Predictors of total hip replacement in community based older adults: a cohort study

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ABSTRACT

Objective: The purpose of this study is to describe predictors of total hip replacement (THR) in community dwelling older adults. A better understanding of predictors of THR can aid in triaging patients and researching preventative strategies.

Design: At baseline, participants had assessment of radiographic OA and cam morphology (from pelvic radiographs), shape mode scores and hip bone mineral density (BMD; from dual energy X-ray absorptiometry (DXA)). After 2.6 and 5 years, participants reported hip pain using WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index), and had hip structural changes assessed using magnetic resonance imaging (MRI). Risk of THR was analysed using mixed-effect Poisson regression.

Results: Incidence of THR for OA over 14 years was 4.6% (37 / 801). As expected, WOMAC hip pain and hip radiographic OA both predicted risk of THR. Additionally, shape mode 2 score (decreasing acetabular coverage) (RR 1.83 per SD; 95% CI 1.1-3.04), shape mode 4 score (non-spherical femoral head) (RR 0.59/SD; 95% CI 0.36-0.96), cam morphology ($\alpha > 60°$) (RR 2.2/SD; 95% CI 1.33-3.36), neck of femur BMD (RR 2.09/SD, 95% CI 1.48-2.94) and bone marrow lesions (BMLs) increased risk of THR (RR 7.10/unit; 95% CI 1.09-46.29).

Conclusion: In addition to hip pain and radiographic hip OA, measures of hip shape, cam morphology, BMD and BMLs independently predict risk of THR. This

supports the role of hip bone geometry and structure in the pathogenesis of end stage hip OA and has identified factors that can be used to improve prediction models for THR.

Key words: hip osteoarthritis, total hip replacement, bone shape, bone mineral density, cam morphology, bone marrow lesions, predictors

INTRODUCTION

Hip osteoarthritis (OA) is a common musculoskeletal condition that is a major contributor to disability globally (1). There are currently no treatments available that prevent hip OA or slow the disease trajectory. Once disease is advanced, total joint replacement surgery is offered. Whilst these surgeries are successful and have high levels of patient satisfaction they are expensive and have a finite life (2). Better understanding of predictors of hip replacement provides some scope for prevention of hip replacement and may aid treatment decisions.

There is ongoing debate as to whether associations exist between radiographic and clinically defined hip OA. The inconsistent literature might be due to different definitions of hip OA, different radiographic protocols and scoring methods (3). However, both predict risk of total hip replacement (THR) (4). Recently, hip morphology has been identified as having an important role in the progression of hip OA (5-8). Particular patterns of hip shape such as reduced acetabular coverage, non-spherical femoral heads and cam impingement (abnormally shaped head of femur leading to abnormal contact between femoral head and acetabulum) predict progression of hip OA and risk of THR (8-11). Hip bone marrow lesions (BMLs), hip cartilage defects and higher bone mineral density (BMD) of the proximal femur are independent risk factors for progression of hip OA (12-17). Greater BMD also increases risk of THR; hip BMLs and cartilage defects may do likewise but these associations have not been studied (18, 19). No studies have reported on all these risk factors in the same population or community-based populations and few have adjusted for pain and/or radiographic osteoarthritis. When they have adjusted for these factors

the result for hip shape was no longer significant, suggesting these risk factors are not independent. (6). Thus, the aim of this study was to examine the effect of hip structural factors as risk factors for THR independent of hip pain and radiographic measures of hip OA in community dwelling older adults.

PATIENTS AND METHODS

Study design and setting

The Tasmanian Older Adult Cohort (TASOAC) study is a prospective, population-based cohort study, which aimed to identify factors associated with development and progression of OA and osteoporosis in older adults. Men and women aged 50-80 years in 2002 were selected from the electoral roll, which is the most complete population listing for adult Australians, in Southern Tasmania (population 229,000) using sex-stratified random sampling (response rate 57%). Participants were excluded if they lived in an aged care facility, or had standard contraindications to magnetic resonance imaging. The Southern Tasmanian Health and Medical Human Research Ethics Committee approved the study, and we obtained written informed consent from all participants.

Baseline data (Phase 1) were collected from February 2002 to September 2004 in 1099 participants. Follow up data (Phases 2 and 3) were collected on average 2.6 (n=875) and 5 years (n=769) later. Participants who had a hip replacement prior to Phase 2 were excluded from analyses in this manuscript (n=16).

Outcome: Total Hip Replacement

Incidence of primary THR was determined by data linkage to the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR), and includes data from both public and private hospitals. Data validation against State and Territory Health Department data is done using a sequential multi-level matching process (20). Matched data were then obtained; this included the date, side of joint replacement, primary or revision joint replacement and the reason for the procedure (e.g., OA, fracture of neck of femur, osteonecrosis, inflammatory arthritis, tumour). In this study, we only considered primary THRs that were due to OA. We include data from the AOANJRR between 1 March 2002 and 21 September 2016, which gives a follow-up period of 14 years. These data excluded participants who died, collected from the Tasmanian Death Registry or who left Australia, which was collected from TASOAC questionnaires.

