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Original article

Diagnostic criteria for early hip osteoarthritis: first steps, based on the CHECK study

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Abstract

Objectives. Although there is a general focus on early diagnosis and treatment of hip OA, there are no validated diagnostic criteria for early-stage hip OA. The current study aimed to take the first steps in developing diagnostic criteria for early-stage hip OA, using factors obtained through history taking, physical examination, radiography and blood testing at the first consultation in individuals presenting with hip pain, suspicious for hip OA, in primary care.
Methods. Data of the 543 individuals with 735 symptomatic hips at baseline who had any follow-up data available from the prospective CHECK cohort study were used. A group of 26 clinical experts [general practitioners (GPs), rheumatologists and orthopaedic surgeons] evaluated standardized clinical assessment forms of all subjects on the presence of clinically relevant hip OA 5–10 years after baseline. Using the expert-based diagnoses as reference standard, a backward selection method was used to create predictive models based on pre-defined baseline factors from history taking, physical examination, radiography and blood testing.
Results. Prevalence of clinically relevant hip OA during follow-up was 22%. Created models contained four to eight baseline factors (mainly WOMAC pain items, painful/restricted movements and radiographic features) and obtained area under the curve between 0.62 (0.002) and 0.71 (0.002).
Conclusion. Based on clinical and radiographic features of hip OA obtained at first consultation at a GP for pain/stiffness of the hip, the prediction of clinically relevant hip OA within 5–10 years was 'poor' to 'fair'.

Key words: early diagnosis, hip osteoarthritis, diagnostic criteria, expert diagnosis

CLINICAL SCIENCE

Rheumatology key messages

- There is currently no accepted or validated reference standard for early-stage hip OA.
- Early diagnosis could facilitate early treatment, and structural changes to the joint might still be reversible.
- Questionnaires, physical examination and radiography were limited in identifying subjects who had clinically relevant hip OA within 5–10 years.

Introduction

The lifetime risk for hip OA has been estimated as one in four, with prevalence increasing with age [1, 2]. In theory, like knee OA, diagnosing hip OA earlier in the disease process would allow for targeted treatment options with potentially greater effectiveness, as joint damage is not yet irreversible and pain has not become chronic [3, 4].

Traditionally, hip OA is diagnosed based on radiographic features, like the Kellgren and Lawrence score [5]. Altman and colleagues showed that the combination

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of radiographic and clinical features best discriminated between patients with hip pain due to OA and those with hip pain due to other causes [6]. More recently, a focus on clinical features useful for the diagnosis of hip OA has emerged [7–10], as most individuals with hip OA are treated in primary care where guidelines recommend against the use of radiography for OA diagnosis [11, 12]. Specific clinical signs and symptoms, like limited range of motion (ROM), tenderness in the groin and age over 60 years, predicted the presence of radiographic hip OA in patients with hip pain aged $\geq$50 years and under treatment of a general practitioner (GP) [8]. In other studies among patients in primary care, ROM tests alone were also proven to be diagnostic for the presence of radiographic features of hip OA [7, 9].

Unfortunately, these studies on the use of clinical signs and symptoms for diagnosing hip OA showed lower specificity for diagnosing early or mild OA [8, 9]. This is not surprising, as structural features of hip OA (used as the reference standard in these studies) develop slowly over time and are generally seen as manifestations of late-stage disease [13] and the known discordance between symptoms and structural features on radiography [14]. Therefore, there is currently no accepted or validated reference standard for early-stage hip OA.

The current study used an expert-based diagnosis of clinically relevant hip OA 5–10 years after the first consultation in primary care with pain/stiffness of the hip as the reference standard (future diagnosis). Next, using the expert-based diagnosis as reference standard, we aimed to find possible early-stage diagnostic criteria based on a set of clinical and radiographic factors obtained at first consultation. As the set of predictive factors have been collected at first consultation and the outcome was established 5–10 years later, the criteria should be seen as diagnostic criteria for early-stage hip OA.

