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Statistical shape modeling of the hip and the association with hip osteoarthritis: a systematic review

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**SUMMARY**

Objective: To summarize available evidence on the association between hip shape as quantified by statistical shape modeling (SSM) and the incidence or progression of hip osteoarthritis.

Design: We conducted a systematic search of five electronic databases, based on a registered protocol (available: PROSPERO CRD42020145411). Articles presenting original data on the longitudinal relationship between radiographic hip shape (quantified by SSM) and hip OA were eligible. Quantitative meta-analysis was precluded because of the use of different SSM models across studies. We used the Newcastle–Ottawa Scale (NOS) for risk of bias assessment.

Results: Nine studies (6,483 hips analyzed with SSM) were included in this review. The SSM models used to describe hip shape ranged from 16 points on the femoral head to 85 points on the proximal femur and hemipelvis. Multiple hip shape features and combinations thereof were associated with incident or progressive hip OA. Shape variants that seemed to be consistently associated with hip OA across studies were acetabular dysplasia, cam morphology, and deviations in acetabular version (either excessive anteversion or retroversion).

Conclusions: Various radiographic, SSM-defined hip shape features are associated with hip OA. Some hip shape features only seem to increase the risk for hip OA when combined together. The heterogeneity of the used SSM models across studies precludes the estimation of pooled effect sizes. Further studies using...
Introduction

Hip osteoarthritis (OA) is one of the most common types of OA, and is a major contributor to the number of years lived with disability worldwide. Hip shape has been recognized as an important risk factor for hip OA. For this reason, the influence of hip shape has been increasingly studied over the last decade. Hip shape variants that are known to significantly increase the risk for hip OA are acetabular dysplasia and cam morphology. These hip shape variations are typically quantified by predefined radiological measurements such as the center-edge angle (CEA) and the alpha angle. However, other hip shape variants that are currently not captured by predefined radiological measurements may also play a role in the etiology of hip OA. The sole use of predefined measurements for hip shape analysis may therefore impede the discovery of further hip shape variants that increase the risk for hip OA.

This limitation has been partially circumvented by the emergence of statistical shape modeling (SSM) as a novel shape analysis technique. SSM allows quantification of the whole shape of the hip and/or pelvis, in contrast to predefined measurements. The application of SSM yields a set of shape variants, called shape modes, that are present in the studied population. When SSM is applied to radiographic images of the hip, the association between each hip shape mode and hip OA can be measured.

SSM has been increasingly used, and many different hip shape modes have so far been associated with hip OA. However, the interpretation of the SSM shape modes can be difficult and there is no thorough overview of the related literature yet. The purpose of this systematic review was to summarize which hip shape variants were found to be associated with incident or progressive hip OA, and to determine if there are any consistent patterns of similar shape variants to be recognized across different studies.

Methods

Protocol and registration

We reported this systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The review protocol was first submitted to PROSPERO on September 23, 2019, and was registered on April 28, 2020 (available from: www.crd.york.ac.uk/prospero/display_ record.php?ID=CRD42020145411).

Eligibility criteria

All publications presenting original research on the association between hip shape and hip OA in human adults were considered eligible, as were conference abstracts published in 2016 or later. The inclusion criteria were:

- Assessment of the longitudinal association between hip shape and OA had to be an aim of the study;
- Hip shape had to be assessed with some form of SSM;
- Hip OA should be either incident or progressive;
- The definition of hip OA could be radiological, clinical, by total hip replacement (THR) status, or a combination of those;
- Studies had to have control subjects that did not develop incident or progressive hip OA during the study.