BMI

Body mass index (BMI) was calculated (weight (in kilograms)/height (in metres)^2) using weight measured to the nearest 0.1 kg (with shoes, socks, bulky clothing and headwear removed) using a single pair of calibrated electronic scales (Seca Delta Model 707), and height measured to the nearest 0.1 cm (with shoes and socks removed) using a stadiometer.

Hip pain.

Self-reported hip pain over the past 30 days was assessed by questionnaire at Phase 2 using the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) index (8, 21). Briefly, the WOMAC pain scale has five items, each rated

on a 10-point numeric rating scale from 0 (no pain) to 9 (most severe pain). Each pain item was summed to create a total pain score (0–45).

Hip radiographs and assessment of hip radiographic OA (ROA) and cam morphology.

Anteroposterior radiographs of the pelvis were obtained at Phase 1, with the individual standing with both feet internally rotated by 10 degrees. Radiographs were read by two trained readers using the OARSI (Osteoarthritis Research Society International) grading system (22). Radiographic features of joint space narrowing (JSN) (axial and superior) and osteophytes (superior, acetabular and femoral) of both hips were graded separately on a 4-point scale (range 0–3 where 0 is no disease and 3 is severe disease. Data from these four features were summed (range 0-12). Any score other than 0 for either JSN or osteophytes was regarded as evidence of radiographic hip OA. Thus, after combining the JSN and osteophytes scores, the presence of radiographic hip OA was defined as a total score of 1 or greater.

The α angle measures the extent to which the femoral head deviates from spherical and is used to quantify cam morphology. It is measured by first drawing the best fitting circle around the femoral head, and then a line through the centre of the neck and the centre of the head. From the centre of the femoral head, a second line is drawn to the point where the superior surface of the head-neck junction first departs from the circle. The angle between these two lines is the α angle. We defined cam morphology by using a previously published standardised cut off point of 60° either in one or both hips (23). The α angle was

calculated from hip radiographs by drawing a circle of best fit based on the statistical shape modeling (SSM) points (SSM B) around the femoral head using custom code in MatLab (v 9.0). This method has good reliability as was shown previously with intraclass correlation coefficient (ICC) for inter-observer reliability of 0.73 and intra-observer reliability of 0.85-0.99 (9).

DXA Imaging and Statistical Shape Modelling (SSM)

Participants had dual-energy X-ray absorptiometry (DXA) images taken of the left hip, unless contra-indicated, using a Hologic Delphi densitometer (Hologic Inc., Waltham, MA, USA) as part of the Phase 1 assessment. Participants were excluded from DXA scanning if their weight exceeded 130 kg (n=3). Left hip images were used to assess bone mass; examined as areal BMD at neck of femur (g/cm^2). This is calculated by dividing the bone mineral content (BMC) by the area measured. Precision was estimated to be 2% *in vivo*.

Using DXA images and radiographs, two statistical shape models (SSM) were developed. SSM A was used to assess hip shape variation, while SSM B was used to calculate the alpha angle. SSM allows quantitative measurements of the whole hip joint on a continuum and incorporates many geometric measures that have been identified as risk factors for hip OA. (6) Briefly the proximal femur and acetabulum were modelled for each image using a template of 85 points placed on defined anatomical landmarks using the Active Shape Modelling toolkit (University of Manchester, UK) (24, 25). The images and points were transferred to the Shape software (University of Aberdeen, UK), where they were rotated and scaled using the Procrustes transform and then subjected to Principal

Component Analysis to generate independent, orthogonal modes of variation. The modes of variation were then normalized to a mean of 0 and expressed as standard deviations from the mean. The modes of variation described decreasing amounts of variation within the model with the first 6 modes describing 68% of the total model variation. To test reproducibility of the measures, two observers (HGA and FRS) assessed joint shape on ten images randomly selected from the TASOAC dataset. Point-to-point variability (the distance between equivalent points placed by each observer) was calculated. The distribution was not normal and the median was 1.6 pixels, which is a small difference given the image dimensions for all images are 252 x 258 pixels. Modes 2 (decreasing acetabular coverage) and 4 (aspherical femoral head), reflecting cam impingement and pistol grip deformity and likely some features of hip dysplasia, have previously been shown to predict THR in this cohort (8) and were the two modes analysed in this study.

Magnetic resonance imaging (MRI).

A subgroup (n=250) had MRI. The right hip was imaged in the sagittal plane during visits at phases 2 and 3 using a 1.5 Tesla GE Signa whole-body magnetic resonance scanner, as previously described (8). Subchondral BMLs and effusion-synovitis were assessed on the short T1 inversion recovery (STIR)–weighted, fat saturation, 2-dimensional fast spin-echo sequence using OsiriX software (Mac version, University of Geneva, Geneva, Switzerland). BMLs were identified as areas of increased signal intensity adjacent to the subchondral bone on the femoral head and/or the acetabulum (8). Intraobserver repeatability was assessed in 25 subjects (at both time points), with a 2-week gap between the

measures. The intra-class correlation coefficient for hip BMLs was 0.98, similar to the reproducibility of our knee quantitative BML measure (26). Hip effusion-synovitis was identified and assessed in STIR images from phases 2 and 3. The observer (HGA) manually selected the MRI slice with the largest effusion-synovitis and determined the maximum cross-sectional area (CSA) of the bright region by manually drawing contours around the outer edges, as previously described. Inter-rater reliability was excellent (0.84) (8). BMLs and effusions were dichotomised as present (CSA >0) or absent (CSA=0).

