

ORIGINAL RESEARCH

Two-year clinical follow-up enhances the diagnosis of early-stage hip osteoarthritis: data from check cohort

Jos Runhaar ¹, Ömer Özbulut,¹ Margreet Kloppenburg,² Maarten Boers ³, Johannes W J Bijlsma,⁴ Sita Bierma-Zeinstra,^{1,5} CREDO expert group

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¹Department of General Practice, Erasmus MC University Medical Center Rotterdam, Rotterdam, Netherlands

²Department of Rheumatology, LUMC, Leiden, Netherlands

³Department of Epidemiology & Data Science, Amsterdam UMC Locatie VUmc, Amsterdam, Netherlands

⁴Department of Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands

⁵Department of Orthopaedics & Sports Medicine, Erasmus MC University Medical Center Rotterdam, Rotterdam, Netherlands

Correspondence to

Dr Jos Runhaar;
j.runhaar@erasmusmc.nl

ABSTRACT

Objective To provide a set of diagnostic criteria for early-stage hip osteoarthritis (OA) in primary care, using signs and symptoms monitored over 2 years in individuals with hip pain and/or stiffness. Additionally, the study aimed to see whether these factors were additive to factors based on baseline signs and symptoms only.

Methods Data of the 543 persons with 735 symptomatic hips were collected from the prospective Cohort Hip and Cohort Knee cohort study. Using data from 5 to 10 years of follow-up, 24 experts (13 general practitioners, 11 secondary care physicians (6 rheumatologists and 5 orthopaedic surgeons)) inspected individuals' medical data on the presence of clinically relevant hip OA. Their diagnoses are used as reference standards. Backward selection method was used to provide models using the factors from baseline to 2 years of follow-up. Additionally, new models were combined with previously published models, using same selection method. Area under the curve (AUC) was calculated after each removal of factors in the final combined models.

Results Radiographic factors and high-sensitive C reactive protein did not end up in any model with change factors only. AUC value (SD) of the final obtained model of change factors was 0.70 (0.01). Adding newly defined factors to previously published models significantly ($p < 0.0001$) increased the AUC value to 0.75 (0.01).

Conclusion Final diagnostic criteria, consisting only of the factors obtained through history taking and physical examination, were able to detect early-stage hip OA associated with clinically relevant hip OA 5–10 years later, with 'moderate' precision.

INTRODUCTION

Hip osteoarthritis (OA) has a huge burden on patients, healthcare systems and society¹ and has a globally increasing prevalence.^{2,3} Many of the hip OA patients are treated in primary care.⁴ General practitioners (GPs) diagnose hip OA according to their personal clinical expertise and preferences,⁵ as there are no accepted and accurate diagnostic criteria in primary care.

As the best impact of key treatment on symptoms and disease course is expected to

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Existing classification criteria for hip osteoarthritis (OA) are known to identify patient with late-stage disease only.
- ⇒ To enable early treatment and the potential to halt the progression of the disease in this 'window of opportunity', early diagnosis is essential.
- ⇒ Previously, diagnostic criteria for early-stage hip OA based on criteria obtained at initial presentation with hip symptoms in primary care showed poor to fair performance.

WHAT THIS STUDY ADDS

- ⇒ The current study improved the existing diagnostic criteria by evaluating the additional value of factor obtained over the first 2 years after the initial presentation.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ The outcome of the current study can help clinicians to diagnose hip OA in an early stage of the disease.

be achieved in the early phase, developing diagnostic criteria for early-stage hip OA is essential.⁶ Since patients first come to primary care with their early signs and symptoms, it is needed to have validated early-stage hip OA diagnostic criteria in primary care. This would enable patient education and treatment in an early phase of the disease.