The exclusion criteria were:

- Hip shape was measured contralaterally to the hip that developed the outcome (e.g., the shape of the contralateral hip in case of THR);
- The studied hip shape variant was explicitly described to be secondary to other conditions (e.g., childhood hip disease, trauma, avascular necrosis, tumors, previous hip surgery);
- The primary outcome was biomechanical injury, or the validation of a novel diagnostic technique;
- The OA outcome reflected ‘early osteoarthritic changes’, such as cartilage damage during arthroscopy or novel magnetic resonance imaging (MRI) techniques like delayed gadolinium-enhanced MRI of cartilage (dGEMRIC), Scoring Hip Osteoarthritis with MRI (SHOMRI), and T1ρ mapping.

Search and deduplication

An experienced information specialist (WB) searched the databases Embase (via Embase.com, since 1971), MEDLINE (Medline ALL via Ovid, since 1946), Web of Science Core Collection (since 1975) and the Cochrane Central Register of Trials (via Wiley, since 1992) from inception until April 25, 2020 (date last searched). A previously published method was used for search development and optimization. The searches combine terms (both thesaurus terms where available, and terms in title and/or abstract) for hip osteoarthritis with terms for anatomy or morphology and terms in title and/or abstract) for hip osteoarthritis with terms for anatomy or morphology and terms in title and/or abstract) for hip osteoarthritis with terms for anatomy or morphology and terms in title and/or abstract) for hip osteoarthritis with terms for anatomy or morphology and terms in title and/or abstract) for hip osteoarthritis with terms for anatomy or morphology and terms in title and/or abstract) for hip osteoarthritis with terms for anatomy or morphology. The full search strategy can be found in Supplement 1. Additionally, we searched Google Scholar and screened the reference lists of the included references for any other relevant articles. The search results from all databases were imported in EndNote and deduplicated.

Study selection

Two reviewers (MvB and RA) independently screened the titles and abstracts of all search results, and after having compared the included references, independently reviewed the full text of all potentially eligible studies. This process was done in EndNote with a predefined method. Subsequently the reviewers held a consensus meeting to discuss each full-text article separately, and to select the final studies to be included. A third reviewer (MN) was consulted to resolve any disagreements.

Data collection/extraction

A custom open-ended electronic data extraction form was developed and pilot-tested with a sample of the included studies. The used data extraction form, including the full list of extracted data, is available upon request.

the same SSM model and definition of hip OA are needed to allow for the comparison of outcomes across studies, and to validate the found associations.

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variables, can be found in Supplement 2. Data extraction was independently performed in duplicate by two reviewers (MvB and RA), and the results were compared in a consensus meeting. For one conference abstract of which the full text was not published yet, the reviewers requested and received the full text manuscript from the authors.

Risk of bias assessment

We used the Newcastle–Ottawa Scale (NOS) to assess the risk of bias of the individual studies18. We used either the cohort version or the case–control version as appropriate. The questions and the scoring key can be found in Supplement 3. The two reviewers (MvB and RA) independently appraised the quality of the individual studies, and disagreements were resolved in a consensus meeting. Publication bias was reduced by searching for recent conference abstracts and by searching Google Scholar for gray literature.

Statistical shape analysis

The application of SSM requires all images (e.g., radiographs) to be annotated by placing a set of points around the outline of the bone. To negate the effect of size and orientation, the outline of the bone (the shape) across images is usually aligned first using a technique called Procrustes analysis. Principal component analysis (PCA) is then applied to identify the main variations in shape (called shape modes) within the given population (i.e., across all images), summarized as a statistical shape model. Shape modes are stored as a set of continuous variables, usually standardized to have a mean of 0 and a standard deviation of 1, and are linearly independent of each other. These shape modes represent the apparent radiographic shape, and may not always match the true anatomic shape due to the influence of subject positioning and radiographic projection effects. Shape modes are ordered by their contribution to the total shape variance, the lower mode numbers being the most contributing. Because the SSM process arbitrarily assigns deviations from the mean shape as either positive or negative, a certain shape variant can either be positively or negatively (inversely) associated with the outcome. Furthermore, due to the nature of PCA the definition of individual shape modes will be data dependent and thus will vary across datasets/studies.

