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# Acetabular dysplasia and the risk of developing hip osteoarthritis at 2,5,8, and 10 years follow-up in a prospective nationwide cohort study (CHECK).

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# ABSTRACT

*Objective:* To assess the relationship between acetabular dysplasia (AD) and the risk of incident and end-stage radiographic hip osteoarthritis (RHOA) over 2,5,8 and 10 years. *Design:* Individuals (n = 1002) aged between 45 and 65 from the prospective Cohort Hip and Cohort Knee

(CHECK) were studied. Anteroposterior pelvic radiographs were obtained at baseline and 2,5,8, and 10-years follow-up. False profile radiographs were obtained at baseline. AD was defined as a lateral center edge angle, an anterior center edge angle, or both  $<25^{\circ}$  at baseline. The risk of developing RHOA was determined at each follow-up moment. Incident RHOA was defined by Kellgren & Lawrence (KL) grade  $\geq$ 2 or total hip replacement (THR), end-stage RHOA by a KL grade  $\geq$ 3 or THR. Associations were expressed in odds ratios (OR) using logistic regression with generalized estimating equations.

*Results:* AD was associated with the development of incident RHOA at 2 years follow-up (OR 2.46, 95% CI 1.00–6.04), 5 years follow-up (OR 2.28, 95% CI 1.20–4.31), and 8 years follow-up (OR 1.86, 95%CI 1.22–2.83). AD was only associated with end-stage RHOA at 5 years follow-up (OR 3.75, 95% CI 1.02–13.77). No statistically significant associations were observed between AD and RHOA at 10-years follow-up.

*Conclusion:* Baseline AD in individuals between 45 and 65 years is associated with an increased risk of developing RHOA within 2- and 5 years. However, this association seems to weaken after 8 years and disappears after 10 years.

## Introduction

Hip osteoarthritis (OA) is a leading cause of poor quality of life [1–8]. Therefore, modifiable risk factors must be identified to allow for preventative measures [9,10]. Risk factors previously identified include age, genetics, trauma, physical workload, and bone morphology [5,8, 11–14]. Acetabular dysplasia (AD) was among the bone shapes with the highest risk for the development of radiographic hip osteoarthritis (RHOA) in prospective studies (pooled OR= 2.38 95% CI 1.84–3.07) [5].

In hips with AD, the under-coverage of the acetabulum relative to the femoral head leads to concentrated focal stress and increases joint load. Increased joint loading may result in premature cartilage deficiency, increased stress on surrounding soft tissues, and ultimately cause hip OA

# [6].

There are several measurements to quantify acetabular coverage of the femoral head. The lateral center edge angle (LCEA) is measured on anteroposterior (AP) pelvic radiographs and quantifies lateral coverage of the femoral head by the acetabulum. The anterior center edge angle (ACEA) is measured on false profile (FP) radiographs and quantifies anterior coverage. Although the LCEA is most commonly used to quantify AD, a recent study demonstrated that only considering the LCEA may lead to over 40% of missed AD cases [15]. To our knowledge, this is the first study of its kind to also include anterior coverage.

A recent meta-analysis of prospective studies found a pooled odds ratio (OR) of 2.2 in hips with AD to develop RHOA, these results however, were heterogeneous [5]. The reported associations in other studies

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Abbreviations: RHOA, Radiographic hip osteoarthritis; AD, Acetabular Dysplasia; LCEA, Lateral center edge angle; ACEA, Anterior center edge angle.

on AD differed, where studies with a long follow-up period seemed to find weaker or no associations between AD and RHOA development [9, 16]. Available prospective studies had a follow-up period between 6 and 22 years but did not analyze multiple follow-up moments within the study population [9]. It is presently unknown how the risk for incident RHOA in the presence of AD varies for different follow-up times.

We aim to determine the relationship between anterior and lateral AD at baseline and the risk of developing RHOA at 2,5,8, and 10 years follow-up.