Clinical classification criteria for hip OA, such as the American College of Rheumatology (ACR),⁷ have shown not to be valid for diagnosing hip OA in primary care.⁵ Several radiographic classifications exist for diagnoses based on structural features of hip OA, such as Croft's grade,⁸ Kellgren and Lawrence (KL) criteria⁹ or Osteoarthritis Research Society International (OARSI)¹⁰ scores. However, most patients with early-stage OA have normal radiographs.¹¹

Table 1 Pooled percentages for selected factors' course over 2 years of follow-up

Pooled percentages			
Questionnaire and physical examination			
	Change <5%	Increase ≥5%	Decrease ≥5%
BMI	75	12	13
Absent			
	Present at either time point	Present at both time point	
Painful/restricted:			
Flexion*	14	32	54
Internal rotation†	40	39	21
External rotation‡	45	38	17
Abduction§	44	30	26
	Stable††	Increase††	Decrease††
WOMAC pain¶			
Walking	48	27	25
Standing	45	29	26
Stairs	44	28	28
Night	37	26	37
Rest	45	25	30
WOMAC stiffness¶			
Morning stiffness	43	24	33
Radiography items	Stable††	Increase††	
Femoral osteophytes**	74	26	
Medial JSN**	86	14	
Superior JSN**	90	10	

*Defined as maximal hip flexion ≤115° or pain at hip flexion.
†Maximal hip internal rotation ≤15° or pain at hip internal rotation.
‡Maximal hip external rotation ≤15° or pain at hip external rotation.
§Maximal hip abduction ≤10° or pain at hip abduction.
¶Presence defined as ≥moderate pain/stiffness.
**Presence defined as ≥ 'minimal'.
††For the WOMAC and radiography items, increase corresponds to 'worsening' and decrease corresponds to 'improvement'. For the radiography items, stable category also includes decrease category
BMI, body mass index; JSN, Joint space narrowing; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

To obtain diagnostic criteria for early-stage hip OA in primary care, we initiated the CREDO project (Criteria for the Early Diagnosis of Osteoarthritis). This project used data from the CHECK (Cohort Hip and Cohort Knee) study.¹² Runhaar *et al* described diagnostic models for early-stage hip OA using baseline characteristics, with 'poor' to 'fair' performance.¹³ These models included individual Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain questions, painful/restricted range of motion of the hip joint and radiographic features of hip OA. As some symptoms related to hip OA fluctuate or emerge over time,¹⁴ monitoring over time could provide better guidance for the diagnosis of hip OA. We designed the present study to establish a set of diagnostic criteria for hip OA to predict clinically relevant established OA 10 years later, using symptoms and signs monitored from baseline to 2 years of follow-up. It was also aimed to see whether newly defined factors

were additive to the previously published criteria based on baseline symptoms and signs only.

PATIENTS AND METHODS

Cohort

Clinical and radiographic data of the 543 persons with 735 symptomatic hips at baseline who had any follow-up data available were selected from the CHECK cohort. The CHECK cohort is a prospective cohort study of individuals consulting their GP with hip and/or knee complaints suggestive of early OA, followed at regular intervals for 10 years. The inclusion criteria of the CHECK cohort were non-traumatic hip pain or stiffness, aged 45–65 years, no former consultation or the first consultation for these symptoms within the last 6 months before enrolment. Subjects were excluded if the existing complaints could be clearly explained by other pathologies, presence of

Table 2 Diagnostic models of change factors for developing clinically relevant hip OA after 5–10 years

OR 95% CI		
Questionnaire, physical examination, radiography items and hsCRP; outcome based on the evaluation of clinical data only		
WOMAC morning stiffness increase	1.53	0.94 to 2.49
WOMAC pain—rest increase	1.52	0.95 to 2.42
Painful/restricted flexion at both time points	1.60	1.08 to 2.37
Painful/restricted abduction at both time points	3.04	1.82 to 5.08
Painful/restricted abduction present once	2.04	1.26 to 3.30
Pooled AUC (±pooled SD)	0.70±0.01	
Questionnaire, physical examination, radiography items and hsCRP; outcome based on the evaluation of clinical and radiographic data		
WOMAC pain—stairs decrease	1.75	1.05 to 2.91
WOMAC morning stiffness increase	1.63	1.01 to 2.63
Painful/restricted flexion at both time points	1.61	1.13 to 2.28
Painful/restricted abduction at both time points	1.69	1.09 to 2.62
Pooled AUC (±pooled SD)	0.66±0.01	
.AUC, area under the curve; hsCRP, high-sensitive C reactive protein; OA, osteoarthritis; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.		