Methods

Cohort

For this study, 543 (out of 588) individuals from the CHECK cohort, with 735 symptomatic hips at baseline, had follow-up data available. Characteristics of the CHECK cohort, a nationwide Dutch cohort of patients with hip complaints in primary care, have been described previously [15]. Briefly, individuals were eligible if they had pain or stiffness of the hip, were aged 45–65 years, and had no prior consultation (when recruited via media campaign) or a first consultation with the GP for these symptoms no longer than 6 months before recruitment. Exclusion criteria were: presence of any other clear pathological condition that could explain the existing complaints (assessed through history taking and/or physical examination), co-morbidity that did not allow physical evaluation or follow-up of at least 10 years, malignancy in the past 5 years, and inability to understand the Dutch language. Patients were followed for 10 years at regular intervals.

Baseline measures

All subjects completed the pain and stiffness (Likert) scales of the Western Ontario and McMaster Universities OA Index (WOMAC) questionnaire (not limb or joint specific) [16] and additional questions on demographics, physical activity, comorbidities, smoking status and alcohol consumption. All hips were physically examined to evaluate the presence of pain at passive flexion, internal rotation, external rotation and abduction and passive ROM for flexion, internal rotation, external rotation and abduction, and BMI was determined [15]. Standardized weight-bearing anterior–posterior (AP) and 'faux profil' (FP) oblique view radiographs were centrally graded (matched read with T2, sequence known) for the presence of femoral osteophytes (grades 0–3), for joint space narrowing (JSN) in the medial and superior aspects of the hip joint (grades 0–3), and Kellgren–Lawrence (KL) grading (grades 0–4) [5, 17]. Statistical shape models determined the presence of cam morphology (α-angle $>60^{\circ}$) and hip dysplasia (Wiberg angle $<25^{\circ}$) on each AP radiograph as previously described [18, 19]. Finally, high-sensitivity C-reactive protein (hsCRP) was determined after a vena puncture to establish systemic inflammation.

Follow-up measures

At 5, 8 and 10 years after baseline, the above procedure was repeated, and patients were additionally questioned for the current presence of hip pain (left/right), subluxation, osteochondritis dissecans, intra-articular fractures, bacterial arthritis, Perthes disease, plica syndrome and Baker's cyst.

Expert diagnoses

A group of 24 experts was recruited: 13 GPs and 11 secondary care physicians (six rheumatologists and five orthopaedic surgeons). Before evaluation of the medical records, all experts were queried on the number of years treating OA patients, number of OA patients treated per week, and their personal assessment of the importance of radiography to diagnose OA ('not important', 'little importance', 'some importance', 'very important').

In the first phase, all experts individually evaluated the medical records for 40–50 CHECK participants; of these, seven records were evaluated by all experts. Software was developed in-house to optimally present demographics and all follow-up measures for each individual. First, the clinical data (questionnaires and physical examination) were presented to the experts. For each joint, the expert then answered the question 'Is clinically relevant OA present in this hip?' for each joint (y/n) and provided a certainty of his/her diagnosis, ranging from 1 ('definitely no clinically relevant OA') to 100 ('definitely clinical relevant OA'), entered into the software system.

So as to solely rely on the expertise of the involved experts, no formal definition of 'clinically relevant OA' was provided to the experts.

Next, the radiographic data for the individual were made available: KL grading and the scores for JSN and osteophytes for each joint at each follow-up time point, but also the actual radiographs. Then the question on the diagnosis of OA and its certainty were repeated for each joint. At that time, the clinical data and corresponding OA diagnoses were still available on a read-only basis.

After completion, the second phase assessed agreement within expert pairs; each pair had one GP and one secondary care physician, except one with two GPs. All cases where the expert pair disagreed on the diagnosis were re-evaluated, except those labelled 'uncertain'; this pre-defined label included all cases where experts disagreed, but both with certainty >30 and <70. Re-evaluation comprised a consensus meeting by conference call (with online access to the data). The expert pair followed the same procedure as before, but now with their individual diagnoses and certainty scores made visible. Cases where consensus could still not be reached were also labelled as 'uncertain'.

