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THE ASSOCIATION BETWEEN HIP PAIN AND RADIOGRAPHIC HIP OSTEOARTHRITIS: THE CHECK COHORT

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Abstract

Background: The diagnosis of hip osteoarthritis is often based on clinical symptoms, such as pain and stiffness, and radiographic features. However, the association between hip pain and radiographic hip osteoarthritis (ROA) remains uncertain.

Aim: To examine the association between hip pain and hip ROA.

Design and setting: Cross-sectional analysis of a Dutch cohort, the Cohort Hip and Cohort Knee (CHECK) study.

Methods: Participants (45-65 years) experienced hip and/or knee pain for which they had no prior consultation or were within 6 months of their first consultation to a general practitioner. Using weight-bearing anterio-posterior pelvis radiographs, definite and early-stage hip ROA were defined as Kellgren and Lawrence grade ≥2 and ≥1, respectively. Presence of ROA and pain was assessed in both hips of all participants. We assessed the association between hip pain and ROA using generalized estimating equations.

Results: The prevalence of definite ROA was 11.0% (218/1982 hips), while the prevalence in painful and pain-free hips was 13.3% (105/789) and 9.5% (113/1193), respectively. The early-stage prevalence was 35.3% (700/1982 hips), 41.2% (325/789) among painful and 31.4% (375/1193) among pain-free hips. Compared to pain-free hips, the odds ratio of painful hips was 1.51 (95% CI 1.16-1.98) for definite and 1.47 (95% CI 1.24-1.75) for early-stage ROA.

Conclusion: Hip pain was associated with definite and early-stage hip ROA, yet the overall ROA prevalence was modest and the prevalence among pain-free hips was substantial. Therefore, radiographs hardly help to identify hip OA patients among patients who recently newly presented with hip or knee complaints.

Keywords: Hip joint; radiographic osteoarthritis; epidemiology; pain.

How this fits in

The diagnosis of hip osteoarthritis (OA) is often based on a combination of clinical symptoms, such as pain and stiffness, and radiographic features. Previous research investigating the association between hip pain and radiographic hip OA (hip ROA) was limited and results were conflicting. In this cross-sectional study, hip pain was only modestly associated with hip ROA in early symptomatic hip OA patients. General practitioners should consider to implement the first steps of OA treatment in clinically suspected hip OA patients. This study affirms that referral of these patients for radiographic confirmation of the diagnosis of hip OA is not necessary.

Introduction

Hip osteoarthritis (OA) is a common cause of morbidity among elderly that is associated with hip pain and stiffness, and impaired mobility (1). Although less prevalent than knee OA, the global all-age symptomatic hip OA prevalence in 2010 was 0.85% (2), while the European prevalence in adults ≥60 years was 7-8% (3, 4). OA currently accounts for up to 2.5% of the gross national product in Western countries, mainly attributable to knee and hip arthroplasties costs (4, 5). In patients ≥45 years, 4% of primary care consultations are registered with an OA ICD code (6) and the overall primary care hip pain consultation rate is approximately 13/1000 consultations (7). On account of an aging world population, the hip OA prevalence and costs are expected to increase (8).

Pain is the most reported symptom among hip OA patients (1, 4). It is often pain and the associated functional disability, participation restriction and loss of independence, which pushes patients to seek health care by a general practitioner (GP) (2, 9-11). Consequently, hip pain is a key clinical feature used to classify or diagnose hip OA in primary care (12, 13). Here, the use of radiographic imaging in the diagnostic process is strongly discouraged, as there is a general mismatch between radiographic signs of OA and patients' symptoms, radiographic findings are thought not to influence the choice of treatment strategy by the GP, and are not predictive for the course of symptoms (4, 13, 14). However, these recommendations are purely based on data obtained in knee OA, while OA in the hip joint is thought to be distinctively different from OA in the knee joint (15).

