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Cam morphology and the risk of developing radiographic hip osteoarthritis within 8 years: an individual participant data meta-analysis of 23 886 hips from the world COACH consortium

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ABSTRACT

Objective To assess the relationship between cam morphology and the development of radiographic hip osteoarthritis (RHOA), overall and in subgroups based on age, biological sex and body mass index (BMI).

Methods Hips with no RHOA at baseline and with available follow-up during 4–8 years were selected from the Worldwide Collaboration on Osteoarthritis PrediCtion for the Hip (World COACH) consortium. Alpha angles were uniformly measured on anteroposterior radiographs, with a threshold of 60° used to define cam morphology. Incident RHOA was defined as the transition from an RHOA-free state at baseline to definite diagnosis of RHOA at follow-up. The association between baseline cam morphology and the development of RHOA was assessed using a three-level mixed-effects logistic regression model, accounting for hip side, individual and cohort-level variation.

Results A total of 23 886 hips were included (mean age: 62.2±8.4 years; 70.6% female; BMI: 27.4±4.5; mean time to follow-up: 6.1±3.0 years). Cam morphology was associated with RHOA (OR: 1.87, 95% CI 1.36 to 2.59), as was a greater alpha angle (OR 1.02, 95% CI 1.01 to 1.03 for every degree increase). The overall relative risk of developing RHOA in hips with cam morphology was 1.62 (95%CI 1.26 to 2.07), greatest for those aged 51–60 years (2.15, 95% CI 1.55 to 2.98) and higher in males (2.50, 95% CI 1.67 to 3.73), compared with females (1.75,95% CI 1.24 to 2.48).

Conclusion Hips with cam morphology have higher odds of developing RHOA within 4–8 years compared with hips without cam morphology. The relative risk was highest in subgroups of participants aged 51–60 years and in males, making cam morphology a potential target for primary or secondary prevention of RHOA.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Cam morphology primarily develops during adolescence and is strongly associated with athletic activity during this period. Although it has been identified as a risk factor for hip osteoarthritis, the strength of this association varies widely across studies, limiting its generalisability.

WHAT THIS STUDY ADDS

⇒ In this individual participant data meta-analysis, including 23 886 hips from nine prospective cohort studies, cam morphology was associated with an increased risk of developing radiographic hip osteoarthritis (RHOA). Specifically, hips with cam morphology had 1.9 times the risk of developing RHOA compared with those without. Subgroup analyses revealed that the association was particularly strong for males and among individuals aged 51–60.

HOW THIS STUDY MIGHT AFFECT RESEARCH PRACTICE OR POLICY

⇒ Cam morphology may be a key target for primary (to prevent the morphology from developing) or secondary (to prevent the development of RHOA) prevention strategies. High-risk subgroups, such as those identified in this study, could benefit from increased clinical attention during the earliest stages of disease development.

INTRODUCTION

Osteoarthritis (OA) is a highly prevalent musculoskeletal condition worldwide, affecting 15% of individuals aged 30 and older.[1] Its global prevalence (7.6% in 2020) is expected to surge in the coming decades, followed by its heavy socioeconomic costs.[2] Currently, hip OA management remains predominantly reactive, given the absence of curative treatments. This underscores the imperative need for a deeper and more thorough understanding of hip OA aetiology and risk factors (both causal and prognostic).