Statistical analysis

Differences between participants who did and did not have hip replacements were assessed using Students' t-tests and chi-squared tests.

Risk of THR in addition to the 'base model' (WOMAC hip pain score, and radiographic hip OA score) was assessed using mixed-effect Poisson regression, in which each potential risk factor was designated as a fixed effect and participant identification as a random effect. The base model was chosen as the features that best represent hip OA and determine the need for a THR and we were interested in additional independent features that predict need for THR. Models were run for each hip separately using Stata's xt function, which enabled us to run side-specific models concurrently. WOMAC pain score and data from radiographs (ROA and alpha angle) used for risk of THR of each hip, while data from DXA (BMD and SSM) and MRI (BML, effusion) had data from one hip only (left hip for DXA, right hip for MRI) and was used to predict risk of THR in either hip. Standard errors were adjusted using the sandwich (robust) estimator of

variance. Given the data was collected at different time points and not all participants had complete data, models were run based on available data, number of participants in each model is indicated in Table 2. All models included the base model (hip ROA and hip pain). Optimal models were chosen by comparing models and using the model with the best fit. Standard model diagnostics were performed. We used WOMAC hip pain as continuous data (range 0-35), but collapsed radiographic hip OA scores into categories as effect sizes were similar within groups. The relationship between each of the risk factors and the incidence of THR during follow-up was assessed using Cox proportional hazards regression models. Two sets of stratified analyses were performed in survival analyses. The first of these evaluated the effect of different combinations of categorical hip pain (no pain [WOMAC score=0], mild [WOMAC score ranged from 1 to 3] and modest-to-severe pain [WOMAC score greater than 3]) based on Kapstad et al (27) and radiographic hip OA (yes or no) on the risk of THR. The second stratification analysis evaluated the effect of cam impingement on the risk of THR, with adjustment for hip pain and radiographic hip OA.Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated. Model assumption was checked and confirmed using the proportional hazards test. We performed a sensitivity analysis, using a competing risk regression model to account for competing risks, which occurred within the study time frame (death, left Australia).

We used Stata 15.0 (StataCorp LP) for all statistical analyses. Statistical significance was defined as a p value ≤0.05 (two tailed).

RESULTS

Eight hundred and one (801) participants had WOMAC hip pain data and data on radiographic hip grade. Of these, 37 individuals had at least one THR for OA after the Phase 2 follow up; 13 participants had bilateral THR. Those who received a hip replacement were more likely to be smokers, have greater WOMAC hip pain scores, greater neck of femur BMD, more severe radiographic hip OA, more likely to have a BML, higher mode 2 and lower mode 4 shape scores, and were more likely to have cam morphology in either left or right hip (Table 1). Study participants were followed for an average of 12.1 years (maximum 14 years).

Table 1

As expected, WOMAC hip pain and radiographic hip OA predicted risk of THR. In addition, greater mode 2 scores (decreasing acetabular coverage) (Figure 1) and lower shape mode 4 scores (non-spherical femoral head) (Figure 2) predicted risk of THR. Cam morphology also increased risk of THR, as did higher BMD at the neck of femur. MRI detected BMLs increased the risk of THR, with significant associations with BMLs in the sub population with MRI available. Age, sex and BMI did not increase the risk of THR independent of WOMAC hip pain and radiographic hip OA (Table 2).

Figure 1

Figure 2

Predictors of total hip replacement

Table 2

We also investigated associations between hip ROA score, hip pain score and cam morphology with incidence of THR over time. The highest cumulative hazard (30% after 14 years of observation) was observed in participants with greater ROA score and higher pain scores (WOMAC pain score ≥4) (Figure 3). Similarly, cam morphology increased incidence of THR by approximately 10% over the study timeframe (Figure 4). Sensitivity analyses were performed to account for competing risks (predominantly competing risk of death) but these did not change the results (data not shown).

Figure 3

Figure 4

DISCUSSION

This prospective population-based cohort study of older adults showed that abnormal hip shape (decreasing acetabular coverage and non-spherical femoral head), cam morphology, higher BMD and BMLs predicted the risk of THR independent of WOMAC hip pain score and radiographic hip OA. Age, sex, and BMI did not predict THR independent of pain and radiographic hip OA. These results, if replicated, can be used to develop predictive models for THR.