The association between hip pain and hip ROA remains uncertain, for relevant literature is scarce and inconsistent (16-19). In prior research, definitions for definite and severe ROA differed considerably, as did pain definitions. Hence, the odds ratios (OR) differed substantially, ranging from 1.6 to 123.4 for severe and 1.3 to 2.8 for definite ROA (16, 17, 19). Since the symptomatic hip ROA prevalence was low in these studies, results were imprecise. Additionally, in one study only participants >60 years were analysed and another analysed these associations only in men, because of an absence of severe ROA in women. Also, pain was related to definite ROA in both sexes in one study (18), while in another study it was associated with severe ROA in men, but not in women (17).

Many scientific studies on hip OA therapies, including conservative interventions (e.g. exercise therapy (20)), analgesics (21), and experimental studies on potential disease modifying drugs (22), restrict the recruitment of patients to those with confirmed structural changes to the hip joint, visible on radiographs. In the absence of knowledge on the true association between hip symptoms and hip ROA, these studies might target the wrong structures (as many individuals with radiographic changes

might not have pain) and potentially exclude many patients with hip symptoms (because of the absence of radiographic changes) that do require medical attention.

We aimed to examine the cross-sectional association between hip pain and prevalent hip ROA in a Dutch cohort study of middle-aged men and women with hip and/or knee pain.

Methods

The CHECK study

The Cohort Hip and Cohort Knee (CHECK) study is a prospective cohort study of 1002 participants with a 10-year follow-up (inclusion 2002-2005). The study protocol and sample have been described before (23, 24). In brief, individuals were eligible if they 1) had knee and/or hip pain or stiffness, 2) were aged 45-65 years old and 3) were enrolled within 6 months of their first visit to the general practitioner (GP) or had not yet sought care for these complaints. Exclusion criteria were 1) any other pathological condition which could cause hip or knee complaints (e.g. other rheumatic disease, previous hip or knee joint replacement, congenital dysplasia, osteochondritis dissecans, intra-articular fractures, septic arthritis, Perthes' disease, ligament or meniscus damage, plica syndrome, Baker's cyst), 2) any comorbidity precluding physical assessment or follow-up, 3) malignancy in the past five years or 4) the inability to understand the Dutch language. Participants were also recruited through daily newspapers or the Dutch Arthritis Society website. All CHECK participants gave written informed consent and the study was approved by medical ethics committees of all participating hospitals.

For the present study, we used data from the first visit ('baseline'), and included all participants with a complete set of radiographs.

Hip pain

Participants were enrolled if they reported pain and/or stiffness in one or both hips and/or knees. During the baseline examination, participants verbally confirmed (yes/no) in which joints they experienced pain and/or stiffness, and body weight and height were measured to calculate body mass index (BMI). Using questionnaires, we obtained age (years), duration of complaints (months), ethnicity ('white' vs. 'other'), education level ('primary', 'secondary', or 'higher'), presence of morning stiffness (yes/no), any pain medication use (yes/no), pain severity (0-10), and WOMAC pain, function, and stiffness scores (all 0-100).

Radiographic assessment

At baseline, weight-bearing antero-posterior pelvis radiographs of all participants were acquired. Both hips were graded according to the Kellgren and Lawrence (K&L) scale (25). A grade was assigned, ranging from 0-4, based on the presence and severity of osteophytes, joint space narrowing, sclerosis and bone-end deformity, in which 0 suggests no ROA and grade 4 suggests severe ROA. Grading was performed by trained readers and images were read paired and in known sequence order. A detailed description of the scoring approach has been published (26).
We defined our main outcome, definite radiographic hip OA, as K&L≥2. Additionally, we evaluated a

secondary outcome, early-stage radiographic hip OA, defined as K&L≥1. Hips with missing baseline K&L scores were excluded from analyses.