Data synthesis

The main outcome measures that we extracted were the measures of association for the relationship between SSM-defined hip shape and OA. These could be odds ratios (OR), relative risk (RR), prevalence ratios (PR), or any other association measures. If present, the covariate-adjusted measures were extracted. We only performed qualitative data synthesis, as the use of SSM models resulting from different studies precludes statistical pooling and thus meta-analysis. To still be able to summarize associations, we qualitatively compared the descriptions (as provided in the original papers) of the different hip shape modes from across studies. The reported shape descriptions are therefore either the literal descriptions by the original authors, or the reviewers’ interpretation of the original figures if these were unambiguous. If neither was the case, we did not report a shape description.

Results

Study selection

The initial database searches yielded 4,618 unique references, which were screened by title and abstract. Twenty-five of these had used SSM to quantify hip shape and were retrieved for full-text reading. The screening and inclusion process as well as the reasons for exclusion are shown in Fig. 1. Finally, we included nine articles in this review19–27.

Study characteristics

The main characteristics of the nine included studies (published between 2007 and 2017) are presented in Table I. The study by Mezhov et al.27 has only been published as a conference abstract as of yet, but we received the full manuscript from the authors upon request. The included studies present data on a total population of 4,706 subjects, with 6,483 hips analyzed with SSM. Not all subjects were unique, since some parts of study populations were used in two separate articles20,23,25,27. The Rotterdam Study population was also used twice, but random samples were drawn, making duplicate entry of subjects unlikely19,24. Factoring in the use of data from these study populations in separate articles, the number of unique hips analyzed with SSM was 4,584. Median sample size was 664 subjects (range 110–831) and median follow-up period was 6.5 years (range 5–19). The overall proportion of females was 69.0%, ranging from 51%22,27 to 100%20,26. The mean age of included subjects ranged from 53.620 to 70.726, with a pooled mean age of 61.8 years across all studies.

Risk of bias

A summary of the risk of bias assessment is presented in Table II, whereas an extensive overview can be found in Supplement 2. Eight of the included studies were deemed as having good methodological quality, with a low risk of bias19–22,24–27. When strictly following the NOS guidelines, one study scored poorly because of self-reported THR assessment and the lost to follow-up rate23. However, the reviewers considered the overall quality of this study sufficient to regard the findings as reliable.

Assessment of exposure and outcome

An overview of the assessment of exposure and outcome in each study can be found in Table III. Seven studies19–22,24–26 used pelvic radiographs to assess hip shape, whereas the other two23,27 used Dual-energy X-ray absorptiometry (DXA). The SSM points used to outline the hip shape varied from 1619 to 8523,27. Three studies only described the femoral head19 or part of the proximal femur21,26. The remaining three studies also included the ischial bones22,23,27. All studies19–27 used the ASM toolkit (University of Manchester, Manchester, UK) to annotate the images. Seven studies also used this toolkit to create the SSM, while two studies23,27 additionally used SHAPE software (University of Aberdeen, Aberdeen, UK) for this. Both the ASM toolkit and the SHAPE software are based on Procrustes analysis and PCA.

Eight studies19,20,22–27 used THR as a definition for hip OA. Other used definitions were Kellgren–Lawrence (KL) grade ≥221,24, an increase in KL grade of ≥3 points compared to baseline19, Croft
Fig. 1 PRISMA flow diagram detailing the literature search, screening and inclusion process. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; OA, osteoarthritis; dGEMRIC, delayed gadolinium-enhanced magnetic resonance imaging of cartilage; SHOMRI, scoring hip osteoarthritis with magnetic resonance imaging.
grade ≥2 