This study extends the literature that hip shape and cam morphology increase risk of THR, independent of hip pain and radiographic hip OA. We assessed cam

morphology as an independent risk factor for THR. Clinically, cam impingement is determined using a combination of radiological and clinical findings such as hip rotation (9). We do not have such data. It is worth noting that whilst cam morphology and shape modes are calculated differently, they are capturing similar aspects of hip morphology and are, therefore, not completely independent measures (28). Both measures, however, reflect changes in the bone, rather than the cartilage, and show that hip OA is driven strongly by bone shape. Of the 6 modes which accounted for 68% of the total variation in the population, mode 2 (decreasing acetabular coverage) and mode 4 (non-spherical femoral head) have been previously associated with THR in this sample (8). They were included in this manuscript for completeness and to compare with other structural measures. Hip shape; specifically, flattening of the femoral head (non-spherical femoral head) and decreasing acetabular coverage were found to predict THR in different community based populations (5-7). One study adjusted for pain, which negated the association (6). Cam impingement has also been found to be a risk factor for THR and accelerated hip OA in a community population study, but this study did not adjust for pain (9).

A recent cohort study showed that the combination of radiographic hip OA and higher BMD as well as the BMD difference between the most affected hip and the contralateral hip predicted progression of hip OA, which included THR (17). A higher BMD may reflect the presence of osteophytes in hip OA or bone hyperplasia (29, 30). The former is unlikely as we adjusted for hip ROA including osteophytes, though we cannot definitively exclude the presence of earlier signs of OA not seen on radiographs. Two case control studies showed

that individuals with high bone mass (HBM) due to a presumed genetic cause had a higher prevalence of bone forming features of radiographic hip OA including osteophytes and subchondral sclerosis as well as THR, suggesting a potential causal pathway of BMD and OA (18, 31). A cross-sectional study showed only modest associations between tibial subchondral BMD and hip and spine BMD, suggesting that there are other factors affecting BMD at the spine and hip. (32) This is the first study to our knowledge to show that BMD, independent of radiographic hip OA, is a predictor for THR. Further longitudinal studies using more sensitive validated techniques are required to support the role of BMD in the pathogenesis of OA.

We demonstrated no associations between advancing age, BMI or sex. A cross-sectional study found that those with a higher BMI (>35kg/m^2) had a THR at a younger age compared to those with BMI <25kg/m^2 and prospective cohort studies have identified increased risk in older, obese people and an increased risk in men (33-36). However, none of these studies assessed relationships independent of hip OA and pain, suggesting that the findings in these cohort studies is mediated by or confounded by hip pain and ROA.

Changes in hip structures seen on MRI (eg. BMLs, cartilage defects) have been previously demonstrated in patients with hip OA (12, 16). Similarly, particular hip shapes correlated to MRI features of hip OA (8). In this cohort, BMLs were significantly associated with a higher risk of THR. This is consistent with data for the knee where BMLs are a strong independent predictor of total knee replacement (TKR) (26). At the hip, BMLs are associated with hip pain, knee pain, cartilage defects and bone density (37-39). However, this is the first study

to show that hip BMLs are an important predictor of joint replacement. The exact pathogenesis of BMLs remains unclear with a previous study suggesting that BMLs reflect a healing process in response to microtrauma (40). BMLs could be a result of continuous bone remodeling and/or bone reabsorption in bone. Studies found elevated bone biochemical markers such as bone alkaline phosphate (ALP) and increase in angiogenesis factors such as vascular endothelial growth factor (VEGF), in bone samples with BMLs, indicating increased bone turnover (41). The evolution of BMLs is variable with some persisting, increasing in size or resolving (26). This might indicate a paracrine effect driven by proinflammatory cytokines such as tumor necrosis factor (TNF) (13). Overall, studies have demonstrated that BMLs play an important role in the early and advanced stages of hip OA and this study extends these findings to include THR (12, 14, 26).

Limitations of this study include the difference in number of participants in some models based on the data from which predictors were collected. In particular, MRI data were only available for a subset of the cohort (215 participants), however the smaller sample size was unlikely to be the reason that why effusions did not predict THR (RR 1.88 (0.24 to 14.78), p=0.50), as they were very common in the sample and mostly physiological. Risk estimates for BMLs from the MRI data are consistent with the knee literature, suggesting that these associations are in the clinically important range, even though the confidence intervals are wide, likely due to the modest sample size.

MRI data and DXA data were only available for one hip, whereas we modelled risk of THR on both hips (in the same model, using STATA's xt function). Studies have

shown that genetic factors are related to hip shapes and therefore it is likely that the shapes are modelled genetically and/or embryonically. (42, 43) The relative symmetry in otherwise normal hips has also been shown. (44, 45) This suggests that for study participants with one normal hip on imaging, that the second (unimaged) hip is likely to be normal. This study minimised the likelihood of the second (unimaged) hip having undetected pathological differences by adjusting for ROA. However, it is possible that occult injury on the contralateral side was missed, which could not be adjusted for using radiographic assessment. If abnormal pathology was missed, this is most likely to have reduced the likelihood of finding an association with risk of THR, rather than finding an association where none existed and therefore associations that were found to increase risk of THR may be underestimates.