A potential causal risk factor for radiographic hip OA (RHOA) is cam morphology.[3] It is characterised by the additional bone formation of varying sizes

around the femoral head-neck junction, typically before growth plate closure, resulting in a non-spherical femoral head.[4 5] This incongruity of the hip joint can result in painful abnormal contact between the femoral head–neck junction and acetabulum during motion, a condition referred to as femoroacetabular impingement (FAI) syndrome.[6] This may cause cartilage damage (even in young adults) and eventually progress to early OA.[7 8]

The association between cam morphology and RHOA has been demonstrated previously.[9–14] A recent systematic review reported ORs ranging from 2.12 to 3.67 (combining data from three prospective studies) and ORs ranging from 4.57 to 10.38 in four cross-sectional studies.[15] Combining data from existing cohort studies and uniformly measuring cam morphology to undertake individual participant data (IPD) meta-analysis could increase the generalisability of findings with larger combined sample size, standardised automated measurements and the ability to consider both cohort- and participant-level heterogeneity jointly.[16]

The primary aim of this study was to assess the association between cam morphology at baseline and subsequent development of RHOA over 4–8 years follow-up period using an IPD meta-analysis based on harmonised data from nine prospective cohorts. Secondary aims included examining whether this association differed by sex, age groups or body mass index (BMI).

METHODS

Study design and participants

The Worldwide Collaboration on OsteoArthritis prediCtion for the Hip (World COACH) consortium is an international collaboration currently comprising nine prospective cohort studies and has previously been described.[17] In this study, we used data from the following included studies: Cohort Hip and Cohort Knee (CHECK) study,[18] Chingford study,[19] Johnston County Osteoarthritis Project (JoCoOA),[20] Multicentre Osteoarthritis Study (MOST),[21] Osteoarthritis Initiative (OAI),[22] Rotterdam Study (RS, including three subcohorts: RS1, RS2 and RS3)[23] and Study of Osteoporotic Fractures (SOF).[24]

Hips were excluded if they had missing baseline demographic data, no or insufficient quality baseline radiographs or absence of RHOA scores at either baseline or follow-up. Data missingness is described in online supplemental table 1. We deliberately included hips that showed no signs of RHOA at baseline to focus on the development of incident RHOA, eliminating potential biases from early RHOA signs, which can influence alpha angle measurements.

Radiographs

At baseline and follow-up, anteroposterior (AP) radiographs of the hip or pelvis were obtained according to the respective protocols.[18–24] The CHECK, OAI and RS cohorts used standardised weight-bearing radiographs, while the Chingford, JoCoOA and SOF cohorts employed standardised supine radiographs. Additionally, the MOST cohort used standardised weight-bearing AP full-limb radiographs of the lower extremities.

Cam morphology

The alpha angle is a recommended radiological measurement to quantify cam morphology.[4] It is the angle between the femoral head–neck axis and a line from the head centre to where the head–neck contour first leaves the best-fitting circle[25] (figure 1). In this study, the alpha angle was automatically and uniformly measured on baseline radiographs.[26] First, the proximal femur's bony margin was automatically annotated with landmark points using the BoneFinder software (The University of Manchester, UK).[27] Subsequently, an in-house, open-access and validated method was used to calculate the alpha angle from these landmarks. The automated method was validated by comparison to manual measurements, with inter-method intraclass correlation coefficients (ICCs) of 0.81 (95%CI 0.46 to 0.92) on dual-energy x-ray absorptiometry images[28] and 0.46 (95%CI 0.12 to 0.70) on AP pelvic radiographs.[29] A validated alpha angle threshold value of ≥60° was used to define the presence of cam morphology.[4 30 31] As dichotomising continuous measures may limit statistical power, we also investigated the effect of the alpha angle as a continuous variable.[4]

Outcome measures

Three classifications for RHOA grading were used in original databases, namely, the Kellgren and Lawrence (KL),[18–21 23] the