Table I  Characteristics of the nine included studies

| Study | Country | Study population | Study design | N subjects | N hips | Age in years, mean (SD) | % Females | Mean follow-up |
|-------|---------|------------------|--------------|------------|--------|------------------------|---------|--------------|
| Agricola et al. (2015) | Netherlands | CHECK study | Prospective cohort | 550 | 1,100 | 55.8 (5.1) | 100% | 5 years |
| Agricola et al. (2013) | Netherlands | Chingford study | Nested case-control | 114 | | 53.6 (3.4) | 100% | 19 years |
| Abed et al. (2017) | Australia | TASOAC study | Prospective cohort | 831 | 831 | 63.2 (7.5) | 51% | 10 years |
| Lynch et al. (2009) | USA | SOF | Nested case-control | 351 | | | | |
| Castano-Bejancourt et al. (2013) | Netherlands | Rotterdam Study | Prospective cohort | 688 | 110 | 68.7 (5.9) | 75% | 6 years |
| Gregory et al. (2007) | Netherlands | Rotterdam Study | Nested case-control | 110 | | | | |
| Mezhov et al. (2017) | Australia | TASOAC study | Prospective cohort | 802 | 799 | 62.5 (7.3) | 51% | 12.1 years |
| Nelson et al. (2014) | USA | JoCoOA project | Nested case-control | 342 | | | | |

The association between hip shape and THR

The results from the studies that used THR as a separate outcome definition are summarized in Table IV, whereas the complete results (including non-significant associations) can be found in Supplement 2. All six studies that used THR as a separate outcome measure found at least one shape mode that was statistically significantly associated with THR (median 2 modes, range 1–6) at the chosen alpha level. The indication for THR was incident hip OA in three studies, and incident or progressive hip OA in the other three studies. One study used Bonferroni correction for multiple testing.

A total of 18 hip shape modes were associated with future THR across the different studies. One of these modes (describing a flattened head–neck junction, a flat major trochanter and a prominent acetabular posterior wall) showed a consistent association in two different populations, namely the CHECK and Chingford populations. Five studies (out of the six that used THR as a separate outcome measure) found at least one shape mode consistent with cam morphology; and four out of six studies found a mode representing acetabular dysplasia. A hip shape variant possibly representing pincer morphology was associated with THR in one study out of the six studies that included the acetabular roof in their model. The description of this shape mode was “more pronounced lateral acetabular rim” in this study.

The association between hip shape and clinical hip OA

One study used a clinical definition of hip OA, namely the ACR criteria, and found no statistically significant associations between baseline hip shape modes and ACR criteria at follow-up. Another study made the distinction between symptomatic radiographic hip OA and overall radiographic hip OA. This study found associations between different shape modes and symptomatic radiographic hip OA in the overall
| Study                        | NOS version | Selection | Comparability | Exposure/Outcome | Total stars | Quality Score |
|-----------------------------|-------------|-----------|---------------|------------------|-------------|---------------|
| Agricola et al. (2015)²⁰  | Case-Control* | ★★★★★ | ★ | ★★★★★ | ★★★★★ | 9 | Good |
| Agricola et al. (2013)²⁵   | Cohort      | ★★★★★ | ★ | ★★★★★ | ★★★★★ | 9 | Good |
| Ahedi et al. (2017)²¹       | Cohort      | ★★★★★ | ★ | ★★★★★ | ★☆★☆ | 7 | Poor |
| Barr et al. (2012)²²        | Case-Control | ★★★★★ | ★ | ★★★★★ | ★★★★★ | 7 | Good |
| Castaño-Betancourt et al. (2013)²⁴ | Cohort | ★★★★★ | ★ | ★★★★★ | ★★★★★ | 9 | Good |
| Gregory et al. (2007)²⁶     | Case-Control | ★★★★★ | ★ | ★★★★★ | ★★★★★ | 8 | Good |
| Lynch et al. (2009)²⁶       | Case-Control | ★☆★★ | ★ | ★★★★★ | ★★★★★ | 8 | Good |
| Mezhov et al. (2017)²⁷      | Cohort      | ★★★★★ | ★ | ★★★★★ | ★★★★★ | 7 | Good |
| Nelson et al. (2014)²¹      | Case-Control | ★★★★★ | ★ | ★★★★★ | ★★★★★ | 9 | Good |

See Supplement 2 for the reviewers' considerations for each question. See Supplement 3 for score calculation. NOS, Newcastle—Ottawa Scale.

