Chapter 5

Association between weight or body mass index and hand osteoarthritis: a systematic review

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ABSTRACT

Objective

To investigate the association between weight or body mass index (BMI) and the development of hand osteoarthritis.

Methods

Systematic review of observational studies. Medical databases were searched up to April 2008. Articles that presented data on the association between weight and hand osteoarthritis were selected. The qualities of these studies were then assessed by two independent reviewers using a 19 criteria scoring system. Using the mean scores of all studies as a cut-off value, the studies were deemed as high or low quality. Study quality and study designs were combined to determine the level of evidence using best-evidence synthesis, which consisted of five levels of evidence.

Results

From the 25 studies included, two had cohort, three case–control and 20 cross-sectional study designs. Fifteen studies were considered high-quality studies. Of these high-quality studies, one cohort, two case–control and seven cross-sectional studies showed a positive association between weight or BMI and hand osteoarthritis. Based on three high-quality studies with preferred study designs (one cohort and two case–control) with a positive association, the level of evidence of the association between overweight and developing hand osteoarthritis is moderate. The approximate risk ratio of this association is 1.9.

Conclusion

Weight or BMI is associated with the development of hand osteoarthritis. The level of evidence of published studies is moderate according to best-evidence synthesis. Further high-quality cohort or case–control studies are needed to elucidate the role of weight in hand osteoarthritis.

5.1. INTRODUCTION

Osteoarthritis is the most common joint disease. Its aetiology is largely unknown and no disease-modifying treatment exists.[1] Overweight is recognised as a risk factor for developing knee osteoarthritis. Being overweight increases the mechanical forces across weight-bearing joints and leads to osteoarthritis.[2] Whether this is the sole explanation is challenged by some studies that showed that overweight is also associated with osteoarthritis of non-weight-bearing joints, such as hand joints.

In a recommendation for the diagnosis of hand osteoarthritis by a task force of the European League Against Rheumatism, obesity was described as a risk factor for hand osteoarthritis.[3] This was based on only four studies. However, in two narrative reviews [1,4] the association of overweight and hand osteoarthritis was inconsistent, but narrative reviews have some shortcomings such as the potential selective inclusion of papers without systematic quality assessment of selected studies.[5] Furthermore, since the latest narrative review, several new studies on this topic have been published.

To summarize data on the association between weight and the development of hand osteoarthritis, which would give more insight into the etiology of osteoarthritis and give consideration as to whether prevention of overweight and losing weight could be a preventive treatment of hand osteoarthritis, we performed a systematic review of available studies.

5.2. MATERIALS AND METHODS

5.2.1. Identification of studies

Together with a medical librarian we searched medical databases up to April 2008 for studies with data on the association between weight or body mass index (BMI) and hand osteoarthritis. No language restriction was applied. Additional articles were searched in the reference lists of identified articles and in Google Scholar.

Table 5.1 Explanation of the criteria used for assessment of methodological quality of included studies.

Item	Criteria	Applicable for
Study population: Definition of Study population		
1.	**Sufficient description of characteristics of study groups** A '1' is given when a paper describes at least setting and time period of the study, ages of the patients (and its range) and man: woman ratio.	C/CC/CS
Study Population: Selection Bias		
2.	**Selected at time point before disease was present** A '1' is given when patients were included before the outcome (hand OA) was present. **Selected at uniform point** A '1' is given when case and control were selected at the same time point concerning disease.	C CC/CS
3.	**Clear description of selection of study subjects** When a paper described how the study subjects were selected from the population level to the study level, a '1' will be given.	C/CC/CS
4.	**Cases and controls were drawn from the same population** This is to exclude the possibility of selection bias.	CC
5.	**Participation rate ≥ 80% for study groups** Eighty per cent was an arbitrary margin chosen to determine the quality of the selection of study subjects.	C/CC/CS
Assessment of overweight as risk factor		
6.	**Weight was measured identical for cases and controls**	CC
7.	**Weight was assessed prior to outcome** In the sequence of assessing, when weight was measured before hand OA was diagnosed, a '1' will be given. In most studies where diagnosis of hand OA was made based on radiograph, a '1' will also be given.	C/CC/CS
Assessment of the outcome: Hand Osteoarthritis		
8.	**Presence of hand OA was according to valid definition and the classification was standardized** ACR criteria did not request radiographic findings in making a diagnosis of hand OA, whereas EULAR recommendation proposed that multiple features on hand radiographs is adequate to make a diagnosis hand OA. A '1' will than given for a study which used ACR criteria or standardized radiological criteria for hand OA.	C/CC/CS
9.	**Hand OA assessment was blinded** A '1' is given if the observers when making a diagnosis (by reading patient's chart) or reading the radiograph did not aware of patients' weigh or body composite.	C/CC/CS

