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Cam Deformity and Acetabular Dysplasia as Risk Factors for Hip Osteoarthritis

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Objective. **Cam deformity and acetabular dysplasia have been recognized as relevant risk factors for hip osteoarthritis (OA) in a few prospective studies with limited sample sizes. To date, however, no evidence is available from prospective studies regarding whether the magnitude of these associations differs according to sex, body mass index (BMI), and age.**

Methods. **Participants in the Rotterdam Study cohort including men and women ages 55 years or older without OA at baseline (n = 4,438) and a mean follow-up of 9.2 years were included in the study. Incident radiographic OA was defined as a Kellgren/Lawrence grade of ≥2 or a total hip replacement at follow-up. Alpha and center-edge angles were measured to determine the presence of cam deformity and acetabular dysplasia/pincer deformity, respectively. Odds ratios (ORs) were calculated to assess the associations between both deformities and the development of OA.**

Results. **Subjects with cam deformity (OR 2.11, 95% confidence interval [95% CI] 1.55–2.87) and those with acetabular dysplasia (OR 2.19, 95% CI 1.50–3.21) had a 2-fold increased risk of developing OA compared with subjects without deformity, while pincer deformity did not increase the risk of OA. Stratification analyses showed that the associations of cam deformity and acetabular dysplasia with OA were driven by younger individuals, whereas BMI did not influence the associations. Female sex appears to modify the risk of hip OA related to acetabular dysplasia.**

Conclusion. **Individuals with cam deformity and those with acetabular dysplasia are predisposed to OA; these associations were independent of other well-known risk factors. Interestingly, both deformities predisposed to OA only in relatively young individuals. Therefore, early identification of these conditions is important.**

Osteoarthritis (OA) of the hip is one of the main causes of musculoskeletal disability with pain and dysfunction in the elderly (1). Epidemiologic studies have identified several risk factors predisposing to hip OA, including increasing age, male sex (after age 55 years, hip OA is more common in women), excess body weight (which has a stronger association with knee OA), trauma, mechanical workload (occupational) and leisure-time physical activity, and gross bony abnormalities (i.e., congenital hip dislocation, Legg-Calvé-Perthes disease, or slipped capital femoral epiphysis) (1–3). Moreover, a review study (4) showed an association between bony abnormalities (e.g., acetabular dysplasia and cam deformity) and hip OA, although the conclusions drawn were based on limited prospective evidence (based on 110 individuals in 1 study of cam deformity, and a total of 1,365 individuals in 5 studies of dysplasia) (5–10).

Recent prospective epidemiologic studies have supported the notion that mild acetabular dysplasia is associated with an increased risk of incident hip OA

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(11–13). In subtle acetabular dysplasia, the femoral head articulates with a small area of the shallow acetabulum. Therefore, more focal stress is placed on this small area, which provides insufficient coverage of the femur (14). Cumulative articular surface contact stress above a critical threshold in dysplastic joints causes joint degeneration (15).

A significant association between cam deformity at baseline and the risk of developing hip OA and/or undergoing total hip replacement (THR) within 2–20 years of follow-up was demonstrated in a few prospective studies with limited sample sizes (11,12,16). Cam-type impingement characterized by excess bone formation at the anterolateral head–neck junction creates a nonspherical femoral head known as a cam deformity (16,17). The cam deformity is forced into the acetabulum during flexion and internal rotation of the hip, leading to structural damage such as acetabular labrum tears and cartilage delamination. This damage might gradually lead to hip OA. To date, there is no evidence available from prospective studies regarding whether the magnitude of the effect of these deformities on hip OA differs according to sex, body mass index (BMI), and age.

Another form of femoroacetabular impingement (FAI), pincer impingement, results from general or localized acetabular overcoverage of the femur, which is called a pincer deformity. Pincer deformity is proposed to compress the labrum and increase stresses on the underlying acetabular rim in the area of acetabular overcoverage during terminal motion of the hip. Retrospective and cross-sectional studies showed conflicting results regarding the association between pincer deformity and hip OA (4), and 2 recent prospective studies demonstrated no association between pincer deformity and the risk of hip OA or THR (12,13).