We used AP pelvis radiographs to measure alpha angle. This method is less sensitive in detecting FAI compared to MRI or Dunn views, (46) however, the net effect would be to reduce the effect sizes rather than artificially inflating them. Therefore, we think this is unlikely to have affected the interpretation of our findings.

SSM generally reflect clinically recognised hip morphology eg acetabular undercoverage, hip dysplasia, CAM morphology, however SSM are generated for specific datasets, and cannot be directly correlated to radiographic morphological measures. However, the fact that SSM modes do predict risk of THR independent

of other measures suggests that hip morphology remains important in assessing risk of THR.

BMLs can and do change over time; therefore BMLs may predict THR more strongly in a site-specific manner. Data from knees in the same cohort demonstrate that BMLs assesed on one knee predict knee replacement in both knees, but the strength of the association is much stronger for the ipsilateral rather than the contralateral side (26). Therefore, in this cohort which only had a right hip MRI, BMLs may more strongly predict right THRs compared to left THRs, meaning that the effect sizes seen may be underestimated for left THRs.

Whilst patient access to THR may be a potential confounder, data from this cohort demonstrates that socio-economic status does not predict time to hip replacement, demonstrating that the publicly funded hospital system in Australia has enabled timely access to THR in TASOAC participants regardless of their socio-economic status (47). Study participants could be lost to follow up due to death, illness or leaving Australia. However, as we were able to perform sensitivity analyses for competing risks (due primarily to death), and results did not change, we conclude that data are not biased by loss to follow up. Strengths of this study are the large cohort of participants, the prospective design and long-term follow up, the completeness of the AOANJRR data, and the analysis of multiple variables in the same population cohort.

CONCLUSION

In this community-based study, hip structural changes as well as BMLs detected on MRI predicted the risk of THR. These risk factors were independent of hip pain and radiographic hip OA, which has not been shown previously. Such factors can lead to better predictive models for THR and enhance our understanding of the pathogenesis of hip OA.

Abbreviations:

Osteoarthritis: OA

Total hip replacement: THR

Dual energy X-ray absorptiometry: DXA

Bone mineral density: BMD

Western Ontario and McMaster Universities Osteoarthritis Index: WOMAC

Magnetic resonance imaging: MRI

Bone marrow lesion: BML

Tasmanian Older Adult Cohort: TASOAC

Australian Orthopaedic Association National Joint Replacement Registry: AOANJRR

Body mass index: BMI

Osteoarthritis Research Society International: OARSI

Statistical shape modeling: SSM

Contributions:

The following authors declare that each made the following contributions to this manuscript:

Veronica Mezhov: Analysis and interpretation of data, drafting of the article, critical revision of the article for important intellectual content, final approval of the article.

Laura L Laslett: Conception and design, acquisition of data, analysis and interpretation of data, drafting of the article, critical revision of the article for important intellectual content, final approval of the article.

Harbeer Ahedi: Analysis and interpretation of data, critical revision of the article for important intellectual content, final approval of the article

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Graeme Jones: Conception and design, acquisition of data, analysis and interpretation of data, drafting of the article, critical revision of the article for important intellectual content, final approval of the article, obtaining of funding

Graeme Jones, Laura L Laslett and Veronica Mezhov take responsibility for the integrity of the work as a whole.

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Competing interest statement:

438 The authors declare that they have no competing interests

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Table 1: Summary of participant characteristics, by hip replacement status

	No hip replacement mean (±SD) n=764	Hip replacement mean (±SD) n=37	p
Left hip replacement	-	16 (43%)	
Right hip replacement	-	10 (27%)	
Bilateral hip replacement	-	11 (30%)	
Age (years)	62.5 (7.3)	62.5 (6.6)	0.98
Sex (% female)	51	41	0.2
Body mass index (weight (kg) / height(m)^2)	27.8 (4.6)	28.1 (4)	0.72
Current smokers (%)	11	24	**0.01**
WOMAC hip pain, Phase 2 (range 0-45)	2.3 (5.2)	7.7 (8.9)	**<0.001**
Radiographic hip OA score, mean of both hips, (range 0-12)	0.69 (1.04)	1.62 (1.77)	**0.004**
Neck of femur BMD (g/cm^2) (Phase 1)	0.77 (0.12)	0.83 (0.14)	**<0.001**
Hip BML (P2 or P3)	22	57	**0.03**
Hip effusion (P2 or P3)	83	83	1
Mode 2, left hip (SD from the mean)	-0.04 (0.98)	0.4 (1.2)	**0.01**
Mode 4, left hip (SD from the mean)	-0.01 (0.98)	-0.5 (1)	**0.014**
Cam morphology (alpha angle ≥60 degrees), mean of both hips	39	67	**<0.001**

*Shape modes were assessed using data from the left hip only

Table 2: Risk factors for THR in addition to WOMAC hip pain and radiographic hip OA