10.	**Presence of hand OA was assessed reproducibly** A '1' is given if hand OA was assessed repeatedly at least in a subgroup, whether by the same observer or different observers.	C/CC/CS
11.	**Hand OA was assessed identical in cases and controls** A '1' is given if assessment of hand OA status was the same in controls as in cases.	CC
Follow-up		
12.	**Prospective study design was used** A '1' is given when a study measured the exposure (weight in this case) before the outcomes hand OA. Cross-sectional study will always scored '0' on this item.	C/CC/CS
13.	**Follow up time ≥ 3 years** Three years are arbitrary margin to say about the acceptable duration of follow-up.	C
14.	**No difference in withdrawal in both groups**	C
15.	**Information on completers vs. withdrawals**	C
Analysis and Data Presentation		
16.	**Weight distribution was given** A '1'is given if the paper describes the distribution of weight or BMI of the study population.	C/CC/CS
17.	**Sufficient information on association sizes were given**	C/CC/CS
18.	**Appropriate analysis techniques were used**	C/CC/CS
19.	**Adjusted for at least age and gender**	C/CC/CS

5.2.2. Inclusion and exclusion criteria

Two reviewers, EY, a PhD student, and MK, a senior rheumatologist, independently read abstracts of all retrieved references for obvious exclusions and subsequently read the full text of remaining references. Studies with data on the association between weight or BMI and hand osteoarthritis, participants with clinical, radiographic or self-reported hand osteoarthritis, were included. Hand osteoarthritis was defined as involvement of at least one hand joint. Reviews, abstracts, letters to the editor, case reports, case series and studies investigating other musculoskeletal disease than osteoarthritis, were excluded. In the case of multiple publications of the same patient population, the publication with the largest study population was selected.

5.2.3. Data extraction

The following data were extracted: (i) study population (patient characteristics, population size, gender and age); (ii) exposure (weight (kg) or BMI (kg/m^2) or other methods); (iii) outcome (methods of assessment of hand osteoarthritis, reproducibility, blinding); (iv) potential confounders (age, gender, smoking, hormone therapy, workload) and (v) association size (relative risk (RR) or odds ratio (OR)).

5.2.4. Assessment of study quality

The same reviewers independently evaluated the quality of the studies using 19 criteria based on previous systematic reviews in the area of musculoskeletal disorders [6,7] with a modification to evaluate studies on the association between weight and hand osteoarthritis (table 5.1). When the criterion was met in the article, '1' was given, otherwise '0'. A '0' was also given when no information was given about the specific criterion mentioned in the article. Differences were solved by discussion. Maximum scores obtainable were 16 for cohort and case–control studies and 13 for cross-sectional studies. Total scores per study were calculated as the percentage of maximum obtainable scores.

5.2.5. Rating the level of evidence

We generated a Forest plot and summarised the evidence using the best-evidence synthesis based on the guidelines on systematic review of the Cochrane Collaboration Back Review Group.[8] This system is a method to summarise evidence in observational studies in which the study population, the assessment of exposure and outcomes and the data analyses are heterogenic.[7] It has five levels of evidence (table 5.2). It puts more weight on studies with a prospective cohort design in which exposure truly precedes outcomes. The next preferred designs are case–control and cross-sectional, respectively.

The mean of the quality scores of all studies was used to classify studies as high or low quality.