In a previous study including a subset of the population-based Rotterdam Study (RS) cohort, Reijman et al observed an association between acetabular dysplasia and an increased risk of incident hip OA (5). Here, we report updated results from the Rotterdam Study analysis in a population that is much larger than that ever investigated, with an additional 4 years of follow-up. Furthermore, we investigated the association between radiographic evidence of cam and pincer deformities and risk of incident hip OA. Finally, we examined whether the associations between hip deformities and future risk of hip OA could be modified by other determinants of hip OA.

PATIENTS AND METHODS

Study population. The study population consisted of participants in the Rotterdam Study, a population-based cohort study, which was established to investigate the occurrence and determinants of diseases in an aging population (18). The Rotterdam Study consists of 3 cohorts. The first cohort (RS-I) was initiated in 1989. All inhabitants of the Ommoord district in Rotterdam, The Netherlands who were 55 years of age or older were invited to participate. The second cohort (RS-II) was initiated in 2000 and consists of individuals who had become 55 years of age or had moved into the study district since the start of the study. Another extension of the study cohort, the third cohort (RS-III), was initiated in 2006 by including all subjects 45 years of age or older who were living in the Ommoord area and were not yet participating in the Rotterdam Study. Written informed consent was obtained from all participants, and the study was approved by the Medical Ethics Committee of the Erasmus Medical Center (18).

Trained interviewers performed an extensive interview to address the demographic characteristics, medical history, risk factors for chronic diseases, and medication use. In the current study, we used data from RS-I (n = 7,983) and RS-II (n = 3,011) cohort participants to investigate the associations of cam deformity and acetabular dysplasia with incident hip OA. After excluding subjects with no baseline or follow-up radiographs, patients with hip OA at baseline, those who did not provide informed consent, patients with rheumatoid arthritis or ankylosing spondylitis, and those who had undergone THR due to a fracture, a total of 3,160 and 1,553 subjects from RS-I and RS-II, respectively, were eligible to be included in the current study (Figure 1) with ~9 years of follow-up.

Outcome assessment. Weight-bearing anteroposterior (AP) pelvic radiographs obtained at baseline and follow-up were scored for the presence and degree of radiographic hip OA according to the Kellgren/Lawrence (K/L) method (grades 0–4) (19). If the K/L grade was 0 or 1 in both hips, the subject was considered to be free of hip OA. The incidence of hip OA was defined as a K/L grade of <2 at baseline and a K/L grade of ≥ 2 or a THR at follow-up.

Deformity measurements. All radiographs of the pelvis digitized to DCM files were converted to JPEG files and subsequently edited with a contrast-enhancing filter. The shapes of the proximal femur and acetabulum were outlined manually using a set of 23 points (see Supplementary Figure, available on the *Arthritis & Rheumatology* web site at http://onlinelibrary.wiley.com/doi/10.1002/art.39929/abstract) and statistical shape-modeling software (ASM tool kit; Manchester University, Manchester, UK). Most of the points were positioned on anatomic landmarks. The other points (e.g., those around the femoral head) were placed at equal distances between the anatomic landmarks. Each point was always placed on the same landmark of the outline, to allow comparison between the shapes. Using this set of points, the alpha and center-edge (CE) angles, parameters that quantify deformities, were calculated using MatLab 7.1.0 (16,17,20).

Cam deformity. The alpha angle indicates the extent to which the femoral head deviates from spherical (17). The center of the femoral head is located by drawing a best-fitted circle around the femoral head based on the points placed on it (see Supplementary Figure, available on the *Arthritis & Rheumatology* web site at http://onlinelibrary.wiley.com/doi/10.1002/art.39929/abstract). The alpha angle is formed by a line through the center of the neck and the center of the head and a line from the center of the femoral head through the point where the femoral head departs from the best-fitting circle around the femoral head (see