² Two versions of NOS were used: NOS case-control for the Chingford population, and NOS cohort for the Cohort Hip and Cohort Knee population.

Table II: Newcastle—Ottawa Scale for risk of bias assessment

Table III: Overview of the exposure and outcome assessments used in the included studies

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| Study                  | Association measure | Subgroup | Shape mode | Explained variance | Shape that is associated with total hip replacement* | Effect size (95% CI) | P-value | Alpha level | Covariates                  |
|------------------------|---------------------|----------|------------|-------------------|---------------------------------------------------|----------------------|---------|-------------|---------------------------------|
| Agricola et al.        | OR                  | Overall  | 12         | 6.0%              | Less concavity superior head-neck junction         | 2.10 (1.46–3.04)     | <0.001  |             | Age BMI Gender                   |
| Agricola et al.        | OR                  | Overall  | 11         | 6.0%              | Shorter femoral neck                              | 0.54 (0.38–0.78)     | 0.001  | 0.002       | Age BMI Gender                   |
| Ahedi et al.           | PR                  | Overall  | 2          | 14.0%             | Greater neck-shaft angle, narrower femoral neck,  | 1.60 (1.20–2.15)     | <0.05** | 0.05        | Age BMI Gender                   |
|                       |                     |          |            |                   | smaller & flatter femoral head, less acetabular coverage | 0.63 (0.50–0.84)     | <0.05** |             |                                |
| Barr et al.            | OR                  | 45-point model | 2  | –               | Poor acetabular coverage, steeper neck-shaft angle | 0.17 (0.04–0.71)     | <0.05** | 0.05        | Baseline KL Clinical factors Geometrical factors | Age Gender |
| Gregory et al.         | OR                  | Overall  | 3          | –                 | Sharp transition from femoral head to the upper neck | 3.71 (1.33–10.42)    | 0.012  | 0.05        |                                |
| Mezhov et al.          | RR                  | Overall  | 2          | –                 | Decreasing acetabular coverage                    | 1.57 (1.01–2.46)     | <0.05** | 0.05        | WOMAC pain OARSI grade          |
|                        |                     |          | 4          | –                 | Non-spherical femoral head                         | 0.65 (0.44–0.97)     | <0.05** |             |                                |

*These shapes are positively associated with the outcome, unless stated otherwise. For a visual impression of what these shape modes look like, we refer to the original articles. Effect sizes are shown per 1 SD increase in shape mode value. An effect size ratio between 0 and 1 indicates that negative SDs are associated with the outcome, and ratios above 1 indicate that positive SDs are associated with the outcome. Descriptions in regular typeface are taken literally from the original papers, while descriptions in italics are interpreted from the figures of the original papers. **Exact P-values were not given, but were under the alpha level of 0.05. /Clinical factors: use of a stick, physical function (from WOMAC), duration of pain; /Geometrical factors: acetabular depth, center-edge angle, baseline minimum joint space width and femoral head migration; /ORs are for OA with THR vs OA without THR; /CI: confidence interval; /OR: odds ratio; /PR: prevalence ratio; /RR: relative risk; /CHECK: Cohort Hip and Cohort Knee; /BMI: body mass index; /KL: Kellgren–Lawrence grade; /WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; /OARSI: Osteoarthritis Research Society International; /SD: standard deviation.