Table 5.2 Best-evidence synthesis used in this review.[8]

Strong	General consistent findings were presented in multiple high-quality cohort studies.
Moderate	One high-quality cohort study and at least two high-quality case-control studies, or when at least three high-quality case-control studies show general consistent findings.
Limited	General consistent findings were found in a single cohort study, or in maximum two case-control studies, or in multiple cross-sectional studies.
Conflicting	Less than 75% of the studies reported consistent findings.
No evidence	No study could be found.

5.2.6. Publication bias

Publication bias was investigated by generating a funnel plot. The association size of weight or BMI and developing hand osteoarthritis on the horizontal axis was plotted against study population size on the vertical axis. Asymmetry in the funnel plot suggests publication bias.[9] We determined symmetry visually.

5.3. RESULTS

5.3.1. Literature flow

From 472 identified references 27 were selected based on inclusion and exclusion criteria (figure 5.1).[10-36] An additional search resulted in another six articles.[37-42] Seven articles were excluded [11,17,25,27,32,35,41] as a result of overlap in the study population. One study was represented by two publications, [20,21] further referred to as reference [20]. In total, 25 studies were included: two cohort, [13,36] one case–control [30] and 20 cross- sectional studies.[10,12,15,16,18-20,22-24,26,28,31,33,34,37-40,42] Two studies [14,29] resembled a case–control design.

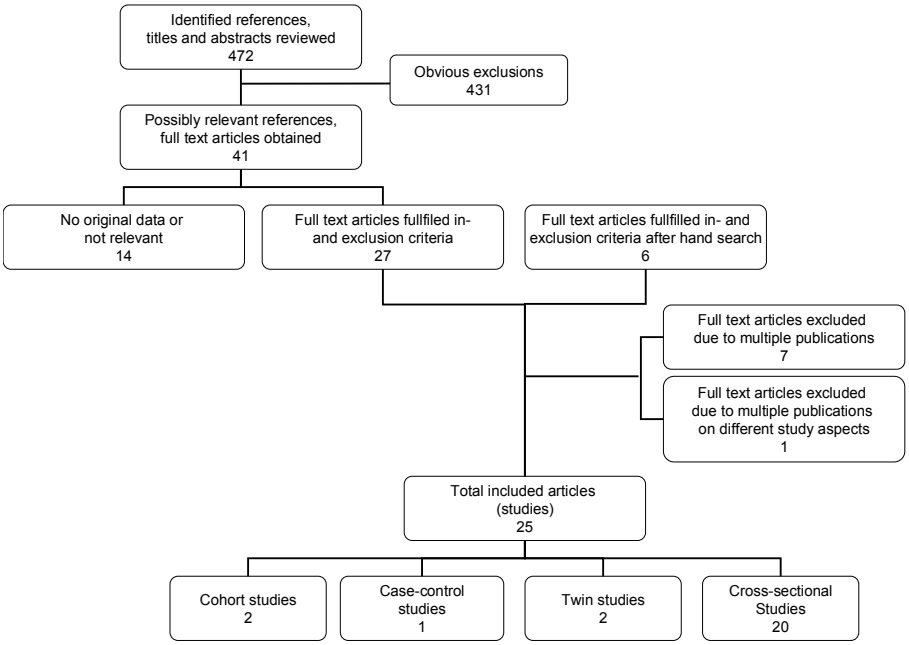

Figure 5.1 Results of the literature search.

5.3.2. Characteristics of included studies

The characteristics of the included studies can be seen in table 5.3. Eight studies investigated only women [13,14,18,23,30,34,37,38] and one [22] only men.

Hand osteoarthritis was diagnosed using radiographic criteria in 21 studies [12-16,18,20,22-24,26,28,30,33,34,36-40,42] ; 18 of them used radiographic criteria only and three [18,30,39] used radiographic and clinical criteria. Clinical criteria only were used in two studies; [10,31] one of them [10] used the American College of Rheumatism criteria for hand osteoarthritis. In two studies, [19,29] hand osteoarthritis was self-reported by the patients.

Table 5.3 Details of the studies included, in order of study design hierarchy and their quality score.