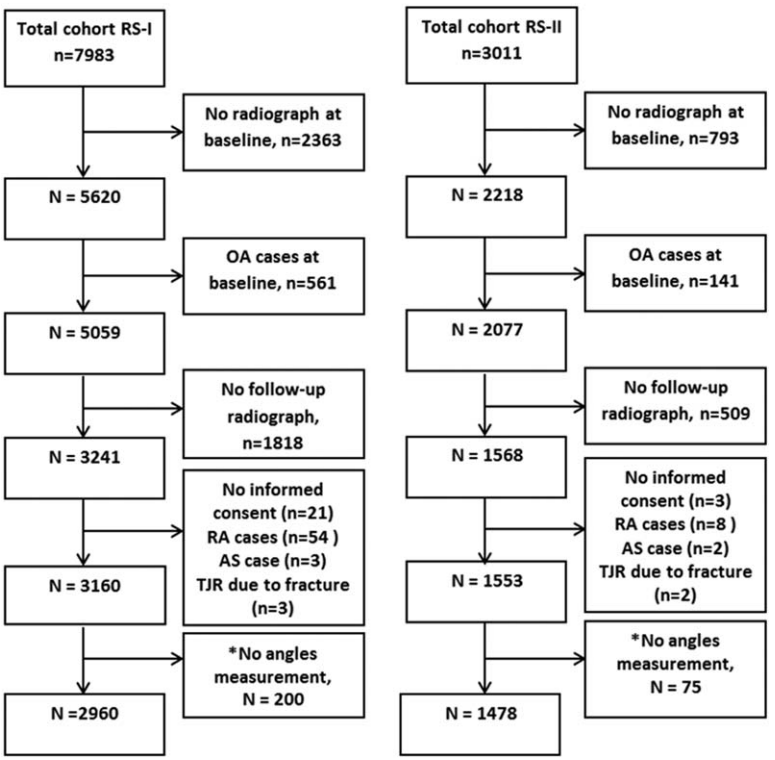

Figure 1. Flow chart of participants in the total Rotterdam Study I (RS-I) and RS-II cohorts who were included in the current study. OA = osteoarthritis; RA = rheumatoid arthritis; AS = ankylosing spondylitis; TJR = total joint replacement. * = Excluded due to poor-quality or damaged radiographs.

Supplementary Figure). The algorithm interpolated this point using the points placed. A cam deformity was defined as the presence of an alpha angle of >60°, based on the cut-off point identified in a previous study (16).

Acetabular dysplasia and pincer deformity. The existence of acetabular dysplasia and pincer deformity was measured with the CE angle, also known as the Wiberg angle. The CE angle is formed by a line from the lateral margin of the acetabular roof through the center of the femoral head and a vertical line through the center of the femoral head perpendicular to the horizontal line connecting the corner of the left and right foramens (see Supplementary Figure, available on the *Arthritis & Rheumatology* web site at http://onlinelibrary.wiley.com/doi/10.1002/art.39929/abstract) (5). Acetabular dysplasia was defined as the presence of a CE angle of <20°. This cut-off point was selected based on the literature, and therefore the results can be compared with those studies. A comparison between the data from this study and the data from a study by Reijman et al (5), in which the CE angle on radiographs was measured by hand in a subgroup of the participants in RS-I, is available in Supplementary Material (available on the *Arthritis & Rheumatology* web site at http://onlinelibrary.wiley.com/doi/10.1002/art.39929/abstract). We defined the presence of a pincer deformity by a CE angle of >40° (13).

Two investigators (MEZ and MV) who were unaware of follow-up data manually positioned the points on hip radiographs obtained from RS-I and RS-II, respectively. To evaluate the intraobserver reliability of both angles, 100 randomly selected radiographs were measured twice for each cohort. To examine interobserver reliability of the alpha and CE angles, the points were positioned by another investigator (FSH) in 50 randomly selected radiographs for each cohort.

The intraclass correlation coefficients (ICCs) for interobserver reliability of the alpha and CE angles were 0.63 (95% confidence interval [95% CI] 0.53–0.71) and 0.86 (95% CI 0.82–0.90), respectively. The intraobserver ICCs for the alpha and CE angles were 0.86 (95% CI 0.83–0.90) and 0.89 (95% CI 0.86–0.92), respectively.

