Subclinical deformities of the hip are significant predictors of radiographic osteoarthritis and joint replacement in women. A 20 year longitudinal cohort study

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Abstract

Objective

Femoroacetabular Impingement (FAI) and Acetabular Dysplasia are common deformities, which have been implicated as a major cause of hip osteoarthritis (OA). We examined whether these subtle deformities of the hip are associated with the development of radiographic OA and total hip replacement in women.

Design

A population-based, longitudinal cohort of 1003 women underwent pelvis radiographs at years 2 and 20. Alpha angle, Triangular Index Height, Lateral Centre Edge (LCE) angle and Extrusion Index were measured. An alpha angle of greater than 65° was defined as Cam-type FAI. Radiographic OA and the presence of a total hip replacement were then determined at 20 years.

Results

Cam-type FAI was significantly associated with the development of radiographic OA. Each degree increase in Alpha angle above 65° was associated with an increase in risk of 5% (OR 1.05 [95% CI 1.01-1.09]) for radiographic OA and 4% (OR 1.04 [95% CI 1.00-1.08]) for total hip replacement. For Acetabular Dysplasia, each degree reduction in LCE angle below 28 degrees was associated with an increase in risk of 13.0% (OR 0.87 [95% CI 0.78-0.96]) for radiographic OA and 18% (OR 0.82 [95% CI 0.75-0.89]) for total hip replacement.

Conclusions

This study demonstrates that Cam-type FAI and mild Acetabular Dysplasia are predictive of subsequent OA and total hip replacement in a large female population cohort. These are independent of age, BMI and joint space and significantly improve current predictive models of hip OA development.
INTRODUCTION

Osteoarthritis (OA) of the hip is a common disease, with a cumulative prevalence of up to 27% [1-4]. The mortality adjusted lifetime risk of Total Hip Replacement (THR) at age 50 is 12% [5]. Losses of earnings due to disability and direct treatment costs have made OA and other rheumatic diseases among the most expensive of all items in any healthcare budget and a major burden to society. Health expenditure towards arthritis related care represents 2.5% of the United States’ entire Gross Domestic Product [6]. Hip Replacement accounts for almost half of the hospitalization costs associated with OA [7], with over three hundred thousand total hip replacements performed in the United States in 2011 [8], which is projected to increase to five hundred and seventy four thousand by 2030 [9].

Historically, 10% of hip OA has been termed secondary and attributed to major deformities of the hip, such as developmental acetabular dysplasia, Legg-Calvé-Perthes disease or slipped capital femoral epiphysis [10]. The remaining 90% of hip OA was termed ‘primary’ or ‘idiopathic’ and presumed some underlying abnormality of articular cartilage. For nearly 50 years authors have suggested some relationship between more subtle deformities of the proximal femur and/or acetabulum and subsequent development of OA of the hip [10-12]. More recently cross-sectional studies have supported this theory; although cannot prove causality [13]. These deformities can be broadly divided into milder forms of acetabular dysplasia, which results in a shallow hip socket, and Femoroacetabular Impingement (FAI), which describes morphological abnormalities of the femoral head-neck junction, acetabulum, or both [14]. Both can be quantified using measurements taken on plain radiographs. These deformities are thought to result in a focal mechanical overload of articular cartilage, leading to subsequent osteoarthritis and joint replacement [14].

FAI and acetabular dysplasia are prevalent and are common in patients with established osteoarthritis of the hip, with concomitant hip malformations seen in 36.6% of women and 71.0% of men with hip osteoarthritis [13]. However, it is not known whether these malformations pre-date or are a result of the OA pathogenic process. Though temporal sequence alone does not prove causality, when combined with the potential mechanism by which impingement or increased contact stress may lead to cartilage damage the likelihood of a causal relationship increases. If the radiographic measurements of mild acetabular dysplasia and FAI are predictive of developing hip OA, they may represent targets for preventative strategies and treatment. Surgical interventions, such as osteotomy and osteochondroplasty have already been developed for these conditions, though their treatment efficacy is unproven. Pharmaceutical and
physical treatments may also become available in the near future[15]. Such interventions may ultimately reduce the burden of end-stage hip osteoarthritis and THR.