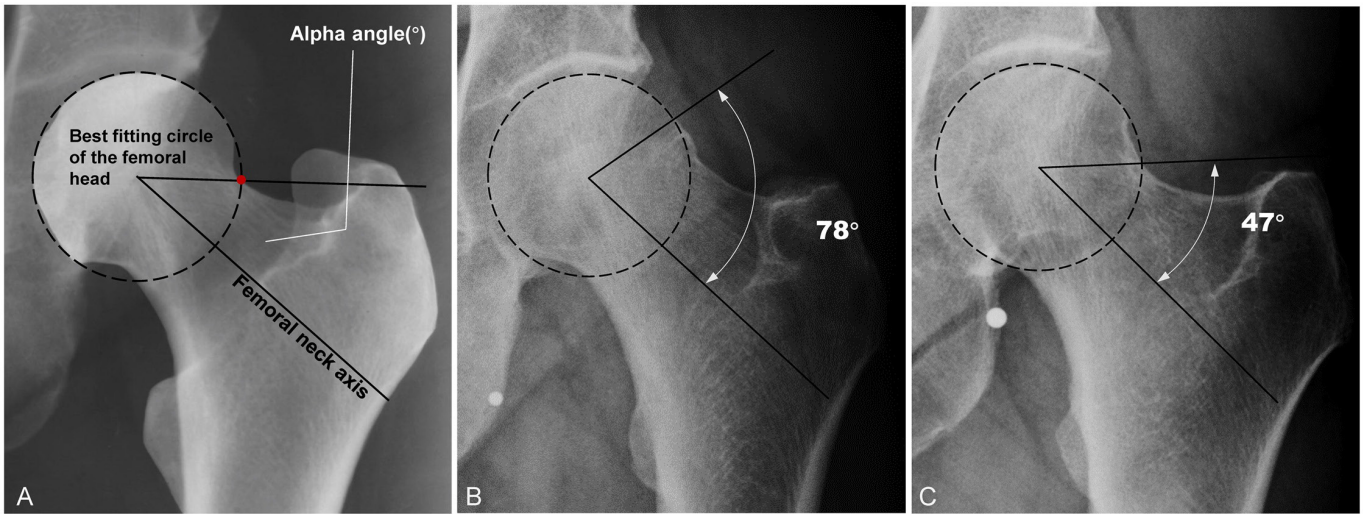

Figure 1 Measurement of the alpha angle on anteroposterior radiographs. (A) The alpha angle is the angle between the femoral neck axis (which passes through the centre of the femoral head and the femoral neck) and a line connecting the femoral head centre and alpha point (red point), where the contour of the femoral head–neck junction begins to leave the best-fitting circle of the femoral head; (B) hip with an alpha angle of 78°; (C) hip with an alpha angle of 47°.

Croft[24] and the atlas of individual radiographic features in osteoarthritis (Osteoarthritis Research Society International atlas).[22] These RHOA scores were harmonised into three ordinal categories through a harmonised interpretation: 'no RHOA' (any score of 0), 'doubtful RHOA' (any score of 1) and 'definite RHOA' (any score ≥2 or total hip replacement). The development of RHOA was defined by a transition from having 'no RHOA' at baseline to having 'definite OA' at follow-up.

Statistics

Descriptive statistics were used to analyse the baseline characteristics, stratified by cohort. Baseline characteristics were compared between included and excluded hips (independent or Welch's t-tests for continuous variables and X^2 tests for categorical variables). Assumptions for all tests were assessed and not violated.

For the primary aim, two statistical models were employed. The first was a three-level mixed-effects logistic regression model (hip side, individual and cohort), accounting for the clustering of two hips per participant and among individuals across cohorts. Multivariate normality for the random effects was assumed. Results were expressed as ORs with 95% CIs, adjusted for age, sex and BMI. The association between continuous alpha angle and RHOA development was assessed using the same method. All analyses were repeated for sensitivity purposes by excluding the MOST cohort.

In the primary analysis, the reference group included hips with either no or doubtful RHOA. The influence of the development of 'doubtful RHOA' to 'definite RHOA' was assessed using a forward continuation ratio model (our second model), given that this transition is often considered a critical and irreversible step. This model treated RHOA as an ordinal outcome and relaxed the ordinality assumption for cam morphology. Results were presented as effect plots of marginal probabilities, adjusted for random effects with mean baseline age and BMI and randomly selected right hip side and stratified by sex.