Statistics

Baseline factors were limited to predefined factors previously described as diagnostic or prognostic for hip OA. These factors were checked for completeness and missing values were replaced through multiple imputation (creating 50 data sets, as 62% of cases had incomplete data, but only six variables had >10% of missing values). Next, categorical factors were dichotomized based on literature and authors' expertise. For WOMAC pain and morning stiffness items, absence of pain/stiffness was defined by merging the 'none' and 'slight' categories. Presence of 'restricted or painful flexion' was defined as maximal hip flexion $\leq 115^\circ$ and/or pain at hip flexion. Presence of 'restricted or painful internal rotation' was defined as maximal hip internal rotation $\leq 15^\circ$ and/or pain at hip internal rotation. Presence of 'restricted or painful external rotation' was defined as maximal hip external rotation $\leq 15^\circ$ and/or pain at hip external rotation. Presence of 'restricted or painful abduction' was defined as maximal hip abduction $\leq 10^\circ$ and/or pain at hip abduction [6, 20]. Osteophytes and JSN were defined present with a grade ≥ 2 (equals 'minimal' or greater). Multicollinearity between factors (variance inflation factor >10) was tested prior to the multivariable regression analyses but was not detected.

To identify early-stage diagnostic factors for the presence of clinically relevant hip OA 5–10 years later, models to predict the expert diagnosis as outcome were created in a stepped approach: first all factors obtained from questionnaires and physical examination were used (model 1). Next, all radiographic factors were added (model 2) and finally hsCRP (model 3). All models applied a backward selection method ($P > 0.1$ for removal). To correct for repeated measures within subjects due to possible bilateral complaints, generalized estimating equations were used. For each model, area under the receiver operating characteristic curve (AUC) was calculated and odds ratio plus 95% CI for each factor within the models was presented.

In sensitivity analyses, continuous measures for age, BMI, duration of complaints and hsCRP were dichotomized. For age and duration of complaints, the upper tertile was compared with the lower two tertiles. BMI was dichotomized using two different cut-offs: <25 *vs* $\geq 25\,kg/m^2$ and <30 *vs* $\geq 30\,kg/m^2$. hsCRP was dichotomized using ≤ 3 mg/l *vs* >3 mg/l [21].

Results

For the 543 selected individuals, mean (S.D.) baseline age was 55.7 (5.2) years, BMI was 26.3 (4.1) kg/m^2, median duration of complaints was 20 months (interquartile range 26), and average WOMAC pain and stiffness (0–100) scores were 27.5 (17.2) and 35.5 (21.0), respectively. Baseline prevalence of the other selected factors, pooled after multiple imputation, are presented in Table 1. Mean baseline concentration for hsCRP was 3.4 (7.9) mg/l.

The experts had 18 (10) years of experience treating OA patients and treated a median of 5 (interquartile range 13) OA patients per week. Prior to evaluating the medical records, most experts deemed radiographs important for the diagnosis (63% somewhat, 17% very important). The remainder (21%) found radiographs to be of minor importance. Both hips of seven individuals were evaluated by all 12 expert pairs (168 diagnoses). There was agreement between expert pairs in 79% of these diagnoses (intra-class correlation coefficient (ICC) 0.682; 95% CI: 0.375, 0.887).

Figure 1 presents the consensus-based diagnosis for all 735 selected hip joints. Based on the clinical plus radiographic assessment, 22% of all hips had clinically relevant OA and in 11% the final diagnosis was uncertain. For optimal contrast, the cases diagnosed without clinically relevant hip OA were compared with the cases diagnosed with clinically relevant hip OA, ignoring the uncertain cases. Several clinical and radiographic baseline features were significantly associated with the diagnosis based on the clinical assessment (Table 2) and that based on the clinical plus radiographic assessment by the experts (Table 3). However, diagnostic accuracy of the models was modest. HsCRP did not end up in any model. Categorizing the continuous variables in the sensitivity analyses did not materially affect the models or their AUC (data not shown).

Discussion

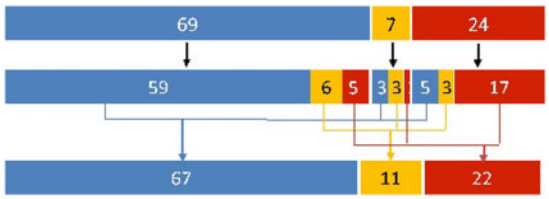
The current study showed that, based on clinical and radiographic features of hip OA obtained at first consultation at a GP for pain/stiffness of the hip, the prediction

TABLE 1 Baseline pooled prevalence for selected factors, presented as percentage of hips with the factor out of 735 hips

