in the analysis.

In the combined analysis of the MOST and OAI cohorts for LLI ≥ 1 cm, the adjusted OR for prevalent RHOA in the shorter leg was 1.47 (95% CI, 1.07–2.02) and the OR in longer leg was 1.09 (95% CI, 0.77–1.55) (Table 2). For LLI ≥ 2 cm, the adjusted OR for prevalent RHOA in the shorter leg was 2.15 (95% CI, 0.87 – 5.34), and the OR in the longer leg was 1.31 (95% CI, 0.46 – 3.74) (Table 3). For incident RHOA in LLI ≥ 1 cm limbs, the OR for in the shorter leg was 1.39 (95% CI, 0.81–2.39), and in the longer leg was 1.56 (95% CI, 0.93–2.60). For LLI >2 cm, the OR for incident RHOA in the shorter leg was 4.20 (95% CI, 1.26 – 14.03), and in the longer leg was 1.32 (95% CI, 0.20 – 8.66) (Table 3).

DISCUSSION

Our study provides mixed evidence that, in individuals with LLI, the shorter limb is at increased risk of radiographic hip OA. For LLI ≥ 1 cm, the shorter limb had a significant 1.47-fold odds of prevalent RHOA in both cohorts combined. For LLI ≥ 2 cm, the OR (2.15 (95% CI, 0.87 – 5.34)) for prevalent RHOA in the shorter leg was increased but findings did not reach statistical significance. The lack of significance may be due to limited numbers of subjects with this degree of LLI.

For incident RHOA, there were no associations with LLI ≥ 1 cm. Among subjects with LLI ≥ 2 cm, there was a significant 4.2-fold greater odds of incident RHOA in the shorter limb. However, this positive association was based on small numbers.

Minor degrees of LLI are common and have been reported to occur up to 70–90% of the population (8–10). LLI may be congenital or acquired with causes ranging from trauma, to infection, or scoliosis causing pelvic tilt (11–13). However, the degree of LLI at which it becomes clinically significant is controversial (8,9,14–17). For our studies, we chose to assess LLI ≥ 1 cm and LLI ≥ 2 cm.

Although it is known that LLI causes abnormal loading of the lower extremities, the pathophysiology of LLI contributing to lower extremity OA is not completely understood. The shorter leg sustains increased impact force with foot strike during gait; thus, transmitting a greater impulse up the ipsilateral leg. A prior cross-sectional study of hip OA

and LLI by Gofton showed an increased prevalence of RHOA in the longer limb in hip arthroplasty patients (18). In the Gofton study, RHOA in the longer limb was postulated to occur because the longer limb sustained excessive load while weight bearing. In cross sectional data from the Johnston County Study in which LLI was assessed using a physical exam measure, there was an association between a shorter leg and ipsilateral right hip OA but not for left hip OA (19). For the longitudinal analyses, there was a non-significant trend for the shorter limb to develop hip OA (20). In our study, we found a modest increase in prevalent RHOA in the shorter limb in the crude analyses. However, we found a significant association of LLI ≥ 2 cm with incident hip OA. In the study of LLI and knee OA in MOST, higher rates of prevalent and incident knee OA occurred in the shorter limb (1).

Among limitations, severe hip OA with femoral head flattening may shorten the affected limb, thus the direction of causality in the cross-sectional analyses is uncertain. For most cases of hip OA, leg length should not be affected. Our positive finding of the incident hip OA in the shorter leg for LLI ≥ 2 was based on a small number (3 out of 36 with LLI ≥ 2 cm developed hip OA in the combined cohort). Similarly, the Johnston County incident hip OA results were based on single digit numbers of outcomes (9 RHOA/62 hips in the shorter leg vs 3 RHOA/57 hips in the longer leg) for LLI ≥ 2 cm. In general, incident hip OA does not occur in large numbers and is difficult to evaluate despite having large cohorts. Furthermore, the follow up period (60 months in MOST and 48 months in OAI) may not be long enough to detect robust numbers of new hip OA. Because our cohorts included participants at risk or with knee OA, our findings may not be generalizable for the general population. For MOST specifically, RHOA was assessed on long limb films, and the limitations of this method have been discussed previously (21,22).