For the secondary aim, we investigated potential interaction effects between cam morphology and demographics (sex, age and BMI) using unadjusted logistic regression. Significant interactions prompted further analysis to compute ORs for each demographic factor, considering females as the reference group for sex and treating age and BMI as continuous variables. Subsequent analyses stratified the data by sex, specific age groups (40–50, 51–60, 61–70 and over 70 years) and BMI categories (normal, BMI <25; overweight, BMI ≥25). It was not possible to perform the analyses in every subgroup due to restricted numbers; instead, we provided descriptive statistics, including absolute and relative risk with 95% CI, for developing RHOA. The 95% CIs for the absolute and relative risk were determined using the Clopper–Pearson exact CI and Katz log method, respectively.

The linearity assumption for quantitative predictors was assessed for all logistic regression models and not violated. Statistical significance was determined as $p<0.05$. Univariate analyses were performed in SPSS (v26.0) and other analyses in R (v4.1.1, The R Foundation, used package: Lme4, GLMMadaptive and ggplot2).

Equity, diversity and inclusion

This study involves participants from diverse ethnic backgrounds across three continents, with a greater proportion of women than men. The author team was gender-balanced and included both junior and senior researchers from varied disciplines and individuals from marginalised communities. All authors actively contributed to writing this manuscript.

RESULTS

Baseline participant characteristics

The World COACH consortium included available data from 77 230 hips. Of these, 38 811 hips were eligible for this study with both baseline and follow-up data (figure 2). From this group, 14 925 hips were excluded due to definite or doubtful signs of RHOA at baseline, leaving 23 886 hips for inclusion in the final analyses. Across all cohorts, the mean interval between the baseline and follow-up radiographs was 6.1±3.0 years.

At baseline, hips excluded for definite or doubtful RHOA were from older individuals and had a higher prevalence of cam morphology (table 1). Results stratified by cohort are provided in online supplemental table 2.

Association between cam morphology and RHOA

The prevalence of cam morphology at baseline was 9.5% (n=2271). The incidence of RHOA was 3.2% in hips with cam morphology and 2.0% in those without. Detailed results per cohort are provided in online supplemental table 2. Cam morphology (alpha angle ≥60°) was associated with the development of incident RHOA with an OR of 1.87 (95%CI 1.36 to 2.59). A significant association was also observed between the continuous alpha angle and RHOA development with an OR of 1.02 (95%CI 1.01 to 1.03) for each degree increase in alpha angle (the crude ORs are provided in online supplemental table 3).

The effect plot of the marginal probabilities of the forward continuation ratio model is provided in figure 3. All marginal probabilities were calculated in males or females aged 62 years with a BMI of 27 kg/m^2. Marginal probabilities indicated that cam morphology increased the likelihood of developing doubtful RHOA to 21% (95% CI 15% to 27%) in females and 23% (95% CI 16% to 30%) in males, compared with 17% (95% CI 11% to 23%) and 18% (95% CI 11% to 25%) in those without cam morphology, respectively. For definite RHOA, probabilities were 5% (95% CI 2% to 10%) in females and 4% (95% CI 1% to 9%) in males with cam morphology vs 2% (95% CI 1% to 6%) in females and 2% (95% CI 1% to 5%) in males without cam morphology.

The sensitivity analysis excluded 2009 hips with full-limb radiographs from the MOST cohort, leading to a total of 21 377 hips for analysis. The association between cam morphology (alpha angle ≥60°) and the development of incident RHOA showed similar results with an OR of 1.82 (95%CI 1.31 to 2.52) and 1.02 (95%CI 1.01 to 1.03) for continuous alpha angle.