	Incident rate ratio (95% CI)
Base model: WOMAC hip pain and radiographic hip OA, n=801	
WOMAC hip pain (per unit)	**1.09 (1.06 to 1.13)**
Hip ROA	
Score 0	1.0 (reference)
Scores 1-3 (Grade 1)	**2.31 (1.14 to 4.68)**
Scores 4+ (Grade 2 or 3)	**6.19 (2.39 to 16.02)**
Base model plus….	
Shape mode 2, n=616	**1.83 (1.1 to 3.04)**
Shape mode 4, n=616	**0.59 (0.36 to 0.96)**
Presence of cam morphology, n=785	**2.20 (1.33 to 3.63)**
Hip BMLs and hip effusions, (Phase 2 or 3) n=215*	**7.10 (1.09 to 46.29)**
	1.50 (0.13 to 17.26)
Neck of femur BMD (per SD), n=801	**2.09 (1.48 to 2.94)**
Age, sex and BMI, n=801#	1.00 (0.95 to 1.06)
	0.65 (0.29 to 1.43)
	0.96 (0.89 to 1.04)

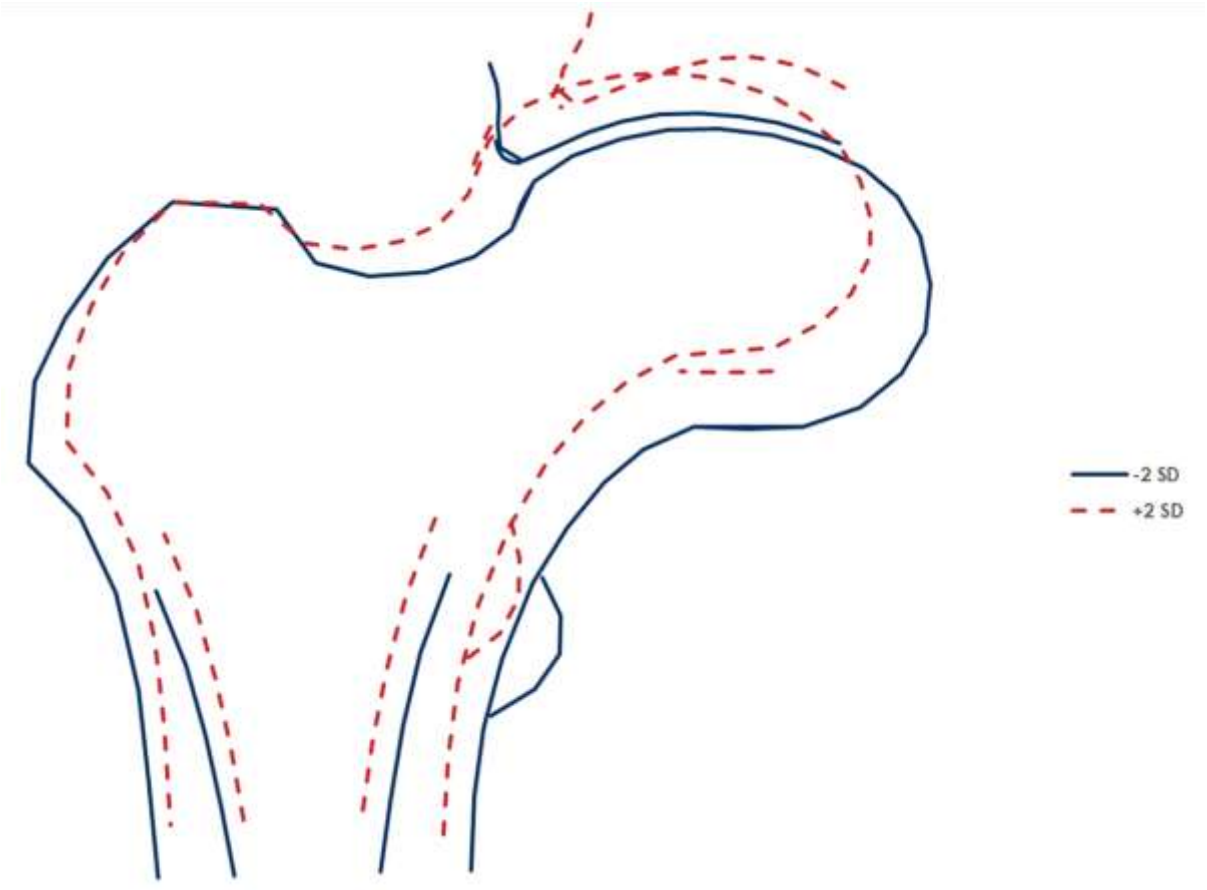

Figure 1: Hip shape mode 2 Variations in shape for +2 (red) and –2 (blue) in mode score from the mean (0) for mode 2.