**Table IV** Hip shape modes significantly associated with total hip replacement outcome
### Table V

| Study                        | Association measure | Subgroup          | Shape mode | Explained variance | Shape that is associated with radiographic hip osteoarthritis* | Effect size (95% CI) | P-value | Alpha level | Covariates          |
|------------------------------|---------------------|-------------------|------------|-------------------|---------------------------------------------------------------|----------------------|---------|-------------|---------------------|
| Castano-Betancourt et al. (2013)²⁴ | OR Overall²⁴        | Baseline KL O⁴    | 5          | –                 | Less covering of the femoral head by the acetabulum           | 0.65 (0.54–0.77)     | <0.0001 | 0.0021      | Age Gender          |
|                              |                     |                   | 9          | –                 | Shorter femoral neck                                          | 1.40 (1.14–1.72)     | 0.001   |             | Gender BMI          |
| Gregory et al. (2007)¹²      | OR Overall¹²        |                   | 12         | –                 | Variation in acetabular version with corresponding rotation of the femur | 1.69 (1.24–2.30)     | 0.00094 |             |                     |
| Lynch et al. (2009)¹⁶        | OR Overall¹⁶        |                   | 3          | 8.9%              | Larger femoral head, longer and thinner femoral neck relative to the size of the trochanters and shaft | 1.73 (1.25–2.39)     | <0.001  | 0.005       | Age Height Hip BMD  |
|                              |                     |                   | 5          | 3.3%              | Larger than average trochanter size, smaller femoral neck size relative to the average size of the femoral head and shaft | 2.31 (1.63–3.28)     | <0.001  |             |                     |
|                              |                     |                   | 9          | 0.8%              | Large femoral head compared to femoral neck, more pronounced trochanter | 1.81 (1.32–2.49)     | <0.001  |             |                     |
| Nelson et al. (2014)²¹       | OR Overall²¹        |                   | 2          | 16.0%             | Alterations in the transition between greater trochanter and femoral neck, a slight reduction in femoral neck width, and a qualitative impression of a longer femoral neck compared to the mean shape | 1.47 (1.03–2.08)     | <0.05** | 0.05        | Age Gender BMI Race Baseline KL |
|                              |                     |                   | 3          | 12.5%             | Alterations in the transition between greater trochanter and femoral neck, a somewhat flatter femoral head | 1.54 (1.09–2.17)     | <0.05** |             |                     |
|                              |                     |                   | Males      | 1                 | Larger trochanter, flatter trochanter, a flattening of the transition between femoral head and neck | 1.66 (1.11–2.48)     | <0.05** |             |                     |
|                              |                     |                   | 2          | 16.0%             | Flattening of the femoral head, somewhat suggestive of cam-type change of femoroacetabular impingement | 1.49 (1.01–2.19)     | <0.05** |             |                     |
|                              |                     |                   | With baseline symptoms | 6 | 3.4%             | Subtle differences in the size of the greater trochanter, the length of the femoral neck, and the transition between the two | 2.11 (1.28–3.50)     | <0.05** |             |                     |
|                              |                     |                   | Without baseline symptoms | 14 | 0.6% | Not described, not shown in figures | 1.80 (1.06–3.07) | <0.05** |             |                     |
|                              |                     |                   |           | 6 | 3.4% | Subtle differences in the size of the greater trochanter, the length of the femoral neck, and the transition between the two | 1.94 (1.20–3.11) | <0.05** |             |                     |
|                              |                     |                   |           | 11 | 1.1% | Alterations in the transition between greater trochanter and femoral neck | 1.52 (1.05–2.17) | <0.05** |             |                     |