comorbidity which did not allow physical examination or follow-up throughout the study, malignancy in the last 5 years and lack of understanding Dutch.¹²

Baseline and second year measures

At baseline, body mass index (BMI) was determined and both hips were examined for painful or restricted function (flexion, internal rotation, external rotation, abduction). Subjects completed the WOMAC questionnaire¹⁵ and questions to state age, sex and duration of complaints. Standardised radiographs (anterior–posterior view) were taken and were centrally graded for the existence of femoral osteophytes (grades 0–3), for medial and superior joint space narrowing (JSN) (grades 0–3). The presence of CAM morphology (alpha angle >60°) and dysplasia (Wiberg angle <25°) was determined.^{16, 17} Finally, blood high-sensitive C reactive protein (hsCRP) was determined. Procedures were repeated after 2 years (T2), except for demographics, duration of complaints, dysplasia, CAM and hsCRP.

Follow-up measures

At 5, 8 and 10 years, patients were again assessed for all clinical and radiographic features. Clinical features

Table 3 Combined diagnostic models with published factors (labelled as ‘baseline’) and newly identified change factors for the presence of clinically relevant hip OA after 5–10 years

OR 95% CI		
Questionnaire, physical examination, radiography items and hsCRP; outcome based on the evaluation of clinical data only		
WOMAC morning stiffness increase	1.95	1.17 to 3.24
WOMAC pain—rest increase	1.98	1.19 to 3.29
Painful/restricted flexion at both time points	2.36	1.16 to 4.79
Painful/restricted flexion Present once	1.91	0.94 to 3.88
Painful/restricted abduction at both time points	2.48	1.43 to 4.29
Painful/restricted abduction present once	1.91	1.15 to 3.20
Absence of WOMAC pain—walking (baseline)	1.97	1.12 to 3.48
WOMAC pain—stairs (baseline)	2.41	1.53 to 3.80
WOMAC pain—night (baseline)	2.14	1.34 to 3.43
Superior JSN (baseline)	2.40	0.94 to 6.13
Pooled AUC (± pooled SD)	0.75±0.01	
Questionnaire, physical examination, radiography items and hsCRP; outcome based on the evaluation of clinical and radiographic data		
WOMAC pain—stairs decrease	1.66	0.98 to 2.80
WOMAC morning stiffness increase	1.64	1.00 to 2.71
Painful/restricted flexion at both time points	1.64	1.15 to 2.35
Painful/restricted external rotation (baseline)	1.44	1.01 to 2.08
Unilaterality (baseline)	1.55	1.01 to 2.38
Pooled AUC (±pooled SD)	0.66±0.01	
.AUC, area under the curve; hsCRP, high-sensitive C reactive protein; JSN, joint space narrowing; OA, osteoarthritis; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.		

comprised BMI, WOMAC scores, the presence of hip pain, hip morning stiffness, pain at internal rotation, external rotation, flexion and abduction, range of motion (internal rotation, external rotation, flexion and abduction) and self-reported presence of other disease (subluxation, osteochondritis dissecans, intra-articular fracture, septic arthritis, Perthes disease, Plica syndrome and Baker’s cyst). Radiographic features comprised KL grade, femoral and acetabular osteophytes, JSN, acetabular cyst, femoral head flattening and femoral neck buttressing, as scored by qualified readers assessing standardised anterior–posterior and faux profile oblique view hip radiographs.¹⁸