Statistical analyses

We performed the analyses using SPSS Statistics Version 25 (IBM, Armonk NY). We calculated means, corresponding standard deviations (SD) and frequencies for baseline characteristics, including hip pain and ROA prevalence. We evaluated the association between self-reported hip pain (yes/no) and both definite and early-stage hip ROA, using generalized estimating equations (GEE), to account for the two hips included per participant. We did not include any covariates, since we wanted to evaluate whether self-reported hip pain was predictive for hip ROA, not whether ROA was causally related to hip pain. A sample size ≥432 would provide ≥80% power for a relative risk ≥2, for an assumed hip pain prevalence of 10% in hips free of ROA (27).
We then performed post-hoc sensitivity analyses. First, since the difference between sexes remained unclear in prior research, we performed sex-stratified analyses and used the Z-test statistic (28, 29) to test for differences in associations between men and women. Second, we repeated the analyses between self-reported hip pain and ROA in a more strictly defined control group, containing only participants without any self-reported hip pain, and thus excluding pain-free hips with a contralateral painful hip. This was done because having contralateral hip pain might increase the risk of having hip ROA in these pain-free hips. Lastly, since knee pain is associated with hip ROA (17), we repeated analyses (i) only in participants who also reported pain in at least one knee (sensitivity analysis III); and (ii) only in participants who reported no knee pain (sensitivity analysis IV).

Results

Baseline radiographic K&L grades of 11 participants (22 hips, 1.1%) were missing. The baseline characteristics of the remaining 991 participants are shown in **Table 1**. Of the participants, 782 (78.9%) were women, mean age was 55.9 years (SD 5.2) and mean BMI was 26.2 kg/m^2 (SD 4.0). 207 participants reported bilateral hip pain, 375 had unilateral hip pain and 409 reported no hip pain on either side. This resulted in 789 (39.8%) painful hips and 1193 (60.2%) pain-free hips.

Prevalence and association

The overall prevalence of definite hip ROA was 11.0% (95% CI 9.6-12.4%) (**Table 2**). When stratified by pain status, 13.3% (95% CI 10.9-15.7%) of all painful hips and 9.5% (95% CI 7.8-11.2%) of all pain-free hips showed definite hip ROA. The overall prevalence of early-stage hip ROA was 35.3% (95% CI 33.2-37.4%). Pain was prevalent in 41.2% (95% CI 37.8-44.6%) of painful hips and 31.4% (95% CI 28.8-34.0%) of pain-free hips. The OR of painful hips for having definite hip ROA was 1.51 in comparison to pain-free hips (95% CI 1.16-1.98). The OR of painful hips for having early-stage hip ROA was 1.47 (95% CI 1.24-1.75) compared to pain-free hips.

Sensitivity analyses

When stratified by sex, the OR of hip pain for definite hip ROA was 1.74 (95% CI 1.06-2.87) and 1.48 (95% CI 1.06-2.06) for men and women, respectively. For early-stage hip ROA these ORs were 1.78 (95% CI 1.23-2.59) and 1.44 (95% CI 1.18-1.75), respectively. Results did not differ significantly between sexes (**Table S1-S3**). When we excluded pain-free hips with contralateral painful hips, results did not differ. Finally, when including only participants with concurrent knee pain, the ORs of

hip pain for definite and early hip ROA decreased to 1.25 (95% CI 0.91-1.72) and 1.36 (95% CI 1.12-1.66), respectively (**Table 3** and **Table 4**).

Discussion

Summary

In this cross-sectional study, presence of hip pain was associated with both definite and early-stage radiographic hip OA in individuals who had recently or not yet presented to primary care. Nevertheless, the difference in prevalence of definite (13.3 vs 9.5%) and early-stage (41.2 vs 31.4%) hip ROA between painful and pain-free hips was small.