Interaction effect and subgroup analyses

The interaction analysis indicated that the association between cam morphology and the development of incident RHOA differed by sex (P value: 0.014), whereas no meaningful interaction was observed with age (P value: 0.417) or BMI (P value: 0.387). Specifically, male hips with cam morphology showed an OR of 3.09 (95%CI 1.38 to 6.90) for developing RHOA compared with those without cam morphology, see online supplemental table 4. In contrast, an OR of 1.36 (95%CI 0.87 to 2.11) was observed in females. The absolute risk and relative risk of developing RHOA for hips with cam morphology in subgroup analyses stratified by sex, age groups and BMI categories are provided in table 2. The highest relative risk was found in the 51–60 years group (2.15; 95% CI 1.55 to 2.98) among

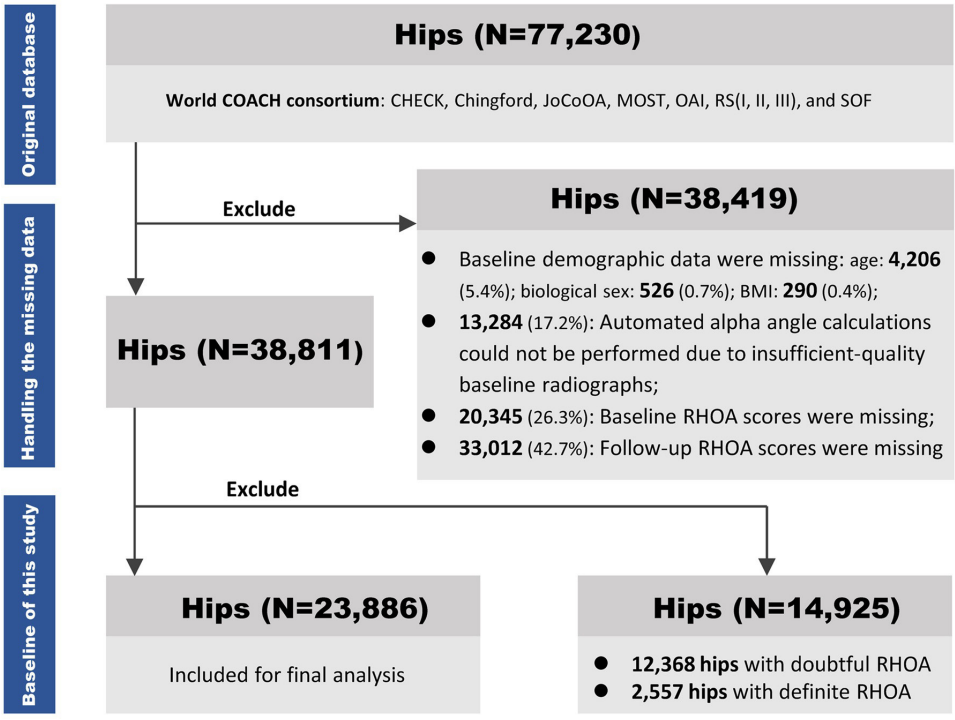

Figure 2 Complete flow of hips from the original dataset to the baseline of this study. BMI, body mass index; CHECK, Cohort Hip and Cohort Knee; JoCoOA, Johnston County Osteoarthritis Project; MOST, Multicentre Osteoarthritis Study; OAI, Osteoarthritis Initiative; RHOA, radiographic hip osteoarthritis; RS, Rotterdam Study; SOF, Study of Osteoporotic Fractures.

three age subgroups, and males showed a higher relative risk (2.50; 95% CI 1.67 to 3.73) compared with females.

DISCUSSION

In this IPD meta-analysis, cam morphology as well as a higher alpha angle was significantly associated with incident RHOA within 4–8 years. Using the largest sample size to date, standardised and repeatable automated measurement and excluding doubtful RHOA cases at baseline, this study provides a robust estimate. Also, the large sample allowed subgroup analysis, confirming that the strength of association was highest in males and in participants aged 51–60 years.