The aim of this study was to determine whether subtle deformities of the hip are associated with the development of radiographic osteoarthritis and end-stage OA (defined by THR) in a population based prospective cohort. To date, no studies have been able to assess the role of hip morphology in the development of structural change and THR in a population cohort without disease at baseline, making this a unique project. Our hypothesis was that a causal relationship exists between subtle deformities of the hip and subsequent osteoarthritis.

METHODS

Study Participants

The Chingford 1000 Women Study is a population-based cohort of 1003 women living in the United Kingdom. In 1989, women registered at a general practice in London of the age range 44-67 years (mean 54.2) were invited to participate in a study assessing musculoskeletal disease, with yearly clinic visits; morphometric, clinical, biologic, and radiographic measurements were obtained at these visits. Standardised supine Anterio-Posterior (AP) pelvis radiographs were taken at years 2, 8 and 20. The local ethics committee approved the study and written consent was obtained from each woman (Outer North East London Research Ethics Committee (formerly Barking & Havering and Waltham Forest RECs), LREC (R&WF) 96). Figure 1 shows flow of participants from the recruitment of the cohort to the final study populations.

Exclusions

Exclusion criteria were applied to ensure that year 2 radiographs were of a minimum acceptable standard. Twenty individuals were excluded due to poor radiograph quality. Poor radiograph quality was a subjective exclusion criterion applied by the principal investigator when a radiograph was either grossly over- or underexposed to the extent that constituent anatomic landmarks were not visible for the purposes of analysis. Five hip joints (3 individuals) were excluded because they already had a THR in situ. Five hip joints (5 individuals) were excluded because it had a dynamic hip screw in situ, indicating previous femoral neck fracture. Seventy-two hip joints (36 individuals) were excluded because they had excessive rotation (measured using Obturator Foramen Index, reference range 0.7 – 1.4) or tilt (measured according to the distance between the sacrococcygeal joint and the pubic symphysis)[16]. A total of 119
hips in 61 individuals were excluded. Baseline characteristics of those excluded from analysis were not significantly different from those included in the analysis.

**Radiographic assessment of morphology**

Hip morphology was analysed using a validated software package called HipMorf 2.0[17]. We used two radiological measurements for Acetabular dysplasia and Pincer-type FAI; the LCE angle [18] and Extrusion Index[19, 20]. LCE measures acetabular coverage of the femoral head and Extrusion Index measures the proportion of femoral head located within the acetabulum. A low LCE indicates acetabular dysplasia, while a high LCE is indicative of Pincer-type FAI. The converse is true with respect to Extrusion Index. Two measurements for Cam-type FAI were also used; the Alpha angle[21, 22] and Gosvig’s Triangular Index Height (the perpendicular height of the femoral head/neck at 1/2r along the femoral neck axis, where r is the radius of the femoral head)[17]. These measurements are in routine clinical use and can be made on standard anterior-posterior pelvis radiographs. Each radiograph was anonymised. All morphological measurements were performed by the principal investigator (GERT), blinded to outcome. Reproducibility of hip morphology measurement was assessed with intra-observer ICC in excess of 0.75 for all measures and inter-observer ICC in excess of 0.81.

**Radiographic assessment of OA**

At baseline (Year 2, n=787) and at Year 20 (n=487) radiographs were scored 'blind' to clinical details according to the method of Kellgren and Lawrence (K & L)[23] using the Atlas of Standard Radiographs by a single trained clinician (GERT). OA was defined as K & L ≥ 2.

**Total Hip Replacement (End-stage Hip Osteoarthritis)**

Details of any operations undergone in the previous year are recorded at each Chingford visit. Confirming that a patient had undergone THR for end-stage OA was done by contacting the patient’s general practitioner and checking the medical records at the hospital at which the surgery was performed.

**Statistical Analysis**

The distribution of morphological measurements (LCE, Alpha Angle, Extrusion Index and Triangular Index Height) was examined using histograms and kernel density plots. Normally distributed variables were compared using the independent 2-tailed Student’s t-test; non-normally distributed variables were compared using the Wilcoxon rank sum test. Participants were only included in an analysis if they had not had the outcome at the start of the study; that is no radiographic OA (K & L < 2) or no THR at baseline. Outcomes were assessed at year 20 according to whether or not the patients had 1) Radiographic OA; 2)
THR. A sensitivity analysis was also performed for development of Radiographic OA which included only hips with baseline K & L = 0.