# Methods

# Study design and participants

All participants were drawn from the Cohort Hip and Cohort Knee (CHECK). CHECK is a prospective, nationwide cohort of 1002 participants (2004 hips) aged 45-65 (mean 55.9 years) at baseline that reported the first onset of pain in either the hip or knee. Participants were recruited by advertisement and referral from general practitioners (GP). Inclusion criteria were; pain or stiffness in the knee or hip and no earlier consultation or a first consultation with a GP within 6 six months for these complaints before entry. Participants were excluded if they had a prior history of hip OA or any other pathological condition that may explain their hip or knee pain. For the hip joints, this includes rheumatic disease, previous hip joint replacement, intra-articular fractures, congenital dysplasia, osteochondritis dissecans, bursitis, septic arthritis, or Perthes' disease [17,18]. It should be noted that included individuals in the CHECK cohort represent a mild form of AD, based on abovementioned criteria, as individuals with a known diagnosis of congenital dysplasia were excluded. Participants were also excluded if it was impossible to perform a physical examination due to comorbidity, if they did not understand the Dutch language, or if malignancy had been present in the past 5 years. We included all hips with AP pelvic radiographs at baseline for the current study. The CHECK cohort initially started obtaining AP hip radiographs from the first included participants but switched to AP pelvic radiographs. Hips with AP hip radiographs were excluded as it was not possible to construct the LCEA reliably. Among the selected hips, we included hips without definite signs of RHOA at baseline (Kellgren & Lawrence (KL) grade = 0 or 1). Finally, we selected all hips with available KL grading at follow-up (Fig. 1). In case variables such as biological sex, BMI, or age were not recorded at baseline but were recorded at follow-up, these measures were used. Written informed consent was obtained from all participants, and the study was approved by the medical ethical committee of each hospital.

# Radiographs

AP pelvic radiographs were obtained at baseline and 2,5,8 and 10 years follow-up, and FP hip radiographs were obtained at baseline according to a standardized protocol that has previously been published [19]. In short, AP radiographs were obtained in a standing position by placing the participant's feet in  $15^{\circ}$  internal rotation. In addition, it was required for the AP radiograph to depict both obturator rings, femoral necks, and a symmetrical pelvis [20].

The weight-bearing FP radiographs were made by rotating the pelvis  $65^{\circ}$  relative to the radiographic table. The rotation was ensured by placing a  $65^{\circ}$  wedge between the patient's back and the table [21,22]

# Radiographic measurements

The osseous outline of the proximal femur and acetabulum were drawn on AP and FP radiographs with a point set using statistical shape modeling (SSM) software (ASM tool kit, Manchester University, UK). This point set was used to automize measurements of the LCEA and the ACEA using a Matlab script (V.7.10) [23].

The degrees of coverage of the femoral head by the acetabulum are



Fig. 1. Flow of hips from CHECK cohort inclusion to the final study population at 2 (T2), 5 (T5), 8 (T8), and 10-years (T10) follow-up.

measured by the center edge angle. A best-fitting circle is outlined around the femoral head based on the SSM points to determine the center of the femoral head. From this center, a line is drawn vertically, and a second line is drawn to the most lateral part of the acetabulum—the angle which can be constructed from these two lines in the center edge angle. To construct the LCEA on the AP radiograph, the vertical line is drawn perpendicular to the horizontal reference line connecting both femoral heads (Fig. 2). To construct the ACEA on the FP radiograph, the vertical line is drawn perpendicular to the horizontal line of the radiographic film (Fig. 3) [24,25]. AD was defined as an LCEA, an ACEA, or both of  $<25^{\circ}$  at baseline.

### Reliability measurement of angles

The reliability of measurements in the CHECK cohort has previously been published [26]. The intraclass correlation coefficients (ICC) of the three observers who annotated the point set for inter-observer reliability were 0.97 (95% CI 0.94–0.99) for the LCEA and 0.99 (95% CI 0.97–0.99) for the ACEA [26]. ICC scores for intra-observer reliability ranged from 0.91 to 0.96 for the LCEA and from 0.97 to 0.99 for the ACEA [26].