Item	Pooled prevalence, %
Questionnaire and physical examination items	
Sex (female)	81
Bilateral pain	52
Painful/restricted flexion[a]	68
Painful/restricted internal rotation[b]	49
Painful/restricted external rotation[c]	37
Painful/restricted abduction[d]	44
WOMAC pain[e]	
Walking	20
Standing	23
Stairs	44
Nigh	38
Rest	32
WOMAC stiffness[e]	
Morning stiffness	50
Radiography items	
Femoral osteophytes[f]	14
Medial JSN[f]	8
Superior JSN[f]	4
CAM morphology[g]	11
Dysplasia[h]	7

[a]Defined as maximal hip flexion $\leq$115° or pain at hip flexion. [b]Maximal hip internal rotation $\leq$15° or pain at hip internal rotation. [c]Maximal hip external rotation $\leq$15° or pain at hip external rotation. [d]Maximal hip abduction $\leq$10° or pain at hip abduction. [e]Presence defined as $\geq$moderate pain/stiffness. [f]Presence defined as $\geq$ minimal. [g]Presence defined as α-angle >60°. [h]Presence defined as Wiberg angle <25°. JSN: joint space narrowing; WOMAC: Western Ontario and McMaster Universities OA Index.

FIG. 1 Percentages for expert diagnoses based on clinical data (upper row), on clinical and radiographic data (middle row) and summed (bottom row)



Blue bars, hips without OA; yellow bars, hips with an uncertain diagnosis; red bars, hips with OA.

of clinically relevant hip OA within 5–10 years was 'poor' to 'fair'.

The expert-based diagnosis of clinically relevant hip OA, used as reference standard, forms both a strength and a weakness of the current study. Given the slow development of structural features of OA, the discordance between signs and symptoms, and the fluctuating nature of OA pain, having clinical experts evaluating individuals' clinical course of signs, symptoms and radiographic features over a 5-year period to establish a diagnosis of clinically relevant hip OA seemed the optimal method to establish a reliable reference standard. With an average of 18 years of experience in treating hip OA patients, the experts seemed well equipped to establish a reliable diagnosis. Of course, the lack of an external validation of the expert-based diagnoses is a limitation to the current study.

Despite the fact that 60% of CHECK participants had radiographic hip OA after 10 years of follow-up, only 16% of CHECK participants fulfilled the clinical ACR criteria for hip OA at that time point [22]. Given the fluctuating nature of OA pain, it is not surprising the prevalence of clinically relevant hip OA during the 5- to 10-year period (22%) was a little higher than prevalence of the clinical ACR criteria at 10 years. Still, the prevalence of clinically relevant hip OA was remarkably lower than the prevalence of radiographic hip OA. This adds to the existing knowledge, mainly coming from knee OA studies [13, 23], that there is mismatch between clinical symptoms and radiographic features of hip OA [14]. Alternatively, one could argue that the experts might have under-diagnosed the presence of clinically relevant hip OA. However, if we also consider the 'uncertain cases' to be cases of hip OA, still the prevalence will only be 33%, which remains lower than the prevalence of radiographic hip OA within this cohort.

The obtained models did not perform as well as expected in separating individuals that developed clinically relevant hip OA within 5–10 years from those who did not, even though all previously identified factors of relevance for diagnosing hip OA (e.g. ROM, duration of symptoms, pain characteristics [7–9]) and factors

predictive for hip OA development (e.g. BMI, female sex, morning stiffness, painful/restricted ROM, dysplasia, CAM deformities [18, 19, 24, 25]) were incorporated in the analyses. Similar methods did result in a 'fair' to 'good' prediction of clinically relevant knee OA [26]. Possibly, incorporating the 2-year course of hip symptoms after the first consultation into the models can increase the discriminatory abilities. Also, choosing stricter cut-off scores for the predictive factors, e.g. $\leq 20^{\circ}$ to define the presence of dysplasia or $\geq$severe pain for the presence of pain, could improve the AUC values. However, this will lower the number of individuals that will meet these criteria and hence limit the clinical applicability. A recent systematic review identified abductor weakness and pain when squatting as factors with potential diagnostic value (high specificity, low sensitivity), but these were not incorporated in the current study [10].