The morphological measurements detailed above were the predictors of interest. We visually assessed evidence of linearity of continuous variables with the outcomes using fractional polynomial plots (see Figure 2). Where evidence of non-linearity was observed, variables were fitted with linear splines. Lateral Centre Edge angle was fitted as a linear spline using tertiles (27.96° and 33.67°). This is consistent with clinical observations, as acetabular over and under-coverage are both implicated in the development of OA. Alpha angle was fitted as a linear spline at 65°, the antimode of its bimodal distribution. Logistic regression analysis was performed to describe the crude (univariate) association of the predictors listed above with radiographic OA and THR as binary outcomes. Secondary analyses were performed by further adjusting for confounders of baseline age, BMI and joint space width. Interactions between the acetabular and femoral morphological measurements were explored. Logistic regression analyses were with robust standard errors and clustering by subject identifier to account for the dependency of two hips from one subject. Area Under Receiver Operating Characteristic (AUROC) as well as McFaddens's pseudo $R^2$ statistic were used to evaluate the discriminatory ability of the morphological measurements. The cut point for non-linearity was examined for alpha angle, as a function of radiographic osteoarthritis and THR. The alternative 'statistical' cut points were determined using fractional polynomial regression modelling which provides a visual assessment of the relationship of alpha angle with outcome (Figure 2), and cut points specific to each outcome chosen on this basis. Logistic regression with these thresholds was performed.
RESULTS
The baseline characteristics of the participants included in this study are summarised in Table 1. 358 participants (670 hips) were included in the analysis of radiographic OA and 726 (1455 hips) in the THR analysis. Participants included were younger. In the radiographic OA analysis participants included were found to be taller (Table 1).

Radiographic OA
Incident radiographic OA was seen in 11% of hips at Year 20 (37% of OA was bilateral).

Femoral measures
Alpha angle and triangular index height were significantly greater in the radiographic OA versus no OA group (p<0.001 in both cases) (Table 2).

Triangular index height and increasing alpha angle above 65° were significantly associated with the development of radiographic OA, and remained significantly associated after adjusting for confounders (Table 3).

Acetabular measures
The acetabular measures, LCE and Extrusion Index were found to be similar in those with and without radiographic OA (Table 2).

Decreasing LCE angle below 28° was significantly associated with the development of radiographic OA, and remained significantly associated after adjusting for confounders.

When femoral and acetabular measures were included in the same model, with use of the same covariates, an alpha angle of greater than 65° was associated with a 5% increased risk of radiographic OA per degree increase in alpha angle (OR 1.05 [95% confidence interval [95% CI] 1.01-1.09]), the increase in risk of radiographic OA per 1° reduction in lateral centre edge angle below 28° was 14% (OR 0.86 [95% CI 0.77-0.96]). Over coverage, consistent with Pincer FAI, was not significantly associated with radiographic OA.

ROC AUC statistic for non-morphological covariates (age, BMI, joint space width) alone as predictors of incident radiographic OA was 57.5% and increased significantly to 66.7% with the inclusion of both LCE and alpha angle (p<0.001). McFadden’s pseudo $R^2$ statistic increased from 1.21% to 7.48% (Table 4).

Total Hip Replacement
Total Hip Replacement was performed on 31 individual (40 hips, 3%).
Femoral measures

Alpha angle and triangular index height were both significantly greater in hips that went on to undergo THR.

Triangular index height was significantly associated with Total Hip Replacement and remained significantly associated when adjusting for the covariates (OR 1.14 [95% CI 1.00-1.30]). Alpha angle was significant in only the univariate analysis (OR 1.04 [95% CI 1.00-1.08]), (Table 3).

Acetabular measures

Acetabular dysplasia at baseline was significantly more common in hips that went on to undergo THR (mean LCE 25.94°, SD 7.53°, mean Extrusion Index 0.25 SD 0.09) than non-THR (LCE 30.94°, SD 6.78° Extrusion Index 0.18, SD 0.08), p<0.001 in both cases.

Univariate logistic regression showed that low lateral centre edge was significantly associated with THR and remained significantly associated when adjusting for the same covariates (OR 0.77 [95% CI 0.63-0.93]).

When femoral and acetabular measures were included in the same model, with use of the same covariates, triangular index height was associated with THR with a 19% increase per unit (OR 1.19 [95% CI 1.01-1.40]). The increase in risk of radiographic OA per 1° reduction in lateral centre edge angle below 28° was 21% (OR 0.79 [95% CI 0.72-0.87]).