First Author, Publication year (reference number)	Study Population	Hand OA Phenotype	Adjusted for	Results[1]	Quality score[2]
Cohort studies					
Carman, 1994[13]	General population from Tecumseh, USA (Tecumseh Community Health Study). n=588 males and 688 females. Age at follow-up 50 to 74 years. Follow-up duration 23 years.	Radiographic (K&L)	Age, gender and smoking.	OA in any hand joint: Ideal weight, RR 1.0 (index) ≥ 20% above ideal weight, RR 3.12 (1.65 to 5.88)	88
Szoeke, 2006[36]	Females from general population in Melbourne (Melbourne Women's Midlife Health Project). n = 224. Mean age at follow up 59 years. Follow-up duration 11 years.	Radiographic (OARSI)	Age, gender, hormone therapy, physical activity, smoking	Osteophytes or JSN in any hand joint: OA per unit BMI (kg/m^2) increase, RR 1.02 (0.9 to 1.1)	75
Case-control studies					
Cicuttini, 1996[24]	Female twins from 2 sources of volunteers: twin registers and twins recruited by phone in London, UK. Case: osteophytes on radiograph (n=78 for DIP, 43 for PIP and 82 for 1st CMC). Control: sib pairs with no radiolographic OA. Mean age 58 years.	Radiographic (Kallman)	Gender, menopausal status, age of menopause, hysterectomy, use of hormone replacement therapy, smoking, physical activity	OA per unit BMI (kg/m^2) increase: DIP, OR 1.07 (0.91 to 1.25) PIP, OR 1.15 (0.9 to 1.45) 1st CMC, OR 1.30 (1.06 to 1.59)	88
Oliveria, 1999[30]	Females from general practice in Worchester USA (Fallon Community Health Plan). Case: hand OA (n = 39). Control: females, matched by closest date of birth (n = 39). Mean age 61 years.	Clinical (ACR) , supported by radiographic OA featrures	Age, gender, estrogen therapy, smoking, number of Fallon health contacts	OA in any hand joint: BMI ≤ 23.80, OR 1 BMI 23.81 – 28.60, OR 5.4 (0.9 to 31.3) BMI > 28.6, OR 8.3 (1.2 to 56.5)	75

Kujala, 1999[29]	Finnish Twin Cohort, Finland. 73 twins discordant for hand OA. Age 39 to 66 years.	Self-reported physican-based	Age, gender	'No differences in BMI among twin pairs discordant for finger OA'	44
Cross-sectional studies					
Sayer, 2003[31]	General population followed since their birth in England, Scotland and Wales. n = 1467 males and 1519 females. Cross- sectional analysis at age of 53 years.	Clinical (Heberden's, Bouchard's nodes, squaring at 1st CMC)	Age, gender, height, social class	OA in any hand joint, men: Weight ≤ 74 kg, OR 1 Weight > 91.8, OR 1.4 'increasing OR with increasing adult weights'	77
Dahagin, 2007[16]	General population of Ommoord, the Netherlands (Rotterdam Study). n = 1499 males and 2086 females. Mean age 66 years.	Radiographic (K&L)	Age, gender, smoking	OA in two of three groups (DIP, PIP, 1st CMC) hand joints: BMI < 27.4, OR 1 BMI > 27.4, OR 1.4 (1.2 to 1.7)	77
Ding, 2008[18]	Female dentists and teacher in Helsinki, Finland. n=532. Mean age 54 years.	Radiographic (modified K&L) and clinical (pain)	Age, gender, occupation, hand-loading leisure-time activities, occupation	Symptomatic OA in DIP joint: BMI < 25, OR 1 (index) BMI 25 to 26.9, OR 1.62 (0.83 to 3.15) BMI ≥ 27, OR 2.39 (1.26 to 4.51)	77
Haara, 2003 and Haara, 2004[20]	General population of Finland from 69 municipalities. n = 1560 males and 2035 females. Age older than 30 years.	Radiographic (K&L)	Age, gender, educational level, smoking, workload	OA in any hand joint (except CMC): BMI ≤ 20, OR 0.50 (0.31 to 0.83) BMI 20 to 24.9, OR 1 (index) BMI 25.0 to 29.9 OR 1.17 (0.96 to 1.43) BMI 30 to 34.9, OR 1.78 (1.37 to 2.33) BMI ≥ 35, OR 1.98 (1.19 to 3.27) OA in 1st CMC joint: BMI 20.0 to 24.9, OR 1 (index) BMI 35, OR ±2	77