*These shapes are positively associated with the outcome, unless stated otherwise. For a visual impression of what these shape modes look like, we refer to the original articles. Effect sizes are shown per 1 SD increase in shape mode value. An effect size ratio between 0 and 1 indicates that the negative SDs are associated with the outcome, and ratios above 1 indicate that positive SDs are associated with the outcome. Descriptions in regular typeface are taken literally from the original papers, while descriptions in italics are interpreted from the figures of the original papers; **Exact P-values were not given, but were under the alpha level of 0.05; *This study used a combined outcome definition (THR or KL ≥ 2) in their methods, but only presented KL ≥ 2 cases in their results; ³This study did not describe what the actual differences between positive and negative SDs were; in the group with baseline symptoms a decrease in mode 6 score was associated with the outcome, while in the group without baseline symptoms an increase in mode 6 score was associated with the outcome; OR for symptomatic radiographic hip osteoarthritis; CI: confidence interval; OR: odds ratio; KL: Kellgren—Lawrence grade; BMI: body mass index; BMD: bone mineral density; SD: standard deviation.
population, as well as in subgroups with or without baseline symptoms (Table V).

Discussion

In this systematic review we have summarized all available evidence from the published literature on the association between SSM-defined apparent radiographic hip shape and hip OA. Our results show that every published study on this topic that was included in this review found at least one hip shape mode statistically significantly associated with incident or progressive hip OA or future THR. Most studies found multiple (up to six) linearly independent hip shape modes associated with hip OA. Most of the included studies used different populations and different SSM point positions for their modeling, which complicates the comparison of hip shape modes between studies. However, in the following we attempt to discuss the overall patterns in radiographic hip shape that were found to be associated with hip OA.

Shape variants that likely represent cam morphology and acetabular dysplasia were consistently found to be associated with future THR and/or incidence or progression of radiographic hip OA. Shape modes that might represent cam morphology were described as “cam-type change of femoroacetabular impingement”, “pistol-grip deformity”, “less concavity of superior head–neck junction”, “less pronounced curve from upper femoral neck into the head”, “less head-neck offset”, “non-spherical femoral head”, “flattening of the head-neck transition”, and “flattening of the femoral head”. Modes that may represent acetabular dysplasia were described as “less/poor/ decreasing acetabular coverage” and “a shallow acetabulum”. The associations between hip OA and both cam morphology and acetabular dysplasia have already been proven in other studies. However, in the cross-sectional studies that were included, the associations were non-significant due to their cross-sectional design. Because there were no baseline OA measurements, it remains unclear whether the shape modes found in these studies preceded hip OA or resulted from it.

A shape mode possibly representing pincer morphology was also associated with THR in one of the studies included in this review. Other studies, using traditional measurements such as the CEA and the crossover sign, did not find a positive association between pincer morphology and hip OA. The magnitude of the reported associations between hip shape and hip OA varied greatly between studies. Due to the different SSM point positions and different outcome definitions, the association measures are not directly comparable. Large ORs or RRs can be interpreted as a strong association nevertheless.

Strengths and limitations

This is the first systematic review on the association between SSM-defined radiographic hip shape and hip OA. It offers an overview of the patterns of hip shape features that are associated with hip OA in multiple populations. The interpretation and implications of the results were carefully discussed within the review group, which contains experts in the fields of both hip OA and SSM. Strengths of the included studies are the relatively large sample sizes and the various populations of differing ages and ethnicities that were included. Overall, the included studies scored well on methodological quality.