ROC AUC statistic for non-morphological covariates as predictors of THR was 63.73% and increased significantly to 83.36% with the inclusion of LCE, alpha angle and triangular index height (p<0.001). McFadden's pseudo R² statistic increased from 4.75% to 22.84% (Table 4).

Alpha Angle Thresholds by Outcome

The cut point for non-linearity varies according to outcome, statistically the threshold for non-linearity for Alpha Angle with Radiographic OA is 41° and with THR is 82° (Figure 2 and Table 5). Logistic regression with these thresholds showed that each degree increase in alpha angle increased the risk of developing radiographic OA by 3% (OR 1.03 [95% CI 1.02-1.05]) and THR by 6% (OR 1.06 [95% CI 1.01-1.11]).
Sensitivity Analysis

Inclusion of only hips with no signs of radiographic osteoarthritis (K&L Grade 0 – Radiographic Osteoarthritis Analysis 556 hips), resulted in no significant change to the results discussed above. (See Appendix).
DISCUSSION

This study of a population-based cohort confirms our hypothesis and demonstrates that radiographic measurements of subtle hip deformities are associated with the longitudinal development of hip osteoarthritis and THR. We found that the deformities associated with Cam-type FAI and mild acetabular dysplasia of the hip were independently predictive of radiographic osteoarthritis and THR 19 years later. These measurements were independently predictive of outcome even when controlling for baseline age, BMI and joint space width and significantly increased the predictive value of the model. This is the first study to demonstrate these findings in a longitudinal population cohort.

FAI has been extensively documented as a cause of groin pain[24]. Whilst associations of abnormal morphology and OA are established[13, 25], prospective longitudinal data, which may provide more convincing evidence of a causal relationship, is lacking. Previous studies examining the development of OA have focused on acetabular dysplasia[26, 27]. Two recent studies have associated cam deformity with OA, but are limited by their cross-sectional nature and used outcome measures which may not be as relevant as using the hard endpoint of THR for example[13, 28]. Longitudinal data is limited to a nested case control using the Chingford cohort[17] and an enriched cohort of symptomatic osteoarthritis patients[29], both of which showed as significant association of Cam-type FAI with THR.

This work demonstrates that women with a Cam-deformity identified by an alpha angle of greater than 65 degrees have an increased risk of radiographic OA and THR with each degree increase in alpha angle conferring a 5% and 3% increase in risk respectively. More severe Cam-type deformities identified by increased triangular index height are predictive of THR at 19 year follow-up with each unit increase conferring a 19% increased risk.

Mild acetabular dysplasia significantly increased the risk of radiographic OA development and THR with each degree reduction in lateral centre edge angle below 28° associated with a 14% and 21% increase in risk respectively, these results are consistent with previously published evidence in relation to incident radiographic OA by Lane et al.[30]. Traditionally the LCE angle is considered normal above 25°, borderline between 20° and 25° and dysplastic below 20°. No significant associations were seen with Pincer-type FAI alone. Evaluation of the models showed statistically significant improvements in our ability to predict radiological OA and THR (p<0.001 in both cases) with the inclusion of morphological measurements as compared to established risk factors of age, BMI, joint space width.
Although we have chosen these thresholds for non-linearity based on the data distribution this statistically might not be the case. On further exploration it was found that the cut point for non-linearity varies according to outcome. The statistical threshold for non-linearity for Alpha Angle with Radiographic OA is 41° and with THR is 82°. When using these statistical thresholds we see a more pronounced association, with a risk increase for THR of 6% per degree when the alpha-angle is greater than 82°. These two methods for calculating the thresholds for non-linearity may have different clinical applications. The use of a threshold based on the distribution has a lower cut off with a lower specificity and a higher sensitivity for OA and THR. These lower thresholds may be used for low-risk treatments for OA. For example, a physical therapy or weight loss treatment might use the lower threshold of 65°. Conversely, a more invasive intervention, such as surgery may wish to identify those patients with a higher risk using a threshold of 80°, which has a higher specificity. Non-linearity should of course not be interpreted as a threshold for clinical intervention, the sensitivity, specificity and level of risk associated with these thresholds requires further evaluation in order allow their use in treatment decisions.