Our study confirmed that cam morphology is a notable risk factor for developing RHOA in individuals without any existing radiographic signs of hip OA. Early identification through simple radiographic measurements can help identify high-risk groups before symptoms develop. Early detection of cam morphology could promote preventive measures, including lifestyle and physical activity interventions, potentially mitigating the risk of developing RHOA. These findings highlight the importance of further investigating the aetiology of cam morphology and specifically primary cam morphology. Although primary cam morphology remains stable after skeletal maturity,[5] its formation could potentially be influenced during growth, making it a target for primary prevention.[32] Adolescents may benefit from targeted load management, periodised training and education.

Interestingly, our results suggest that the risk posed by cam morphology for developing RHOA may be slightly lower than previously reported. It was reported that not all shape variants captured by alpha angle ≥60° are relevant to RHOA development.[33] Future research may focus on further subclassifying cam morphology (eg, by shape or volume) and integrate imaging findings with clinical symptoms of FAI syndrome to improve risk prediction.[34]

Descriptive subgroup analyses, addressing our second aim, indicate that the risk of developing RHOA due to cam morphology does not consistently increase with age. Individuals aged 51–60 may especially benefit from preventative strategies. Additionally, males have a higher risk of RHOA than females, likely due to their higher mean alpha angle, which is associated with cartilage defects and labral tears[35] and the absolute higher prevalence of cam morphology. These insights highlight the need to consider various demographic and physical characteristics in RHOA prevention strategies.

The considerable variability in previous findings may stem from differences in population, alpha angle measurement and RHOA definition. First, demographic characteristics varied widely in previous studies, such as a mean age <50 years[35] versus >60 years[10], a mean BMI >30[36] versus <26[37] and asymptomatic

Table 1 Difference in characteristics between included and excluded hips at baseline

	Baseline of this study		
Baseline characteristic	Included hips (n=23 886)	Excluded hips (n=14 925)	P value
Age in years: mean (SD)	62.21 (8.36)	65.40 (8.43)	<0.001
Women, no (%)	16 875 (70.6)	10 636 (71.3)	0.195
BMI, kg/m²: mean (SD)	27.35 (4.48)	27.56 (4.75)	<0.001
Alpha angle, °: mean (SD)	46.40 (10.17)	48.11 (11.98)	<0.001
Cam morphology: no (%)	2271 (9.51)	2128 (14.26)	<0.001
No RHOA: no (%)	23 886(100)	0 (0)	–
Doubtful RHOA: no (%)	0 (0)	12 368 (82.90)	–
Definite RHOA: no (%)	0 (0)	2557 (17.10)	–

Standard independent t-test for age and Welch's t-test for BMI and alpha angle to account for unequal variances were used.
BMI, body mass index; RHOA: radiographic hip osteoarthritis.

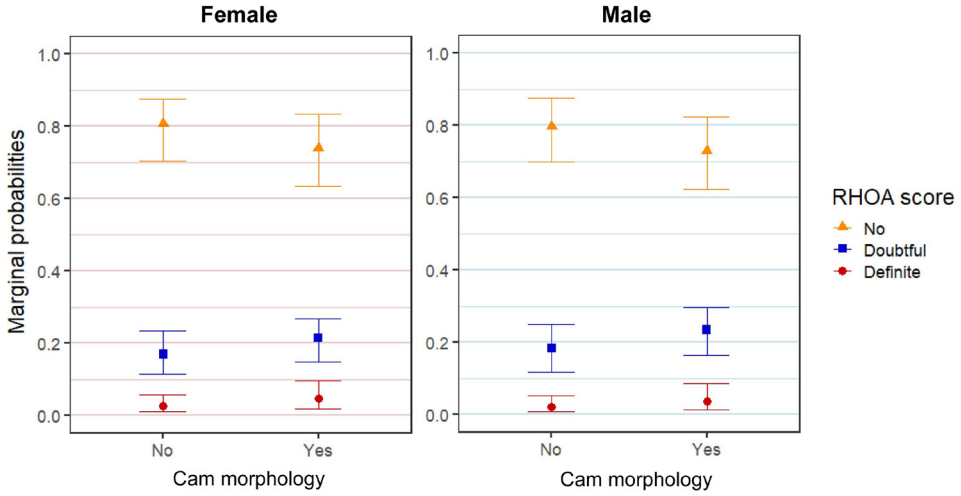

Figure 3 Effect plot of the marginal probabilities of RHOA within 4-8 years for females and males, aged 62 years, and BMI of 27 kg/m^2. BMI, body mass index; RHOA, radiographic hip osteoarthritis.