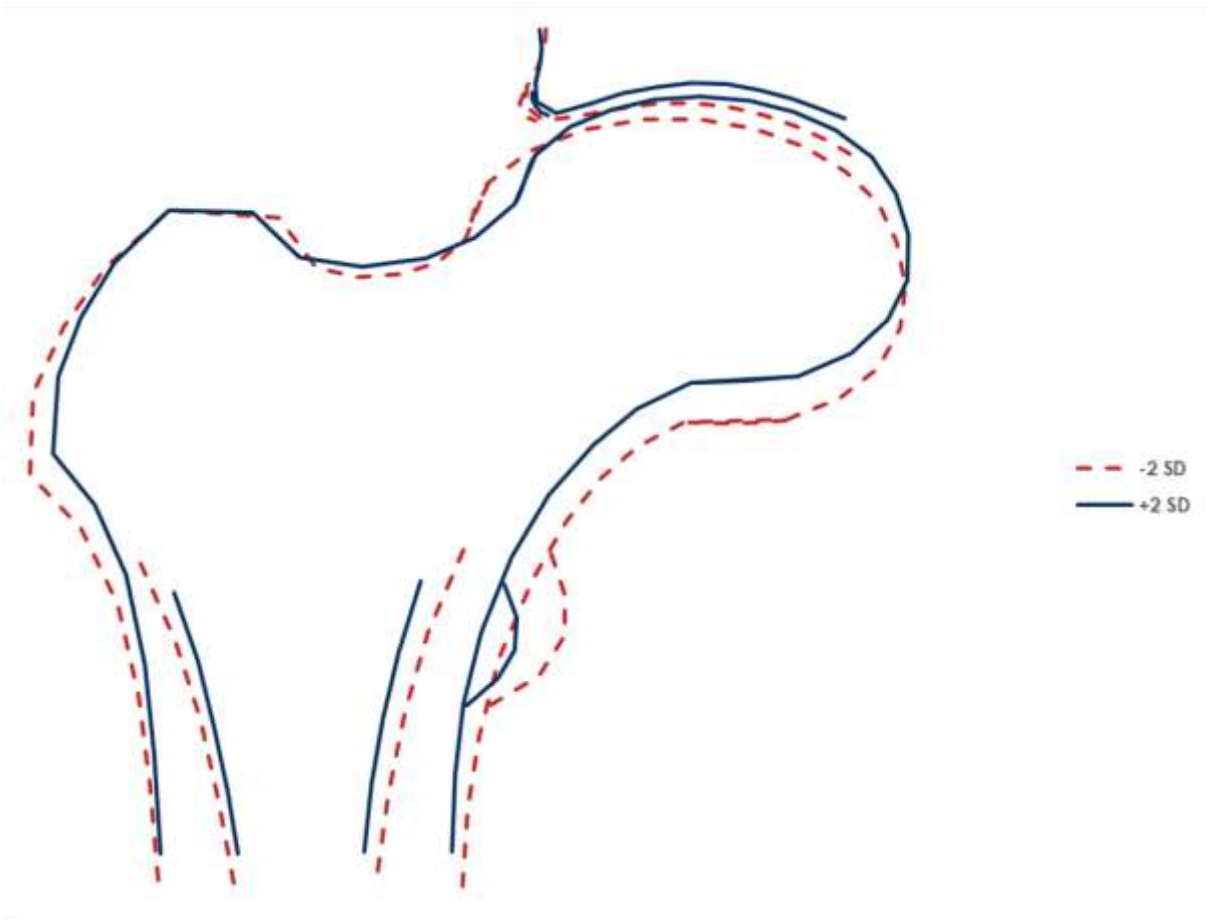

Figure 2: Hip shape mode 4. Variations in shape for +2 (red) and –2 (blue) in mode score from the mean (0) for mode 4.