#### Outcome measures

The KL radiographic classification was used to grade all AP radiographs at baseline, 2,5,8, and at 10 years follow-up [27,28]. Each participant's radiographs of all time points were scored simultaneously, so that information on all available images was used for the KL scoring at each time point. Disclosing all available images is more reliable than scoring a single radiographic image [28]. Incident RHOA was defined by a KL grade  $\geq 2$  or total hip replacement (THR) at each follow-up moment. End-stage RHOA was defined by a KL grade  $\geq 3$  or THR at each follow-up moment.

### Statistical analysis

All statistical analyses were performed in SPSS version 28.0. Univariate baseline differences between included and excluded hips were determined by the independent sample's T-test for age, body mass index (BMI), body height, and body weight and by the chi-square test for biological sex. The association between baseline AD and the development of RHOA was determined using logistic regression with generalized estimating equations (GEE), adjusted for baseline age, biological sex, BMI, and repeated measures within persons, expressed in odds ratios (ORs) with 95% confidence intervals (95% CI).



Fig. 2. The lateral center edge angle (LCEA) is measured on an AP pelvic radiograph. The white line represents the best fitted circle around the femoral head. The green line represents the horizontal reference line. The blue lines represent the measurement of lateral acetabular coverage (LCEA). AD was defined as an LCEA<25°



Fig. 3. The anterior center edge angle (ACEA) is measured on an FP radiograph. The white line represents the best fitted circle around the femoral head. The blue lines represent the measurement of anterior acetabular coverage (ACEA). AD was defined as an ACEA<25°

# Results

# Participants

1253 hips were included for analysis at 2 years follow-up, 1262 hips at 5 years follow-up, 1188 hips at 8-years follow-up, and 1169 hips at 10-years follow-up. Baseline demographic data is outlined in Table 1. Differences in baseline demographics between included and excluded hips are included.

# RHOA classification

Incident RHOA had developed in 69 hips (5%) at 2 years, 178 hips (14%) at 5 years, 279 hips (24%) at 8 years, and in 495 hips (42%) at 10 years follow-up. End-stage RHOA had developed in 7 hips (<1%) at 2 years, 22 hips (2%) at 5 years, 43 hips (4%) at 8 years, and in 62 hips

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Baseline characteristics and differences between included and excluded hips.

Characteristic	Included hips ( $n = 1265$ )	Excluded hips ( $n =$ 739)	p- value
Age in years: mean (±SD)	55.7 (5.2)	56.2 (5.2)	0.06
Women, no. (%)	1038 (82.1)	540 (73.0)	0.01
BMI, kg/m2: mean (±SD)	26.1 (4.1)	26.2 (3.7)	0.76
Length in cm: mean (±SD)	169.5 (8.1)	170.6 (9.0)	0.03
Weight in kg: mean (±SD)	75.1 (13.7)	76.6 (14.1)	0.05
KL grade 0, no (%)	943 (74.5)		
KL grade 1, no (%)	322 (25.5)		
LCEA $\leq$ 25°, no. (%)	144 (11.4)		
ACEA $\leq 25^{\circ}$ , no. (%)	112 (9.0)		
LCEA & ACEA $\leq 25^{\circ}$ , no.	47 (3.7)		
(%)			

(5%) at 10 years follow-up.

# Association between acetabular dysplasia and RHOA over time

The associations between acetabular dysplasia and RHOA are summarized in Table 2. At 2 years follow-up, a combination of lateral and anterior AD was associated with incident RHOA. At 5 years follow-up, anterior AD and a combination of lateral and anterior AD was associated with incident RHOA, whereas lateral AD and a combination of lateral and anterior AD was associated with end-stage RHOA. At 8 years follow-up all forms of AD were associated with incident RHOA, whereas none were associated with end-stage RHOA. At 10 years follow-up, no significant associations were found between any forms of AD and neither incident nor end-stage RHOA.