vs symptomatic individuals.[37] Lastly, some studies defined the development of RHOA as a transition from KL grade <3 at baseline to KL grade >3 at follow-up,[36] while others defined it as a KL grade ≥2 at follow-up from KL grade <2 at baseline. These inconsistencies limit generalisability. By accounting for these variabilities, our study found a lower OR of 1.87 (95% CI 1.36 to 2.59), compared with previously reported results. The result for the continuous alpha angle showed similar lower strength (OR 1.02 (95% CI 1.01 to 1.03)), compared with previous OR of 1.63 (95% CI 1.58 to 1.67) found in the UK Biobank study.[38]

Excluding hips with doubtful RHOA at baseline likely accounted for the lower association strength compared with prior studies. Despite removing 12 368 such cases, the large sample size still allowed for robust analysis. Previous research often included doubtful cases in the non-RHOA groups, potentially during early RHOA transitions. Doubtful RHOA, characterised by uncertain joint space narrowing and possible osteophyte formation,[39–41] often precedes more definitive RHOA, thereby influencing outcomes. Our forward continuation ratio model confirmed higher marginal probabilities for developing both doubtful and definite RHOA in hips with cam morphology. For example, the CHECK study previously reported a 23.8% 8-year RHOA incidence,[37] while we observed 13% RHOA incidence in the same cohort with our updated criteria. Including doubtful cases may overestimate RHOA prevalence and misclassify baseline cam morphology, as early RHOA signs can elevate alpha angle readings. This was supported by our findings: excluded hips displayed larger alpha angles than those included, suggesting early structural changes indicative of RHOA progression. This study is the first to apply a methodology that establishes a clear association between cam morphology and RHOA without the influence of doubtful RHOA. We recommend that future research adopt a similar strategy, provided that the sample size is sufficient to support robust analyses.

While an AP radiograph is not the gold standard for measuring cam morphology, its effectiveness in predicting RHOA has been demonstrated in our findings and previous studies.[11 42] Cam morphology is a three-dimensional structure, and different planes in CT and MRI images provide more detailed information. However, the use of CT and MRI for large-scale screening is limited; CT and MRI scans are time-consuming, expensive and require specialist facilities and radiologists. Therefore, radiographs may be the best solution as a screening tool for large samples. Although lateral views (eg, Dunn 45 or frog-leg) are more sensitive for detecting cam morphology, they are less commonly used than AP views in most cohort studies. Cam morphology is mostly located at the anterosuperior part of the femoral head–neck junction, and the more superiorly located cam morphologies are captured well on AP views.[43] Our sensitivity analysis, which excluded the MOST study with full-limb radiographs, indicates that minor differences in radiographic protocol had a limited impact on the results of this study.

Table 2 Absolute risk and relative risk for developing radiographic hip osteoarthritis stratified by age, sex or body mass index groups