It has been proposed that FAI leads to shear forces being applied to acetabular cartilage with displacement of the labrum[31]. This may lead to delamination of the acetabular cartilage, and detachment of the labrum at the chondro-labral junction. Developmental dysplasia leads to increased contact stress and cartilage degeneration[32]. The mechanism by which morphological abnormalities lead to OA are likely to be similar in both men and women.

This study has several strengths and potential limitations. This is the only cohort study at present which includes long term follow up in a normal population with validated records of THR. Loss to follow-up appears to be non-differential, and expected with the median age of the cohort reaching seventy four. In addition only women are included in the study. Baseline characteristics of women in the study were similar to the UK general population in terms of weight (65 kg in the UK, 67 kg in Chingford), height (1.61 m v 1.62 m) and BMI (25.4 v 25.6 kg/m²)[33]. This study did not consider a wide range or ethnic groups, as 98% of the women were white and predominantly middle class (but with a range of all social groups) The use of anteroposterior pelvis radiographs only for the assessment of morphology must be acknowledged as a limitation, while lateral projections of the hip are more sensitive for detecting FAI no large population cohort exists which includes this imaging. In addition radiographic OA was not considered as an exclusion criteria in the THR analysis.
Cam-type FAI appears to be twice as frequent in men as in women[25, 34], and acetabular dysplasia approximately 20% more frequent in women as in men[13]. The role of Cam-type FAI in OA may therefore be underestimated in this population cohort and a long-term epidemiological study involving male subjects is needed to confirm the natural history of these anatomical abnormalities in men.

In summary this study provides longitudinal evidence in a large population cohort that measurements of hip morphology characteristic of Cam-type FAI and undiagnosed dysplasia are predictive of OA development (radiographic OA and THR), independent of age, BMI and joint space width. These measurements can be made on a simple anteroposterior pelvis radiograph, and significantly improve our ability to identify individuals at risk of hip OA development. Pincer-type FAI was not predictive of subsequent OA or total hip replacement.
ACKNOWLEDGMENTS

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CONTRIBUTIONS

All authors made substantial contributions to the conception and design of the study, or acquisition of data, or analysis and interpretation of data. GERT drafted the article and all authors were involved in revising it critically for important intellectual content as well as final approval of the version to be submitted.

FUNDING

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COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

NKA has received consultancy fees from Merck, Roche, Smith & Nephew, Q-Med, Nicox and Flexion, grants from Novartis and Schering-Plough, and payment for lectures from Novartis, Schering-Plough, Smith & Nephew, Q-med, Servier, GSK, Amgen, Schering-Plough, Rottapharm and Lilley. SGJ has received consultancy fees, grants and payment for lectures from Zimmer.
References


Appendix: Sensitivity Analysis Baseline K&L Grade = 0 - Radiographic Osteoarthritis Analysis 556 hips

**Logistic regression: Hip morphology at Year 2 Predicting 20 Year Outcome, OR (95% CI)**

<table>
<thead>
<tr>
<th>Hip Morphological variables</th>
<th>Radiographic Osteoarthritis (baseline KL Grade=0)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariate</td>
</tr>
<tr>
<td></td>
<td>OR (95% CI) p-value</td>
</tr>
<tr>
<td>Alpha Angle</td>
<td></td>
</tr>
<tr>
<td>&lt;65 (per unit)</td>
<td>1.00 (0.95, 1.06) 0.862</td>
</tr>
<tr>
<td>&gt;65 (per unit)</td>
<td>1.04 (1.00, 1.09) 0.05</td>
</tr>
<tr>
<td>LCE</td>
<td></td>
</tr>
<tr>
<td>&lt;28 (per unit)</td>
<td>0.85 (0.76, 0.95) 0.004</td>
</tr>
<tr>
<td>28-33.7 (per unit)</td>
<td>1.18 (1.00, 1.38) 0.044</td>
</tr>
<tr>
<td>&gt;33.7 (per unit)</td>
<td>0.99 (0.88, 1.10) 0.801</td>
</tr>
<tr>
<td>Extrusion Index (per SD)</td>
<td>1.10 (0.71, 1.71) 0.672</td>
</tr>
<tr>
<td>Triangular Index Height (per unit)</td>
<td>1.10 (0.97, 1.23) 0.124</td>
</tr>
</tbody>
</table>