Expert diagnoses

Follow-up data from 5, 8 and 10 years were used to establish a clinical expert-based diagnosis of OA, as was done in the study aiming to establish diagnostic criteria based on baseline factors only.¹³ 24 experts (13 GPs, 11 secondary care physicians (6 rheumatologists and 5 orthopaedic surgeons), all with a completed training as specialist or in-training for such, but with a PhD in OA research, and all currently treating patients with OA in their clinical practice, were recruited and divided into 12 pairs. Each pair consists of one GP and one secondary care physician, except one pair of two GPs.^{13 19 20} Experts within the same team independently inspected the same subjects' medical documents, using in-house developed software. First, experts were presented with the clinical data only. Experts were inquired to decide whether 'clinically relevant OA' was present for each joint during follow-up and provided a certainty score of their diagnosis, ranging from 1 to 100 (1 indicated 'definitely no OA' and 100 indicated 'definitely OA'). Next, experts were enabled to evaluate the radiographic data and asked to provide new diagnoses and new certainty scores. All hips with agreement among the experts (ie, diagnosed as yes/no clinically relevant hip OA by both experts) were labelled as such. All other hips on which experts had opposed diagnoses, except those marked as 'uncertain' (predefined as opposed diagnoses, but with both certainty scores >30 and <70), were reassessed in a consensus meeting using identical procedures.

Statistics

Diagnostic models were created with the change in clinical and radiographic factors from baseline to T2 as determinants and the consensus-based final expert diagnoses as outcome. Multiple imputation procedure handled missing data in the predictors. Changes in predictors from baseline to T2 were calculated and categorised as follows: change in BMI as ≥ 5 unit decrease, less than 5 units change and ≥ 5 unit increase (person level); selected WOMAC items as decrease of one grade or more, stable or increase of one grade of more (person level); change in osteophyte and JSN as stable or increase of one grade or more (joint level); the change of painful and/or restricted rotations as absent at both time points, present at either time point and present at both time points (joint level). First, all factors obtained from questionnaires and physical examination were used to derive the diagnostic model (model 1). Backward selection method ($p > 0.1$ for removal) with generalised estimating equations was used, to correct for repeated measures within subjects due to possible bilateral complaints. In the case of bilateral complaints, person-level measures were assigned identically to both joints. For model 2, the change in radiographic factors was added to the clinical factors and finally (model 3) baseline hsCRP was added. Expert diagnoses after evaluating clinical data only and after clinical plus radiographic data were used as separate outcomes. The area under the receiver operating

curve (AUC) was calculated for each model and OR's plus 95% CIs for each factor within the models were presented.

As the factors obtained through these methods might be additive to the previously published factors from models based on baseline factors only,¹³ new models combining previously published models and currently newly identified factors were created, using identical selection methods as described above. To assess stepwise contribution of significant factors in the final combined models, the backward selection method was continued and after each removal, AUC was calculated.

Patient and public involvement

Two patients were members of the Steering Committee of CHECK and therewith actively involved in designing and conducting the study. Results from the CREDO cohort will be disseminated to OA patients through the Patient Platform initiated and managed by the Department of General Practice of Erasmus MC (www.artrosegezond.nl).

RESULTS

The study sample comprised 81% of women, with mean (SD) age at baseline 56⁵ years, BMI 26.3 (4.1) kg/m² and median duration of complaints 20 months (IQR 26). Of 735 hips, 178 (24%) and 162 (22%) were diagnosed with clinically relevant hip OA based on the evaluation of clinical data only and clinical plus radiographic data, respectively. [Table 1](#) shows the categorisation of the predicting factors.

From all factors presented in [table 1](#), factors ending up in the predictive models are presented in [table 2](#). Radiographic factors and hsCRP did not end up in any model. Predictive ability of the final obtained models using the evaluation of the clinical data only or using the clinical plus radiographic data as outcome were very similar, with AUC values (SD) of 0.70 (0.01) and 0.66 (0.01), respectively.

Previously published models based on baseline factors resulted in AUC values (SD) of 0.71 (0.01).¹³ Adding change factors significantly ($p < 0.0001$) increased the AUC value to 0.75 (0.01) using the outcome based on clinical data only ([table 3](#)). Using the outcome based on clinical plus radiographic data, the combined model resulted in AUC values of 0.66 (0.01), which was not significantly different from the baseline factors-only model (see online supplemental table 1).