Subgroup		N (%)	Alpha angle, °: mean (SD)	Cam morphology: No (%)	RHOA		Absolute risk in % (95% CI)	Relative risk (95% CI)
					In hips with cam morphology	In hips without cam morphology		
Age in years	40–50	**2083** (8.7)	**48.27** (11.38)	**287** (13.8)	5	49	1.74 (0.23 to 3.26)	0.64 (0.26 to 1.59)
	51–60	**8155** (34.1)	**46.90** (10.56)	**853** (10.5)	43	171	5.04 (3.67 to 6.73)	2.15 (1.55 to 2.98)
	61–70	**9340** (39.1)	**45.84** (9.82)	**768** (8.2)	17	143	2.21 (1.29 to 3.52)	1.33 (0.81 to 2.18)
	Over 70	**4308** (18.0)	**45.78** (9.57)	**363** (8.4)	7	61	1.93 (0.78 to 3.93)	1.25 (0.57 to 2.71)
Biological sex	Female	**16 875** (70.6)	**44.26** (8.65)	**853** (5.1)	34	364	3.99 (2.78 to 5.53)	1.75 (1.24 to 2.48)
	Male	**7011** (29.4)	**51.56** (11.62)	**1418** (20.2)	38	60	2.68 (1.90 to 3.66)	2.50 (1.67 to 3.73)
BMI, kg/m^2	<25	**7880** (33.0)	**45.30** (9.82)	**602** (7.6)	24	169	3.99 (2.57 to 5.87)	1.72 (1.13 to 2.61)
	³25	**16 006** (67.0)	**46.95** (10.30)	**1669** (10.4)	48	255	2.88 (2.13 to 3.80)	1.62 (1.19 to 2.19)

BMI, body mass index; RHOA, radiographic hip osteoarthritis.

However, the potential influence of using full-limb radiographs may be underestimated due to the relatively small contribution of the MOST cohort (9% of the total sample).

Our analyses included participants' baseline age, biological sex and BMI as confounders. Structural changes of RHOA have been found to occur with increasing age and showed differences between sexes.[44] Although the causal association of obesity in the incidence and progression of OA is more pronounced in the knee joint compared with the hip,[45 46] recent studies suggest a potential causal role for obesity in hip OA as well.[47–49] Generally, obesity can lead to abnormal biomechanical loading on weight-bearing joints, as well as altered metabolism and inflammation.[50] Therefore, we included BMI as a confounder in analyses, despite obesity's inconclusive role in hip OA.

Limitations and strengths

This study has several limitations. First, limitations relating to our data. We relied solely on AP radiographs to quantify cam morphology. While we recognise the practicality of radiographs for large-scale studies, they are less detailed compared with MRI or CT scans and underestimate both the magnitude of the alpha angle and the prevalence of cam morphology. This underestimation may also differ by sex, due to subtle differences in the typical location of cam morphology between males and females.[51] In addition, ethnicity data were not included, as these were incomplete across part of the original datasets. Inclusion of ethnicity would therefore reduce the sample size of the current study. We acknowledge that incorporating this information could enhance generalisability of our findings. Our findings are also limited by the age demographics of our sample, with a mean age of 62 years, making them less applicable to individuals under 40 years old, as the age range spanned from 40 to over 70 years. In addition, we did not consider the influence of other hip morphologies, such as hip dysplasia or pincer morphology, which may also contribute to the development of RHOA and thus impact the association between cam morphology and RHOA.

Second, methodological limitations should be considered. Although the harmonised three-level RHOA grading system is the most appropriate approach for a study of this scale, we acknowledge that variability in assessors' experience and grading protocols across part of the original cohorts could have influenced the results. Additionally, the inter-rater and inter-method ICCs for alpha angle measurements were low to moderate, potentially limiting the sensitivity of this metric for identifying individuals at risk. Additionally, we only adjusted for age, biological sex and BMI, so unmeasured confounders may be of importance in the association and should be studied in future work.

Important strengths of this analysis include the combination of populations from diverse cohorts, uniform calculation for alpha angle and more strict definition for the development of RHOA, supporting the robust and generalisable nature of our findings.

CONCLUSION

Cam morphology defined by alpha angle ≥60° measured on AP pelvic radiographs and greater continuous alpha angles is associated with the development of RHOA over 4–8 years follow-up. Our results highlight the need for research on primary and secondary prevention of cam morphology development and its early hip disease consequences. Such measures could impact the development and burden of hip OA.

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