*adjusted for Age, BMI and Joint Space

Area Under Receiver Operating Characteristic (AUROC) statistic as well as McFadden's pseudo R² statistic were used to evaluate the discriminatory ability of the morphological measurements

<table>
<thead>
<tr>
<th>Radiographic Osteoarthritis (baseline KL Grade=0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model with Age, BMI, Joint Space</td>
</tr>
<tr>
<td>R2 AUC</td>
</tr>
<tr>
<td>0.69% 0.55 (0.47-0.62)</td>
</tr>
</tbody>
</table>

*Alpha Angle, LCE, MTIH

**Comparison of Logistic regression Analysis for association of Alpha Angle (univariately) with 20 Year Outcomes using Distribution and Statistical thresholds of non-linearity**

<table>
<thead>
<tr>
<th>Radiographic Osteoarthritis (baseline KL Grade=0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distribution Threshold OR (95% CI) p-value</td>
</tr>
<tr>
<td>Alpha Angle &lt;65 (per unit)</td>
</tr>
<tr>
<td>&gt;65 (per unit)</td>
</tr>
</tbody>
</table>
Figure 1
Flow Diagram summarising selection for inclusion and analyses

Figure 2
Fractional polynomial plots showing probability of outcome versus Alpha Angle (95% CI) - Non-linear effect demonstrated
Table 1: Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Full cohort (n=1003)</th>
<th>Radiographic Osteoarthritis</th>
<th>Total Hip Replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Subjects not used in this analysis (n=663)</td>
<td>Subjects used in this analysis (n=340)</td>
<td>p-value</td>
</tr>
<tr>
<td>Age (years), median (IQR)</td>
<td>54.00 (49.00, 60.00)</td>
<td>57.00 (50.50, 61.00)</td>
<td>52.00 (48, 56)</td>
</tr>
<tr>
<td>Height (m), mean (s.d.)</td>
<td>1.62 (0.06)</td>
<td>1.61 (0.06)</td>
<td>1.62 (0.06)</td>
</tr>
<tr>
<td>Weight (kg), median (IQR)</td>
<td>65.00 (58.50, 73.00)</td>
<td>65.70 (58.45, 73.75)</td>
<td>64.6 (58.50, 71.80)</td>
</tr>
<tr>
<td>BMI (kg/m²), median (IQR)</td>
<td>24.86 (22.63, 27.61)</td>
<td>25.15 (22.67, 28.19)</td>
<td>24.59 (22.60,27.01)</td>
</tr>
</tbody>
</table>
Table 2. Hip Morphology At Year 2

<table>
<thead>
<tr>
<th>Hip Morphological Variable</th>
<th>Control (n=564)</th>
<th>Radiographic OA at Year 20 (n=70)</th>
<th>p-value</th>
<th>Control (n=1426)</th>
<th>Total Hip Replacement (n=40)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCE, mean (SD)</td>
<td>30.56 (6.44)</td>
<td>30.03 (8.11)</td>
<td>0.456</td>
<td>30.94 (6.78)</td>
<td>25.94 (7.53)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Extrusion Index, mean (SD)</td>
<td>0.25 (0.11)</td>
<td>0.26 (0.15)</td>
<td>0.4563</td>
<td>0.18 (0.08)</td>
<td>0.25 (0.09)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alpha angle*, median (IQR)</td>
<td>46.47 (43.53, 55.23)</td>
<td>55.81 (44.09, 87.60)</td>
<td>&lt;0.001</td>
<td>46.75 (43.53, 58.83)</td>
<td>73.10 (47.47, 94.57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triangular Index Height*, mean (SD)</td>
<td>22.90 (2.09)</td>
<td>23.69 (2.52)</td>
<td>&lt;0.001</td>
<td>22.97 (2.12)</td>
<td>24.15 (3.13)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*P-values in this analysis are a guide only, and do not account for clustering
Table 3: Logistic regression: Hip morphology at Year 2 Predicting 20 Year Outcome, OR (95% CI)