# Discussion

This prospective cohort study of individuals with the first onset of hip and knee pain without evidence of definite RHOA at baseline showed an increased risk of developing RHOA within 2–8 years in individuals with lateral or anterior AD or a combination of both. Associations between AD and RHOA were observed at 2 and 5 years follow-up, but the association seems to weaken at 8 years follow-up and disappears at 10 years follow-up.

To the best of our knowledge, no other studies have investigated the risk in individuals with AD to develop RHOA at multiple follow-up moments in time. Our results may explain why previous studies have reported conflicting results. A systematic review by van Buuren et al. aimed to summarize the association between hip shape as quantified by statistical shape modeling and the incidence or progression of hip OA and found that the shape variants representing AD were consistently associated with THR and incidence or progression of hip OA [29]. These findings did not align with conclusions drawn by studies with a single, long-term follow-up moment. One prospective study with one follow-up moment at 22 years concluded that no AD measure correlated with the onset of OA [14]. Jacobsen et al. conducted a case-control study with a

single follow-up moment at 10 years follow-up and found no difference in joint space narrowing between individuals with AD and individuals without AD [30]. Our results support these findings and suggest that AD is a considerable risk factor for the rapid development of RHOA, while this association blurs at later follow-up moments. Given the steady increase in the prevalence of RHOA over 10 years, individuals without AD at baseline seemed to have developed RHOA at a slower rate and for other reasons.

Our study demonstrates that hips with AD and first complaints of hip or knee pain for which the GP was consulted were at risk of rapidly developing RHOA compared to hips without AD. It is relatively easy to detect AD with AP radiographs, which are already more or less standard of care in the orthopedic setting. Nevertheless, FP radiographs should be obtained considering their added value. In our study, 83 (7% of all included hips), 104 (8%), 98 (8%), and 97 (8%) cases of anterior AD at 2,5,8, and 10 years follow-up, respectively, would have been missed had FP radiographs not been obtained. We studied a population where hips with a known diagnosis of congenital dysplasia were excluded. We likely included hips with a mild form of AD, which had a high prevalence in our population (12%). The results from our study allow healthcare professionals to inform at-risk individuals about potentially developing RHOA and may contribute to preventative strategies [31]. AD is an essential risk factor to target, as it may be modifiable, has a high prevalence, and is easy to detect [31].

Our study has several strengths. The first strength is the availability of LCEA and ACEA to define AD. As a result, we obtained a more extensive assessment of the acetabular coverage of the femoral head compared to other large cohorts with only AP pelvic radiographs. A second strength of our paper are the five close follow-up moments. Having multiple follow-up moments within 10 years allowed us to monitor the development of RHOA closely over time. Finally, a third strength is the prospective design of the study.

Our study had several limitations that must be acknowledged. First, it is impossible to construct a horizontal reference line for calculating the ACEA on FP radiographs, as only one hip is depicted. However, an FP view is still more sensitive for the diagnosis of dysplasia when compared

Table 2

Association between acetabular dysplasia at baseline and RHOA at 2,5,8 and 10 years follow-up. Significant associations are in bold.