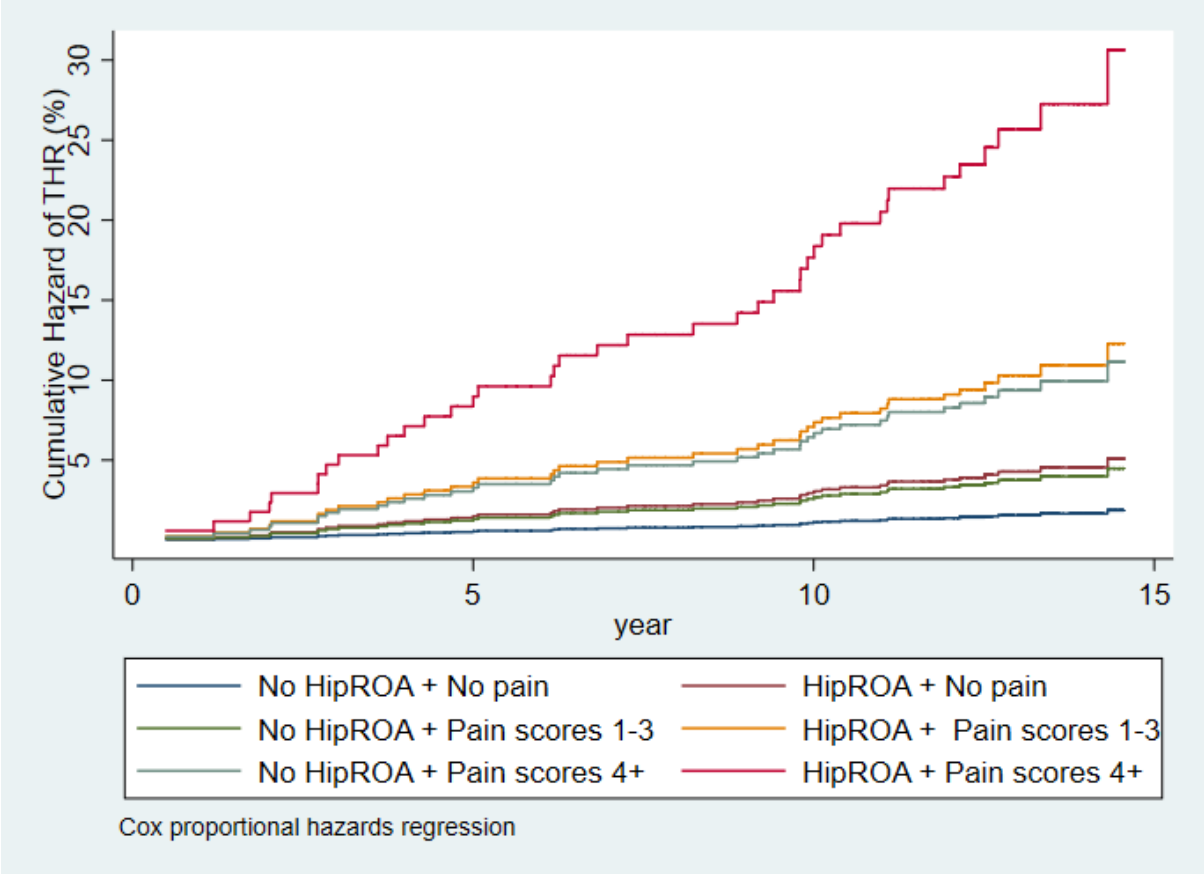

Figure 3 Cumulative hazard of THR, by presence of radiographic hip OA and WOMAC hip pain intensity.

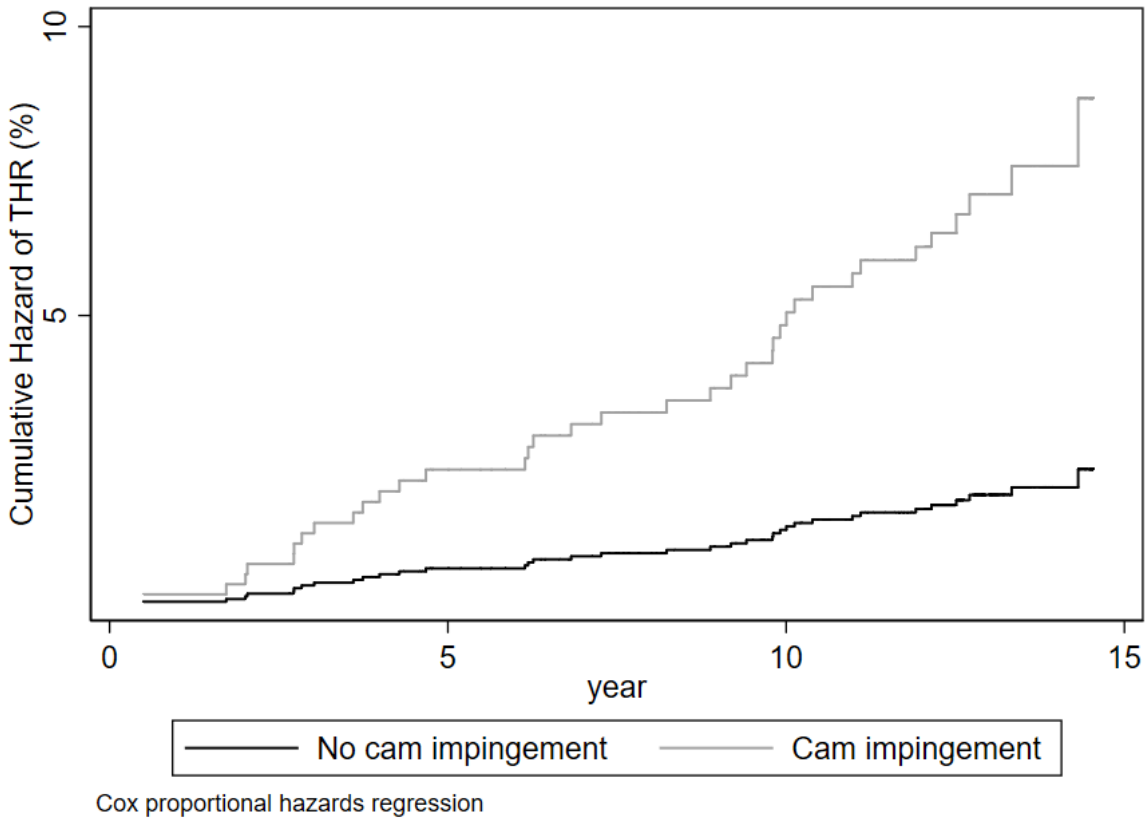

Figure 4: Cumulative hazard of THR, by presence of cam morphology.