Strengths and limitations

Firstly, all participants were included based on the presence of knee or hip pain in at least one joint, so we did not have a fully pain-free control group. In sensitivity analysis II, we examined the associations with a control group consisting of only participants without any hip pain. This showed only a marginal effect on the ORs, suggesting that hip pain is not associated with a higher likelihood of having hip ROA in the contralateral pain-free hip. However, in a prior study, knee pain was associated with hip ROA (17), which could indicate that our observed association might underestimate the true relation in the population or that the OR of knee pain is simply different from contralateral hip pain.
Secondly, we used radiographic K&L scores in our analyses that were read and scored with images paired and in known sequence (26). This approach is believed to produce more reliable and valid scores than those assigned to a single image with no follow-up images. Using this scoring approach, more hips were assigned K&L≥2 compared to a single radiograph scoring approach (26). In primary care, the single scoring approach might resemble common practice most, since no follow-up radiographs are yet available. As hip ROA might be diagnosed less often using this approach, this suggests that our results may overestimate the associations found in primary care. That said, the purpose of our present study was to understand the association between pain and ROA, and not to predict the prevalence of ROA in a clinical setting in which some cases of ROA might be missed.
Thirdly, it should be noted that we only studied pain prevalence as an exposure for hip ROA. Previous research suggests associations between pain severity and K&L≥2 (30) and between pain duration and joint space narrowing (JSN) (31) as well. Additionally, we only studied K&L grades as outcomes. However, this might differ from the associations between hip pain and individual features of ROA (e.g. JSN). Another limitation is that we performed cross-sectional analyses in this study, which prevents us from evaluating causal associations between pain and ROA. Future studies could evaluate whether the presence of pain predicts future onset or progression of structural OA features.
Lastly, our participants were mainly of white ethnicity. Therefore, the external generalizability of our results might be limited. However, as mentioned, two of the few prior studies are Asian population-based studies and research studying the association in Europe and the white ethnicity are scarce (16, 17). Since the ROA prevalence differed within the Asian and European samples (4, 32-35), the association within the white ethnic population might differ as well and knowledge about this association is important.

Comparison with existing literature

The observed association between pain and definite hip ROA is in contrast with several previous studies (16, 17, 19). Although two Asian population-based studies (16, 17) observed a relation between hip pain and more severe hip ROA (K&L≥3), no association was found between hip pain and definite hip ROA (K&L=2). This might be due to the different definite ROA definitions. Nevertheless, in these studies the painful ROA prevalence was low (n=29, 0.75% (16) and n=26, 0.02% (17)), leading to imprecise results. Moreover, due to cultural and ethnical differences and since the (symptomatic) hip ROA prevalence in Asia is lower than in Europe and the United States, these associations might not be generalizable to the European population (4, 32-35). One European study assessed the association between hip pain and moderate hip ROA (K&L2-3) (19). Although K&L2-3 were combined, hip pain was not associated with hip ROA. Few symptomatic participants (n=56) and only men were included in this analysis.

In the study by Jacobsen et al. (18), hip pain was associated with definite hip ROA. However, data about uni- or bilateral hip pain was missing. The radiographic most affected hips (uni- or bilateral) were selected as painful hips, which might have overestimated the association.

Previous research suggested that the association between hip pain and hip ROA differed between sexes (16, 17). We did not find such difference for definite and early-stage ROA. However, previous research showed that the association differed most in individuals with K&L≥3, which was not analysed in the current study due to the low prevalence of more severe ROA in our participants (0.7%). Also, our sample included predominantly women, which could cause the sex-stratified analyses to be underpowered.