Statistical analysis. Missing values (range 1–13%) (see Supplementary Table 1, available on the *Arthritis & Rheumatology* web site at http://onlinelibrary.wiley.com/doi/10.1002/art.39929/abstract) for the covariates were imputed based on the correlation structure within the data, using an iterative Markov chain Monte Carlo method that can be used when the pattern of missing data is arbitrary (monotone or non-monotone). This method fits a model using all other available variables in the model as predictors and then imputes missing values for the variable being fit. The method continues until the maximum number of iterations is reached, and the imputed values at the maximum iteration are saved to the imputed data set.

The association of cam and pincer deformities and acetabular dysplasia at baseline with the development of hip OA was calculated using generalized estimating equations (GEEs) and expressed in terms of odds ratios (ORs). GEEs take into account the correlation between the left and right hip. Hips with either a pincer deformity or dysplasia were

Table 1. Baseline characteristics of the study populations*

Characteristic	RS-I			RS-II		
	Total cohort (n = 7,983)	Study population (n = 2,960)	Lost to follow-up (n = 1,818)	Total cohort (n = 3,011)	Study population (n = 1,478)	Lost to follow-up (n = 509)
Age, mean ± SD years	70.6 ± 9.8	65.1 ± 6.4	71.6 ± 8.2	65.2 ± 8.4	62.9 ± 6.4	68.1 ± 9.5
Female	61.1	56.6	58.0	56.2	55.5	50.7
BMI, mean ± SD kg/m^2	26.3 ± 3.7	26.2 ± 3.5	26.3 ± 3.9	27.2 ± 4.1	27.1 ± 3.9	27.3 ± 4.2
Height, mean ± SD cm	166.6 ± 9.5	168.3 ± 9.0	165.9 ± 9.3	168.3 ± 9.2	168.5 ± 9.1	168.1 ± 9.8
Weight, mean ± SD kg	72.9 ± 12.0	74.3 ± 11.6	72.4 ± 11.9	77.3 ± 13.4	77.0 ± 13.1	77.2 ± 14.0
Smoking status						
Current	22.6	21.4	27.4	23.3	23.1	25.2
Former	40.7	46.7	39.7	10.7	10.1	12.4
Never	36.6	31.9	32.9	66.0	66.7	62.4
Lower education level†	56.1	46.6	61.8	54.4	52	56.0
Positive family history of hip OA	18.9	22.0	18.8	NA	NA	NA
Alcohol intake, mean ± SD gm/day	10.4 ± 15.2	11.1 ± 14.6	9.8 ± 15.9	7.2 ± 13.8	8.0 ± 13.0	4.9 ± 10.0
Heavy mechanical workload	12.0	12.4	17.7	NA	9.9	NA
Hip pain	12.7	11.1	11.8	15.2	13.5	12.2
Hip alpha angle >60°						
Left	–	8.3	–	–	7.2	–
Right	–	6.4	–	–	7.0	–
Hip CE angle <20°						
Left	–	3.4	–	–	3.8	–
Right	–	5.4	–	–	6.2	–
Hip CE angle >40°						
Left	–	13.5	–	–	10.9	–
Right	–	8.6	–	–	8.9	–
Hip K/L grade 0						
Left	–	56.7	–	–	87.3	–
Right	–	65.9	–	–	84.2	–
Hip K/L grade 1						
Left	–	43.3	–	–	12.7	–
Right	–	34.1	–	–	15.8	–

* Except where indicated otherwise, values are the percent. RS = Rotterdam Study; BMI = body mass index; CE = center-edge; NA = not available; K/L = Kellgren/Lawrence.
† Including primary education, primary education plus higher education that was not completed, and lower vocational education.

compared with a reference group of hips with a CE angle of ≥20° and ≤40°, respectively, representing normal acetabular coverage. The magnitude of confounding was estimated by the degree of discrepancy between the unadjusted and adjusted estimate, with 10% as a cut-off point to designate an important change in the estimate. Crude ORs were calculated, as well as ORs adjusted for age, sex, BMI, baseline K/L grade, and follow-up duration. We further investigated whether these associations were modified by age (>65 years), sex, BMI (>25 kg/m^2), baseline K/L grade (0 or 1), and follow-up duration. Two-sided *P* values less than 0.05 were considered significant. IBM SPSS Statistics 21.0 was used for all analyses.