LLI is likely treatable with shoe modifications such as heel lifts which are simple and inexpensive. Hip OA is a disease with few significant modifiable risk factors, and current nonsurgical treatment modalities are of only moderate efficacy. The current study provides suggestive evidence that equalizing leg lengths may reduce risk of hip OA.

In summary, leg length inequality increased risk of prevalent and incident radiographic hip osteoarthritis, with a greater effect on risk in the shorter limb. Leg length inequality is easily correctable, so this association might identify a correctable cause of hip osteoarthritis.

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TABLE 1

Subject characteristics in MOST and OAI

Subject characteristic	MOST (n=1966)	OAI (n=2627)
Age = mean(SD)	61.9 (7.9)	61.0 (9.1)
Gender (male n(%))	777 (39.5%)	1114 (42.4%)
White vs non-white N (%)	1671 (85.0%)	2144 (81.6%)
BMI mean(SD) kg/m ²	29.9 (5.1)	28.2 (4.6)
Height (cm) mean(SD)	169.4 (9.4)	168.2 (9.5)
Leg length difference category N (col %)		
Difference less than 1 cm	1709 (86.9%)	2285 (87.0%)
Difference between 1 cm and 2 cm	240 (12.2%)	304 (11.6%)
Difference ≥ 2 cm	17 (0.9%)	28 (1.1%)

TABLE 2

Leg Length Inequality ≥ 1 cm and Hip OA

	Degree of Leg Length Inequality		
	from -1 to 1 cm	Shorter limb where LLI is ≥ 1 cm	Longer limb where LLI is ≥ 1 cm
Prevalent Hip OA			
Hips, $n/N(\%)$	450 / 7969 (5.6%)	51 / 587 (8.7%)	39 / 588 (6.6%)
Crude OR	(reference)	1.58 (1.16–2.16)	1.18 (0.84–1.67)
Adjusted OR *	(reference)	1.47 (1.07–2.02)	1.09 (0.77–1.55)
Incident Hip OA			
Hips, $n/N(\%)$	141 / 6971 (2.0%)	15 / 505 (3.0%)	17 / 516 (3.3%)
Crude OR	(reference)	1.50 (0.89–2.53)	1.65 (1.00–2.72)
Adjusted *OR	(reference)	1.39 (0.81–2.39)	1.56 (0.93–2.60)

 n/n = hips with outcome/hips in leg-length inequality category

* Adjusted for age, sex, race (white/nonwhite), BMI, and height (sex-specific quartiles)

TABLE 3

Leg Length Inequality 2 cm and Hip OA

		Leg Length Inequality					
		from -1 to 1 cm (reference)	Shorter limb where LLI is 1 cm but 2 cm	Longer limb where LLI is 1 cm but 2 cm	Shorter limb where LLI is 2 cm	Longer limb where LLI is 2 cm	
Prevalent Hip OA							
Hips, <i>n/N</i> (%)		450 / 7969 (5.6%)	45 / 543 (8.3%)	35 / 543 (6.4%)	6 / 44 (13.6%)	4 / 45 (8.9%)	
Crude OR		(reference)	1.50 (1.09–2.08)	1.15 (0.80–1.65)	2.60 (1.09–6.22)	1.62 (0.58–4.57)	
Adjusted OR *		(reference)	1.41 (1.01–1.97)	1.07 (0.74–1.55)	2.15 (0.87–5.34)	1.31 (0.46–3.74)	
Incident Hip OA							
Hips, <i>n/N</i> (%)		141 / 6971 (2.0%)	12 / 469 (2.6%)	16 / 478 (3.3%)	3 / 36 (8.3%)	1 / 38 (2.6%)	
Crude OR		(reference)	1.30 (0.73–2.30)	1.67 (1.00–2.79)	4.17 (1.26–13.76)	1.41 (0.23–8.47)	
Adjusted OR		(reference)	1.20 (0.66–2.16)	1.57 (0.93–2.66)	4.20 (1.26–14.03)	1.32 (0.20–8.66)	

n/n = hips with outcome/hips in leg-length inequality category

* Adjusted for age, sex, race (white/nonwhite), BMI, and height (sex-specific quartiles)