The OA illness (complaints) and disease (structural/radiographic changes) could be seen as two separate entities, since hip pain is not experienced in all hip ROA cases and is present in many cases without hip ROA (19, 35). Due to this structure-symptom discordance, reliable clinical diagnostic criteria to adequately initiate treatment when needed, are important, yet remain unsettled. Recent diagnostic criteria for early-stage hip OA showed ‘poor’ to ‘fair’ diagnostic accuracy (36). The ACR classification criteria were constructed for epidemiologic purposes in secondary care and showed poor reliability in primary care (12, 37). The NICE diagnostic criteria are more applicable in primary care, yet unspecified to hip OA, are primarily based on knee OA studies, and have not been validated (13, 38). When applied to the CHECK cohort, 62.7% of participants with hip complaints would be hip OA diagnosed according to the ACR criteria (39), while according to the NICE criteria all painful hips would be clinically diagnosed with OA. This, while only 13% of painful hips showed definite hip ROA. Due to their diagnostic purpose, the NICE criteria have a high sensitivity, while specificity is low. As a result, hips are diagnosed with OA, while the pain might be associated with another disease, such as low back pain or knee pain (17) based on referred pain or through e.g. central sensitization (40). Hip OA treatments might not be as effective for these hips.

Our sensitivity analyses showed that in hips with concurrent knee pain, the ORs for ROA decreased, for definite ROA even to an insignificant level, while the ORs in hips without concurrent knee pain increased. It is known that knee OA is associated with central sensitization, which could lead to decreased pain thresholds (40, 41). The difference between participants with and without knee pain might indicate the role of central sensitization in patients presenting with multiple painful joints or might have been found since participants with knee pain or OA have an increased risk to have hip OA (17, 42).

Implications for research and practice

Since most painful hips did not have hip ROA and the association between hip pain and ROA was only moderate, radiographs likely do not help us in identifying patients with hip OA in primary care. This is in line with recent diagnostic criteria for early stage hip OA in primary care, where the addition of radiographic variables did not increase diagnostic certainty(36). This suggests that prior guideline recommendations, mostly based on knee OA data, which stated that radiographic evidence was unrequired for the OA diagnosis, apply for hip OA as well (13, 14).

An important question in these patients is whether the absence of radiographic evidence changes the treatment approach for patients who fulfil the clinical criteria for hip OA. Based on our results, we argue that a GP could - without radiographic confirmation of OA - consider these patients as having early OA and initiate appropriate treatments, such as education, exercise and weight loss. Therefore, referral for radiography will not likely change clinical decision making in these patients.

In the CHECK cohort, no hip joint specific pain scores were collected at baseline. Hence, the influence of pain intensity in this association remains unknown. In knee OA pain, intensity was associated with knee ROA (43). Also in knee OA research, the association between pain and ROA strongly differed between cohort-level analyses and within-person analyses (44, 45). In within-person analyses, knee pain was strongly associated with knee ROA. In hip OA, no research has been conducted to examine the association in a within-person design. Lastly, although hip pain is of limited diagnostic value, it might still be of prognostic value for hip ROA. It is unknown whether hip pain is associated with an increased risk of hip ROA development. These uncertainties could be assessed in further research.

In conclusion, in patients recently or not yet presenting in primary care, hip pain was moderately associated with hip ROA and the difference in hip ROA prevalence between painful and pain-free hips was only modest. Therefore, radiographs hardly aid general practitioners in the identification of patients with hip OA. In hips that fulfil the clinical criteria of hip OA, general practitioners should consider to start guideline-recommended conservative OA treatments, without radiographic confirmation.

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Ethical approval
The CHECK study was approved by medical ethics committees of all participating hospitals.

Provenance
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Competing interests
The authors have declared no competing interests.

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Table 1

Baseline characteristics

Characteristic	N= 991 participants
Age, years, mean ±sd	55.9 ± 5.2
Women (%)	782 (78.9%, 95% CI [76.4-81.4])
BMI, kg/m^2, mean ±sd	26.2 ±4.0
White ethnicity (%)	965 (97.5%, 95% CI [96.5-98.5])
Highest level of education (%)	
- Primary	372 (19.3%, 95% CI [16.8-21.8])
- Secondary	874 (45.3%, 95% CI [42.2-48.4])
- Higher	682 (35.4%, 95% CI [32.4-38.4])
Hip pain (%)	
- No pain	409
- Hip pain	582
o Unilateral pain	375
o Bilateral pain	207
Morning stiffness in any hip (%)	343 (35.9%, 95% CI [32.9-38.9])
Knee pain in any knee (%)	821 (82.8%, 95% CI [80.5-85.1])
Duration of complaints, months, mean ±sd	24.6 ±24.2
Standardised WOMAC score, mean ±sd	
- Total (0-100)	24.6 ±16.5
- Pain (0-100)	25.3 ±17.2
- Stiffness (0-100)	33.1 ±21.0
- Function (0-100)	23.5 ±17.2
NRS hip and/or knee pain past week (0-10), mean ±sd	3.6 ±2.1
Using any pain medication (%)	369 (38.0%, 95% CI [35.0-41.0])