RESULTS

Of 3,160 and 1,553 eligible subjects from RS-I and RS-II, 200 and 75 subjects, respectively, were excluded because of poor-quality or damaged radiographs that would not allow measurement of bony deformities, leaving totals of 2,960 and 1,478 subjects in the studies for RS-I and RS-II, respectively (Figure 1).

Table 1 shows the baseline characteristics of the included individuals. Our study population in both cohorts was younger, consumed more alcohol, and had a higher level of education compared with the total cohorts, while there were no significant differences for BMI, weight, height, and current smoking status between the study populations and the total cohorts. The percentages of current smokers and subjects with a heavy mechanical workload were highest in the population that was lost to follow-up.

At the follow-up times, 234 and 162 cases of hip OA were identified in RS-I and RS-II, respectively. Incident hip OA was defined in 281 hips in RS-I, of which 12.1% (n = 34) had cam deformity, 14.9% (n = 42) had pincer deformity, and 8.2% (n = 23) had acetabular dysplasia, while of 199 hips with incident hip OA in RS-II, 17.6% (n = 35) had a cam deformity, 14.6% (n = 29) had pincer deformity, and 8% (n = 16) had acetabular dysplasia.

In pooled crude data analyses, a significant association between the presence of cam and pincer deformities

Table 2. Associations of cam deformity, acetabular dysplasia, and pincer deformity with hip OA, stratified by age, sex, BMI, K/L grade at baseline, and follow-up time, in pooled data*

	No. of hip with OA/without OA	Cam deformity	Dysplasia	Pincer deformity
All subjects	480/8,393	2.11 (1.55–2.87)	2.19 (1.50–3.21)	1.24 (0.93–1.66)
Age, years				
≤65	261/5,168	3.07 (2.05–4.60)	2.59 (1.62–4.16)	1.37 (0.93–2.00)
>65	219/3,225	1.36 (0.86–2.16)	1.74 (0.90–3.37)	1.10 (0.71–1.71)
Sex				
Female	319/4,672	1.71 (1.02–2.85)	2.96 (1.93–4.53)	1.21 (0.86–1.70)
Male	161/3,721	2.40 (1.60–3.59)	1.09 (0.49–2.41)	1.33 (0.78–2.25)
BMI				
≤25 kg/m^2	135/3,066	2.16 (1.18–3.96)	2.36 (1.22–4.58)	1.18 (0.69–2.02)
>25 kg/m^2	345/5,327	2.06 (1.44–2.95)	2.21 (1.38–3.53)	1.33 (0.94–1.87)
K/L grade at baseline				
0	179/5,984	1.42 (0.76–2.64)	3.06 (1.88–4.99)	1.60 (1.02–2.51)
1	301/2,409	2.39 (1.65–3.46)	1.79 (1.05–3.05)	1.16 (0.81–1.65)
Follow-up duration†				
≤9.2 years	109/2,669	2.54 (1.41–4.58)	1.76 (0.76–4.06)	0.58 (0.28–1.21)
>9.2 years	371/5,720	1.91 (1.32–2.76)	2.46 (1.60–3.78)	1.50 (1.09–2.07)

* The models were adjusted for age, sex, body mass index (BMI), Kellgren/Lawrence (K/L) grade at baseline, cohort, and follow-up time. For the analyses of pincer deformity and dysplasia, a reference group of hips with normal acetabular coverage (center-edge angles of ≥20° and ≤40°, respectively) was used. Values are the odds ratio (95% confidence interval).
† The duration of follow-up was categorized according to the mean follow-up time (9.2 years) in the combined data.

and acetabular dysplasia and the development of hip OA was observed (data not shown). The associations for cam deformity and dysplasia remained significant after adjustment for age, sex, BMI, K/L grade at baseline, follow-up duration, and cohort (Table 2), in particular among subjects younger than age 65 years, and for both obese (BMI >25 kg/m^2) and non-obese (BMI ≤25 kg/m^2) subjects. Moreover, acetabular dysplasia increased the future risk of hip OA only among women, while cam deformity was associated with incident hip OA in both men and women. These bony deformities were independently associated with outcome when included in the same model (for cam deformity, OR 2.12 [95% CI 1.55–2.90]; for hip dysplasia, OR 2.26 [95% CI 1.56–3.29]; for pincer deformity, OR 1.20 [95% CI 0.90–1.60]). We observed no significant interaction between cam and pincer deformities.