<table>
<thead>
<tr>
<th>Hip Morphological Variable</th>
<th>Radiographic Osteoarthritis</th>
<th>Total Hip Replacement</th>
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<tbody>
<tr>
<td></td>
<td>Crude (Univariate)</td>
<td>Adjusted*</td>
</tr>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>p-val</td>
</tr>
<tr>
<td>Alpha Angle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 (per unit)</td>
<td>0.99 (0.95, 1.04)</td>
<td>0.818</td>
</tr>
<tr>
<td>&gt;65 (per unit)</td>
<td>1.05 (1.01, 1.09)</td>
<td>0.008</td>
</tr>
<tr>
<td>LCE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;28 (per unit)</td>
<td>0.89 (0.81, 0.98)</td>
<td>0.017</td>
</tr>
<tr>
<td>28-33.7 (per unit)</td>
<td>1.10 (0.95, 1.27)</td>
<td>0.199</td>
</tr>
<tr>
<td>&gt;33.7 (per unit)</td>
<td>1.03 (0.93, 1.15)</td>
<td>0.539</td>
</tr>
<tr>
<td>Extrusion Index (per SD)</td>
<td>1.09 (0.74, 1.61)</td>
<td>0.67</td>
</tr>
<tr>
<td>Triangular Index Height (per unit)</td>
<td>1.14 (1.03, 1.26)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

* adjusted for Age, BMI and Joint Space
Table 4: Area Under Receiver Operating Characteristic (AUROC) statistic as well as McFadden’s pseudo R2 statistic were used to evaluate the discriminatory ability of the morphological measurements.

<table>
<thead>
<tr>
<th>Radiographic Osteoarthritis</th>
<th>Total Hip Replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model with Age, BMI, Joint Space</td>
<td>Model + Morph Variables*</td>
</tr>
<tr>
<td>R²</td>
<td>AUC (95% CI)</td>
</tr>
<tr>
<td>1.21%</td>
<td>0.57 (0.49-0.64)</td>
</tr>
</tbody>
</table>

*Alpha Angle, LCE, TH
Table 5: Comparison of Logistic regression Analysis for association of Alpha Angle with 20 Year Outcomes using Distribution based and Statistical thresholds of non-linearity

<table>
<thead>
<tr>
<th></th>
<th>Distribution Threshold</th>
<th>OR (95% CI)</th>
<th>p-val</th>
<th>Statistical Threshold</th>
<th>OR (95% CI)</th>
<th>p-val</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radiographic Osteoarthritis</strong></td>
<td>Alpha Angle</td>
<td></td>
<td></td>
<td>Alpha Angle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 (per unit)</td>
<td>0.99 (0.95, 1.04)</td>
<td>0.818</td>
<td></td>
<td>&lt;41 (per unit)</td>
<td>0.55 (0.39, 0.78)</td>
<td>0.001</td>
</tr>
<tr>
<td>&gt;65 (per unit)</td>
<td>1.05 (1.01, 1.09)</td>
<td>0.008</td>
<td></td>
<td>&gt;41 (per unit)</td>
<td>1.03 (1.02, 1.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Total Hip Replacement</strong></td>
<td>Alpha Angle</td>
<td></td>
<td></td>
<td>Alpha Angle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 (per unit)</td>
<td>1.02 (0.97, 1.08)</td>
<td>0.384</td>
<td></td>
<td>&lt;82 (per unit)</td>
<td>1.02 (1.00, 1.05)</td>
<td>0.045</td>
</tr>
<tr>
<td>&gt;65 (per unit)</td>
<td>1.04 (1.00, 1.08)</td>
<td>0.038</td>
<td></td>
<td>&gt;82 (per unit)</td>
<td>1.06 (1.01, 1.11)</td>
<td>0.011</td>
</tr>
</tbody>
</table>
Figure 1: Flow diagram summarising selection for inclusion and analyses

Invited to participate (n=1353)

Participating at baseline data collection (n=1003)

Participating at Year 2 with adequate AP Pelvis Radiographs (n=793)

Excessive tilt/rotation = 110 hips (55 participants)
Prosthesis in situ = 10 hips (8 participants)

Morphology data at baseline
1466 hips (734 participants)

Death n = 199
Withdrawal from study n = 128
KL ≥ 2 at baseline = 90 hips (67 participants)

Radiographic Osteoarthritis Analysis
634 hips (340 participants)

Osteoarthritis (KL≥2): 70 hips (11%)
No Osteoarthritis(KL<2): 564 hips (89%)

Total Hip Replacement Analysis
1466 hips (734 participants)

THR: 40 hips (3%) in 31 participants
No-THR: 1426 hips (97%) in 725 participants