Previous studies did show that factors like limited ROM (either in a single plane or in multiple planes) [7, 9] or a combination of factors from history taking and physical examination [8, 10] did have acceptable to good diagnostic abilities for diagnosing hip OA. As indicated, all these factors were incorporated in the current study, but only resulted in 'poor' to 'fair' diagnosis. Three factors likely contributed to this discrepancy: (i) the outcome measure/reference standard, (ii) handling of the predictors, and (iii) the study design. Previous studies using clinical features to diagnose hip OA all used radiographic features of hip OA as a reference standard [7–10]. Apparently, it is easier to predict the presence of radiographic features of hip OA based on clinical features than the presence of clinically relevant hip OA, which will be strongly influenced by the presence of pain and functional limitations. In contrast to some of the previous studies, predictive factors based on ROM were dichotomized in the present study. Despite the potential loss of statistical power, the clinical feasibility of a dichotomous factor was deemed of greater importance. Finally, the indicated studies all had a cross-sectional design [7–9]. In the present study, we intended to create criteria to diagnose early-stage hip OA. As there is no validated reference standard for early-stage hip OA, the best available option is to relate potential diagnostic factors to a relevant outcome in the future. Intuitively, a period of 5–10 years between the assessment of potential diagnostic factors and the establishment of the reference standard will reduce the strength of their association compared with a cross-sectional assessment of both factors.

Table 2 Obtained models for developing clinically relevant hip OA after 5–10 years based on the evaluation of clinical data only

Item	Odds ratio (95% CI)
Questionnaire and physical examination items	
WOMAC pain—walking	0.57 (0.33, 0.98)
WOMAC pain—climbing stairs	2.44 (1.57, 3.80)
WOMAC pain—night	2.23 (1.36, 3.65)
WOMAC pain—rest	0.58 (0.35, 0.98)
Painful/restricted flexion	1.73 (1.12, 2.68)
Painful/restricted abduction	1.72 (1.14, 2.60)
Pooled AUC (pooled S.D.)	0.698 (0.007)
Questionnaire, physical examination and radiographic items	
WOMAC pain—walking	0.62 (0.36, 1.07)
WOMAC pain—climbing stairs	2.43 (1.55, 3.80)
WOMAC pain—night	2.24 (1.37, 3.65)
WOMAC pain—rest	0.56 (0.33, 0.94)
Painful/restricted flexion	1.76 (1.13, 2.74)
Painful/restricted abduction	1.81 (1.19, 2.74)
Femoral osteophytes	1.70 (1.03, 2.80)
JSN superior	0.29 (0.09, 0.94)
Pooled AUC (pooled S.D.)	0.714 (0.007)

AUC: area under the curve; JSN: joint space narrowing; WOMAC: Western Ontario and McMaster Universities OA Index.

Table 3 Obtained models for developing clinically relevant hip OA after 5–10 years based on the evaluation of clinical and radiographic data

Item	Odds ratio (95% CI)
Questionnaire and physical examination items	
WOMAC pain—standing	1.63 (0.98, 2.72)
WOMAC pain—night	1.56 (0.97, 2.50)
WOMAC pain—rest	0.59 (0.35, 1.01)
Painful/restricted flexion	1.79 (1.11, 2.88)
Age	1.03 (1.00, 1.07)
Bilateral complaints	0.64 (0.41, 0.98)
Pooled AUC (pooled S.D.)	0.620 (0.002)
Questionnaire, physical examination and radiographic items	
Painful/restricted flexion	1.70 (1.04, 2.77)
Painful/restricted internal rotation	1.38 (0.94, 2.03)
Bilateral complaints	0.66 (0.43, 1.01)
Femoral osteophytes	2.20 (1.50, 3.22)
Pooled AUC (pooled S.D.)	0.626 (0.010)

AUC: area under the curve; JSN: joint space narrowing; WOMAC: Western Ontario and McMaster Universities OA Index.

From the presented models in Tables 2 and 3, it is notable that some associations were counterintuitive. For example, the presence of pain at rest or superior JSN was associated with reduced odds for having clinically relevant hip OA after 5–10 years. However, one must keep in mind that these are factors within a multivariable model; the presented associations are only true when adjusted for the other factors in the model. This is illustrated by the non-significant associations of pain at rest, pain when walking and superior JSN with the presence of clinically relevant hip OA when tested univariately (i.e. single factor models; data not shown).

In conclusion, features obtained through history taking, physical examination, radiography and blood testing at the first consultation in individuals presenting with hip pain, suggestive for early-stage hip OA, in primary care predicted the presence of clinically relevant hip OA within 5–10 years only marginally. Additional factors need to be identified to come to acceptable diagnostic criteria for early-stage hip OA in primary care.

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Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

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