The results were very similar in both cohorts. The adjusted analyses showed a significant association of cam deformity and acetabular dysplasia with the development of hip OA among those in RS-I (OR 1.82 [95% CI 1.18–2.81] for cam deformity and OR 2.25 [95% CI 1.37–3.69] for dysplasia) and RS-II subjects (OR 2.72 [95% CI 1.71–4.33] for cam deformity and OR 2.30 [95% CI 1.23–3.31] for dysplasia) (Table 3).

Multivariate analyses excluding THR cases (for hip OA, n = 397; for no hip OA, n = 8,393) showed that all 3 deformities were associated with a significantly increased risk of hip OA (for cam deformity, OR 2.11 [95% CI 1.51–2.94]; for pincer deformity, OR 1.36 [95% CI 1.01–1.84]; for dysplasia, OR 1.68 [95% CI 1.07–2.63]), while analyses including THR as the outcome (for THR, n = 83; for no THR, n = 8,790) showed a significant association only for dysplasia (OR 4.84 [95% CI 2.57–9.14]; for cam deformity, OR 1.63 [95% CI 0.85–3.32]).

The associations of cam and pincer deformities and acetabular dysplasia with the incidence of hip OA stratified according to age, sex, BMI, K/L grade at baseline, and follow-up for both cohorts are shown in Supplementary Table 2 (available on the *Arthritis &*

Table 3. Associations of cam deformity, acetabular dysplasia, and pincer deformity with future risk of hip osteoarthritis, stratified according to cohort*

	RS-I (n = 281 hips)	RS-II (n = 199 hips)
Cam deformity	1.82 (1.18–2.81)	2.72 (1.71–4.33)
Age	1.02 (0.99–1.04)	1.05 (1.03–1.08)
Female	2.48 (1.81–3.39)	1.48 (1.04–2.11)
BMI	1.05 (1.02–1.09)	1.01 (0.97–1.05)
Dysplasia	2.25 (1.37–3.69)	2.30 (1.23–3.31)
Age	1.02 (1.0–1.04)	1.06 (1.03–1.09)
Female	2.55 (1.84–3.51)	1.20 (0.83–1.74)
BMI	1.05 (1.02–1.09)	1.02 (0.97–1.06)
Pincer deformity	1.26 (0.87–1.83)	1.21 (0.74–1.97)
Age	1.02 (0.99–1.04)	1.06 (1.04–1.10)
Female	2.00 (1.47–2.73)	1.24 (0.86–1.79)
BMI	1.06 (1.03–1.10)	1.01 (0.97–1.06)

* Values are the odds ratio adjusted for age, sex, body mass index (BMI), Kellgren/Lawrence grade at baseline, and follow-up (95% confidence interval). RS-I = Rotterdam Study I.

Rheumatology web site at http://onlinelibrary.wiley.com/doi/10.1002/art.39929/abstract). We observed a significant association of both acetabular dysplasia and cam deformity with incident hip OA among subjects younger than age 65 years in the RS-I cohort. In subjects with a K/L grade of 1 at baseline, there was an association between cam deformity and hip OA, while in subjects with a K/L grade of 0, there was a stronger association between acetabular dysplasia and hip OA. BMI did not modify the associations of acetabular dysplasia and cam deformity with incident hip OA, although the significance levels differed. Acetabular dysplasia increased the risk of hip OA in female subjects, while pincer deformity was significantly associated with hip OA in men.

Among subjects in RS-II, a significant association was shown for cam deformity and incident hip OA in males and for both age and BMI groups and follow-up periods, while the presence of mild acetabular dysplasia was associated with an increased risk of hip OA in female subjects, subjects younger than 65 years of age, and the second follow-up period. The magnitude of the association of cam deformity and acetabular dysplasia with incident hip OA was almost similar in subjects with a BMI of $\leq$25 kg/m^2 and those with a BMI of $>$25 kg/m^2 in RS-II. Given the limited power, these results should be interpreted with caution.