				Incident RHOA		End-stage RHOA	
Total hips per follow-up $(n=)$	Hips with incident OA ( <i>n</i> =)	Hips with end- stage OA ( <i>n</i> =)	Hips with AD per radiographic view (n=)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
T2 ( <i>n</i> = 1255)	69	7	LCEA<25 ( <i>n</i> = 136) ACEA<25 ( <i>n</i> = 123) LCEA & ACEA<25 ( <i>n</i> = 53)	1.71 (0.91–3.19) 1.83 (0.90–3.74) 2.29 (0.95–5.53)	1.69 (0.90–3.16) 1.93 (0.93–4.01) <b>2.46</b> (1.00–6.04)	2.84 (0.54–14.79) 1.51 (0.18–12.73) 3.82 (0.45–32.50)	3.02 (0.51–18.00) 1.39 (0.17–11.72) 5.73 (0.69–47.69)
T5 ( <i>n</i> = 1262)	178	22	LCEA<25 ( $n = 157$ ) ACEA<25 ( $n = 123$ ) LCEA & ACEA<25 ( $n = 53$ )	(1.44 (0.92–2.27) 1.99 (1.26–3.13) 2.28 (1.20–4.31)	(1.44 (0.90–2.30) 2.07 (1.28–3.34) 2.43 (1.25–4.76)	<b>2.65</b> (1.07–6.56) 1.39 (0.38–5.07) 3.55 (0.97–13.00)	2.65 (1.06–6.66) 1.35 (0.37–4.94) 3.75 (1.02–13.77)
T8 ( <i>n</i> = 1188)	279	43	LCEA<25 (n = 146) ACEA<25 (n = 115) LCEA & ACEA<25 (n = 48)	(1.09–2.24) 1.86 (1.23–2.80) 1.82 (1.01–3.27)	$\begin{array}{c} 1.56 \\ (1.08-2.26) \\ 1.86 \\ (1.22-2.84) \\ 1.88 \\ (1.03-3.42) \end{array}$	1.52 (0.70–3.29) 0.83 (0.26–2.67) 1.91 (0.53–6.88)	1.47 (0.66–3.29)         0.78 (0.24–2.55)         1.79 (0.46–7.01)
T10 ( <i>n</i> = 1169)	495	65	LCEA<25 ( <i>n</i> = 144) FP ACEA<25 ( <i>n</i> = 112) LCEA & ACEA<25 ( <i>n</i> = 47)	1.22 (0.88–1.69) 1.12 (0.77–1.64) 1.26 (0.71–2.25)	1.21 (0.86–1.69) 1.11 (0.75–1.66) 1.29 (0.71–2.35)	1.69 (0.91–3.14) 1.25 (0.54–2.90) 1.43 (0.45–4.55)	1.65 (0.87–3.13) 1.17 (0.50–2.75) 1.34 (0.40–4.45)

Odds ratios ORs were adjusted for age, BMI, and biological sex at baseline. AD= acetabular dysplasia, LCEA= lateral center edge angle, ACEA= anterior center edge angle, RHOA= radiographic hip osteoarthritis, OR= odds ratio.

to the AP view alone [15]. Secondly, the individuals in the CHECK cohort represent a mild form of AD, as individuals with a known diagnosis of congenital dysplasia were excluded from the CHECK cohort. Finally, in our present study, it should be noted that 35% of all participants had developed incident RHOA at 10 years follow-up. This is high compared to other studies where the incidence of developing RHOA was 6–11% [32,33]. However, this is can be explained by the inclusion criteria of having pain or stiffness in the hip or knee at baseline, which could represent the first signs of OA. However, the CHECK cohort is a unique population of individuals first seeking medical help for potential complaints of OA. This offers a unique opportunity to diagnose and treat complaints of OA at the onset.

In conclusion, AD was a risk factor for developing incident and endstage RHOA within 2–8 years. However, as time passed, the risk of developing both incident and end-stage RHOA disappeared in individuals with AD compared to individuals without this bone shape variation. In addition, as acetabular dysplasia can be diagnosed before severe hip damage occurs, this may provide an opportunity to prevent the development of RHOA in the future.

### CRediT authorship contribution statement

N.S. Riedstra: Conceptualization, Visualization, Formal analysis, Methodology, Writing – original draft, Writing – review & editing, Data curation. R. Vinge: Methodology, Writing – review & editing. J. Herfkens: Writing – review & editing, Methodology. D. Eygendaal: Writing – review & editing, Methodology. S.M.A. Bierma-Zeinstra: Writing – review & editing, Methodology. J. Runhaar: Writing – review & editing, Formal analysis, Methodology. M.M.A. van Buuren: Writing – review & editing, Methodology. R. Agricola: Conceptualization, Formal analysis, Methodology, Writing – review & editing, Writing – original draft.

### **Declaration of Competing Interest**

No conflict of interest to disclose.

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#### Supplementary materials

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