Stepwise contribution of factors in the combined models are presented in online supplemental figures 1 and 2.

For optimal contrast, hips that were diagnosed as 'uncertain' were excluded in all analyses above. If the uncertain cases were defined either as OA cases or non-OA cases, the predictive ability of all models was only affected minimally (see online supplemental table 2).

DISCUSSION

Based on the change of clinical factors during 2 years after the first consultation, we were able to create diagnostic criteria which were able, with 'moderate' precision, to detect early-stage hip OA, associated with clinically relevant hip OA 5–10 years later, among 45–65 aged individuals in primary care with hip symptoms suggestive for hip OA. Change factors were also statistically additive to previously published models of baseline factors only, by increasing AUC from a value of 0.71–0.75. Only factors obtained through history taking and physical examination during the first 2 years after the first consultation were predictive for clinically relevant hip OA. Most likely, this is because clinical factors change much more than radiographic features in 2 years. Our results emphasise the importance of repeated history taking and physical examination to diagnose hip OA in an early disease stage.

Current non-surgical treatment strategies for hip OA focus on relieving symptoms; there is no approved disease-modifying treatment.²¹ Therefore, diagnosing patients at an early stage and starting key treatment, such as education and exercise seems crucial.²¹ This study provided the unique and essential diagnostic criteria for early-stage hip OA in primary care, with most of the predictors available through low cost physical examination and history taking. Moreover, Kim *et al* also stated that early-stage hip OA is frequently missed if clinicians solely rely on radiographs.²² Second, all of our patients in the current study were recruited at or prior to their first consultation in primary care, the relevant population to diagnose early-stage hip OA. This will overcome the problem that currently available criteria, like the in secondary care developed ACR criteria, were shown not to be valid in primary care.⁵

Prior to considering the implementation of current diagnostic models, external validation is required. Moreover, acceptance and willingness of early diagnosis of hip OA among potential patients and caregivers is essential to ascertain uptake in clinical practice. With GPs under-diagnosing hip OA by $\pm 100\%$, through labelling many patients as 'hip pain' rather than 'hip OA',²³ education of GPs on the importance of early diagnosis of hip OA seems essential. This education should also include recommendations on the usage of terminology, as diagnostic labels (eg, 'hip degeneration', 'persistent hip pain' and 'hip osteoarthritis') can influence the attitude and beliefs of patients towards conservative interventions, the perception that surgery is the recommended treatment option, and their worries about their condition.²⁴ Of course, whether these findings also hold true for diagnostic labels in early diagnosis of hip OA is to be determined.

Our study has some limitations. First, we cannot determine the validity of the expert diagnosis. However, having an expert-based diagnosis is also unique side of the CREDO study. Furthermore, the uncertain cases were excluded from the main analyses; the effect of uncertain cases on the predictive ability of diagnostic model was very small (see online supplemental table 2). Although

the newly defined change factors were statistically additive to previously defined baseline factors, it is hard to make a firm conclusion on whether the increase in AUC values was clinically relevant. Given the applicability of measurements and the low cost, the update to our diagnostic criteria seems worthwhile and promising. Finally, the female dominance in the current cohort might represent clinical practice, it does lead to the uncertainty of generalisability of current results towards men.

In conclusion, the current study updates our diagnostic criteria for the diagnosis of early-stage hip OA in primary care with items obtained through 2-year follow-up. Further external validation in other datasets is required.

X Jos Runhaar @JosRunhaar

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Data availability statement Data are available in a public, open access repository. Data are available on reasonable request. Data from the CHECK study are publicly available through <https://dans.knaw.nl/en/>.

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ORCID iDs

Jos Runhaar <http://orcid.org/0000-0002-6293-6707>

Maarten Boers <http://orcid.org/0000-0002-6969-283X>

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