DISCUSSION

The current prospective study of the influence of bony deformities of the hip on the development of hip OA in a large population of subjects (age $>$55 years) with no radiographic hip OA at baseline showed a strong independent association of cam deformity and acetabular dysplasia with the development of hip OA that is present only in younger individuals (age $\leq$65 years). Moreover, female sex appears to modify the risk of hip OA related to acetabular dysplasia, while BMI does not.

Our finding on the association between cam deformity and hip OA is consistent with the results reported by Agricola et al (16) in participants in the Cohort Hip and Cohort Knee (CHECK) study (n = 723) with a follow-up duration of 5 years. Consistently, in a more recent longitudinal study of participants in the Chingford 1,000 Women Study (n = 734), a positive association was observed between cam deformity and the development of hip OA and THR at 20-year follow-up (11,12). Furthermore, 2 cross-sectional studies also showed an association between cam morphology and hip OA (21,22).

Cam deformity appears to be more frequent in men than in women (23,24). Consistently, in our study, cam deformity was detected in 12.7% of measured hips in men (combined cohorts) compared with only 3.1% of measured hips in women. However, we reported increased risk estimates for both men and women, showing that the mechanisms by which this abnormality leads to hip OA are likely to be similar in men and women. The association between cam deformity and hip OA appears to be strongest in subjects with a K/L grade of 1 at baseline. The development of hip OA in subjects with a K/L grade of 0 might require a length of time that is longer than the follow-up period, which could explain the stronger association in subjects with a K/L grade of 1 at baseline. In our study population, however, the frequency of cam deformity was twice as high (11.7%) in hips with K/L grade of 1 compared with hips with a K/L grade of 0 (5.4%).

Measurement of the alpha angle might be influenced by the presence of osteophytes. Although we avoided the osteophytes while placing the points, we cannot completely exclude the influence of existing osteophytes on our alpha angle measurements. Moreover, we observed a higher prevalence of cam deformity in subjects age older than 65 years (9.1%) than in subjects age 65 years or younger (6.1%), while the analyses adjusted for baseline K/L grade showed a significant association between cam deformity and the risk of hip OA among only younger subjects. On the other hand, this raises the question of whether cam deformity could be a reactive osteophyte in the setting of existing hip OA. However, some studies have shown that idiopathic cam deformity seems to be an entity distinct from hip OA–induced osteophytes, in particular in young individuals (25,26). In addition, assuming that cam deformity develops during puberty and adolescence and remains rather stable (16,27,28), it could not be a consequence of hip OA.

Previous investigations in participants in the Chingford and CHECK studies showed that subclinical acetabular dysplasia is a significant predictor of radiographic hip OA and THR (11–13). These findings are consistent with the positive association between acetabular dysplasia and the development of hip OA found in this study and with the previous study by Reijman et al in a subset of the Rotterdam Study cohort (5). Although the prevalence of hip dysplasia was similar in men (4.7%) and women (4.6%) in our study, we found a significant association between hip dysplasia and the development of hip OA only in women. Different alignment of the lower extremity in women and consequently the influence on dynamic joint function and mechanical

loading of the hip joint as well as abnormal underlying joint laxity, estrogen metabolism, and pregnancy-associated pelvic instability might explain the difference (29). Alternatively, it might be possible that men had already developed hip OA before onset of the study due to a more heavy work and were therefore excluded from our study. However, the exact reason is not yet clear. Moreover, we found a strong association between acetabular dysplasia and incident hip OA in subjects with a K/L grade of 0 in the present study. This supports the notion that the association was not biased by a preexisting K/L grade of 1 at baseline.