One limitation of this review is that we were not able to conduct a meta-analysis. This is inherent to SSM, because the shape modes will be defined by the population from which they were created. This was already taken into account when designing the review protocol. The lack of a meta-analysis makes validation of associations difficult. We therefore subjectively described patterns of hip shape that seemed to be consistently associated with hip OA across the included studies. A second limitation is that the interpretation and description of the shape modes are relatively subjective processes, which were left to the authors of the included papers. Still, we purposefully reported only the literal descriptions from the original articles to reduce bias by our own interpretation. Another limitation is that none of the included studies have validated the found associations in an independent test dataset. Internal validation would have been possible if the datasets had been divided into a training set and a test set. This is something that future SSM studies could possibly address. One more consideration is the influence that hip OA may have on hip shape. As some studies have shown, hip OA may not only result from certain hip shape variants because one statistical shape mode often consists of more than one shape feature, extra caution has to be taken when singling out just one shape feature. The association with hip OA may only be present when there is a combination of multiple shape features. This is precisely the advantage of SSM. One combination that consistently appears to be associated with hip OA is cam morphology combined with dysplastic acetabular features, a combination that has been previously described in the literature. It is still not entirely clear why this combination would increase the risk for hip OA, because theoretically a cam would be less likely to impinge with a dysplastic acetabulum. However, one computer simulation study has demonstrated that impingement can still occur, but more proximally and more medially than with a normal acetabulum. It remains unknown whether the higher risk is due to the cam morphology alone, the dysplastic acetabulum, or the interaction between the two. Another reported shape combination was the presence of a cam morphology with acetabular retroversion, which could be theoretically explained by femoroacetabular impingement happening earlier during hip flexion and internal rotation. The combination of a valgus hip with acetabular dysplasia was associated with hip OA in two studies. From a biomechanical perspective, this could be explained by higher vertical joint reaction force acting on a smaller surface during weight bearing. This combination has also been previously described. Besides the aforementioned combinations, variations in the size of the trochanters, the length and width of the femoral neck, and the apparent rotation of the femur and pelvis were found, but no obvious patterns were seen in these variations.

The magnitude of the reported associations between hip shape modes and hip OA varied greatly between studies. Due to the different SSM point positions and different outcome definitions, the association measures are not directly comparable. Large ORs or RRs can be interpreted as a strong association nevertheless.

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but can also cause changes in hip shape. This is not a problem in incidence studies where all analyzed hips were free of OA at baseline, but the hip shape modes found in progression studies could already be a result of early hip OA. Further limitations of the included studies are the heterogeneity of pelvic radiograph protocols and outcome definitions, and the varying use of covariate adjustment. Further research is required to investigate whether significant covariates (e.g., gender) may require independent shape models instead of simply adjusting for them. Lastly, most studies only described shape modes that were significantly associated with hip OA at their chosen alpha level, but some studies used Bonferroni correction, whereas others did not. This may have led to some reporting bias, even more so because statistical significance does not always translate to clinical significance. In our opinion, the use of multiple testing correction in SSM analysis should depend on the goal of the analysis. When SSM is used for hypothesis generation, you could argue not using a correction because you would want to find any possible leads. The associations found in this way should not be taken as evidence though, but have to be investigated further. In other cases, a method like the Bonferroni correction is warranted. In any case, authors should preferably explain their reasoning for (not) using multiple testing correction.

Conclusion

This systematic review suggests that several radiographic hip shape features and combinations thereof are associated with the incidence or progression of radiographic hip OA and with future THR. Associations of both cam morphology and acetabular dysplasia with hip OA have been found by SSM in multiple studies. In addition, hip shape features other than these well-known variants also appear to be associated with hip OA. Moreover, certain combinations of (sometimes subtle) hip shape features, rather than single features, may increase the risk for development or progression of hip OA when present together. More research with SSM is needed to validate these associations, and a standardized set of SSM point positions should be used to allow comparison between studies. When SSM is used to generate hypotheses, the found associations could be tested with traditional radiographic measurements in an independent sample. This would both validate the associations and make them more easily transferrable to clinical practice.

Author contributions

Conception and design: MvB, NA, SBZ, WB, JM, AN, MN, RA.
Screening of abstracts and full texts: MvB, RA.
Collection and assembly of data: MvB, RA.
Analysis and interpretation of the data: MvB, NA, SBZ, NC, DF, GJ, NL, CL, NM, JM, AN, MN, PV, JV, HW, RA.
Statistical expertise: MvB, CL, RA.
Drafting of the article: MvB, WR, RA.
Critical revision of the article for important intellectual content: MvB, NA, SBZ, WB, NC, DF, GJ, NL, CL, NM, JM, AN, MN, PV, JV, HW, RA.
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Conflict of interest statement

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Supplementary data

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