BMI= Body Mass Index; WOMAC= Western Ontario and McMaster Universities Osteoarthritis Index, in which 0 corresponds to no complaints; NRS= Numeric Rating Scale, in which 0 corresponds to no pain. CI = confidence interval.

Table 2

K&L grading among all hips and stratified to pain-status

K&L grade	Total (n=1982)	Painful hips (n=789)	Pain-free hips (n=1193)
0	1282 (64.7%)	464 (58.8%)	818 (68.6%)
1	482 (24.3%)	220 (27.9%)	262 (22.0%)
2	205 (10.3%)	95 (12.0%)	110 (9.2%)
3	13 (0.7%)	10 (1.3%)	3 (0.3%)
4	0 (0.0%)	0 (0.0%)	0 (0.0%)
Early-stage ROA ≥1	700 (35.3%) [95% CI 33.2-37.4%]	325 (41.2%) [95% CI 37.8-44.6%]	375 (31.4%) [95% CI 28.8-34.0%]
Definite ROA ≥2	218 (11.0%) [95% CI 9.6-12.4%]	105 (13.3%) [95% CI 10.9-15.7%]	113 (9.5%) [95% CI 7.8-11.2%]

ROA = radiographic hip OA. CI = confidence interval.

Table 3

Association between hip pain and definite radiographic hip OA within sensitivity analyses

Analyses	***Painful hips included***	***Prevalence K&L≥2 in painful hips***	***Pain-free hips included***	***Prevalence K&L≥2 in pain-free hips***	***OR [95% CI]***
Primary analysis	All painful hips	105/789 (13.3%)	All pain-free hips	113/1193 (9.5%)	1.51 [1.16, 1.98]
Sensitivity analysis II	All painful hips	105/789 (13.3%)	Pain-free hips of participants without *any* hip pain	70/818 (8.6%)	1.71 [1.19, 2.46]
Sensitivity analysis III	Painful hips without concurrent knee pain	40/217 (18.4%)	Pain-free hips without concurrent knee pain	11/117 (9.4%)	2.30 [1.26, 4,19]
Sensitivity analysis IV	Painful hips with concurrent knee pain	65/572 (11.4%)	Pain-free hips with concurrent knee pain	102/1076 (9.5%)	1.25 [0.91, 1.72]

Table 4

Association between hip pain and early-stage radiographic hip OA within sensitivity analyses

Analyses	***Painful hips included***	***Prevalence K&L≥1 in painful hips***	***Pain-free hips included***	***Prevalence K&L≥1 in pain-free hips***	***OR [95% CI]***
Primary analysis	All painful hips	325/789 (41.2%)	All pain-free hips	375/1193 (31.4%)	1.47 [1.24, 1.75]
Sensitivity analysis II	All painful hips	325/789 (41.2%)	Pain-free hips of participants without *any* hip pain	239/818 (29.2%)	1.75 [1.37, 2.23]
Sensitivity analysis III	Painful hips without concurrent knee pain	114/217 (52.5%)	Pain-free hips without concurrent knee pain	52/117 (44.4%)	1.49 [1.05, 2.12]
Sensitivity analysis IV	Painful hips with concurrent knee pain	211/572 (36.9%)	Pain-free hips with concurrent knee pain	323/1076 (30.0%)	1.36 [1.12, 1.66]