We found no significantly increased risk of hip OA in the presence of pincer deformity. Consistently, 2 recent prospective studies in participants in the Chingford (19 years of follow-up) and the CHECK (5 years of follow-up) cohorts showed no increased risk of hip OA or THR in presence of a pincer deformity (12,13). However, a significantly increased risk of hip OA was observed for pincer deformity among subjects with longer follow-up times. Because the prevalence of pincer deformity was the same for both follow-up periods (10.8%), this might suggest that the pincer-type FAI produces a rather slow process of degeneration. Moreover, pincer deformity increased the risk of hip OA in subjects with a K/L grade of 0 at baseline. It may suggest a true association for pincer deformity that was missed in the main analyses due to the influence of the preexistence of a K/L grade of 1 at baseline.

We demonstrated similar risk estimates for hip OA among persons with a low BMI ($\leq$25 kg/m^2) and those with a high BMI (>25 kg/m^2) for all hip deformities. This indicates that BMI does not modify the associations between hip deformities and the development of hip OA. In support of this notion is the fact that 2 cross-sectional studies showed no association between BMI and the prevalence of cam deformity (23) and acetabular dysplasia (30). We also observed that the prevalence of cam and pincer deformities and hip dysplasia was similar in subjects with a low BMI and those with a high BMI in our study population. Intuitively, one might expect a stronger association between hip deformities and hip OA in individuals with a high BMI, because the mechanical load is higher. A lower activity level in those with a high BMI might explain the lack of a stronger association between bone deformities and incident hip OA in individuals with a high BMI. We did indeed observe that subjects with a high BMI had more lower limb disability compared with those with a low BMI (16.9% versus 9.9%), but we did not find a stronger association for all deformities in subjects with a higher BMI after adjustment for lower limb disability.

We observed a significant association only for dysplasia when THR was defined as the outcome. THR is more closely related to severe pain and disability compared with the K/L score for the joint. In our study, 28% of patients with THR had hip pain at baseline compared with 15.4% of all patients with incident hip OA. Moreover, the mean lower limb disability index was higher among THR cases compared with all cases of incident hip OA. The study by Nicholls et al (12) showed an association of both cam deformity and dysplasia with THR. Inconsistencies in the results might be attributable to different subjects' inclusion criteria or the variability of pain and disability in subjects with hip OA leading to THR rather than hip OA itself in these studies. Our study subjects were free of radiographic changes at baseline, while those in the Nicholls study were free of THR at baseline.

This study is the first to actually evaluate the associations according to age. We observed that the associations of cam deformity and acetabular dysplasia with hip OA were enhanced by an age younger than 65 years. This finding might explain why the reported association for dysplasia among participants in the CHECK cohort (13) is stronger (OR 2.83 [95% CI 1.54–5.20]) than the association in our study, because the CHECK participants were younger (mean age 60 years) than our study subjects. Given that cam deformity develops during adolescence, some individuals develop hip OA at a relatively young age, and persons with cam deformity who do not develop hip OA get older without developing hip OA. Therefore, as individuals get older, the association with hip OA becomes less strong, which fits with the observed trend in the Rotterdam Study cohort toward cam deformity (and also dysplasia) and hip OA as the age of the subjects increases. Further studies on the influence of these deformities on the development of hip OA in younger individuals are warranted.

Our study had several limitations that must be taken into account. First, our study subjects were ages 55 years or older at baseline. At this age, some individuals already have hip OA, and those with OA at baseline were excluded from the study. Therefore, the influence of deformities might be underestimated because of this exclusion. Second, many subjects were lost to follow-up, and as a consequence, some baseline characteristics of subjects in the total cohort differed from those of subjects who were included in the study. The subjects who were lost to follow-up were probably less mobile and unable to visit the center. Another possible reason is that these individuals did not survive during follow-up period. Both of these factors could have led to the relatively healthier and younger study population. Finally, because we used AP radiographs to measure the angles,

we cannot exclude the possibility that deformities were underestimated in our data.

In conclusion, both cam deformity and acetabular dysplasia are strongly related to the development of hip OA, even in a population of subjects ages 55 years or older. These associations are independent of known risk factors for radiographic hip OA, including age, sex, and BMI. Because cam deformity and acetabular dysplasia can be diagnosed before severe hip damage occurs, this might provide an opportunity to prevent the development of hip OA.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Saberi Hosnijeh had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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