Hart, 1993[39]	Females from a large general practice in Chingford, near London, UK (The Chingford Study) n=985. Mean age 54 years.	Radiographic (K&L) and clinical (pain and stiffness)	Age and gender	BMI < 23.4, OR 1 (index) OA in DIP joint: BMI 23.4 – 26.4, OR 1.64 (0.84 to 3.21) BMI > 26.4, OR 1. 71 (0.88 to 3.33) OA in PIP joint: BMI 23.4 – 26.4, OR 1.19 (0.39 to 3.62) BMI > 26.4, OR 0.71 (0.22 to 2.29) OA in CMC joint: BMI 23.4 – 26.4, OR1.68 (0.88 to 3.21) BMI > 26.4, OR 1. 85 (0.96 to 3.56)	77
Jones, 2002[24]	Patients with OA and their family in Tasmania, Australia. n = 174 males and 348 females. Mean age males 53 years, females 57 years.	Radiographic (OARSI) or clinical (Heberden's nodes)	Age, gender, and family effects	BMI < 25, OR 1 Radiographic OA in DIP joint: BMI ≥ 25, OR 1.22 (0.70 to 2.14) Radiographic OA in CMC joint: BMI ≥ 25, OR 0.99 (0.54 to 1.52)	77
Kessler, 2003[28]	Patients with hip or knee OA severe enough for arthroplasty in Ulm, Germany (Ulm Osteoarthritis Study). n = 242 males and 397 females. Median age 65 years.	Radiographic (OARSI)	Age, gender, physical exertion, and hip or knee OA	OA in two or more IP joints: OA per unit BMI (kg/m^2) increase, OR 1.02 (0.98 to 1.07) OA in at least one of 1st CMC joint: OA per unit BMI (kg/m^2) increase, OR 1.01 (0.96 to 1.06)	77
Van Saase, 1989[42]	General population of Zoetermeer, near the Hague, the Netherlands. n = 1071 males and 1097 females. Age 45 to 64 years.	Radiographic (K&L)	Age and gender	♂, association between overweight and OA: DIP (p≤0.001), MCP (p ≤0.001), 1st CMC (p ≤0.15), wrist (p ≤0.29), PIP (p ≤0.001), CARP (p ≤0.06) ♀, association between overweight and OA: DIP (p ≤0.002), MCP (p ≤0.39), 1st CMC (p ≤0.30), PIP (p ≤0.001), CARP (p ≤0.003), wrist (p ≤0.12)	77

Andrianakos, 2006[10]	General population of Greece (ESORDIG study). Urban, suburban and rural. n = 4269 males and 4471 females. Age 19 to 99 years old, mean: 47 years.	Clinical (ACR)	Age, gender, education level, occupation, alcohol consumption, cigarette smoking, rural residence, socioeconomic status.	Clinical OA: BMI ≤ 30, OR 1 (index) BMI ≥ 30, OR 1.3 (0.98 to1.8)	69
Cvijetic, 2000[15]	General population of Zagreb, Croatia. n = 304 males and 306 females. Mean age male and female 63 years.	Radiographic (K&L)	Age, gender, duration of postmenopause, cigarette smoking, blood pressure	β values of multiple regression analysis: ♂: DIP: 0.25, p<0.001, PIP: 0.08, 1st CMC: 0.07 ♀: DIP: 0.17, PIP: 0.02, 1st CMC: 0.02	69
Sowers, 2000[34]	Females from two cohorts: General population of Michigan, USA (Michigan Bone Health Study), n=510 and volunteers from Study of Women's Health Across the Nation, n=543. Age 27 to 53 years, median 44 years.	Radiographic (K&L)	Age, gender, previous injury, smoking	OA in any hand joint: OA per unit BMI (kg/m^2) increase, OR 1.05 (1.03 to 1.08)	69
Bergstrom, 1986[12]	Seventy-year old People Study in Goteborg, Sweden. n = 190 males and 162 females. Cross-sectional analysis of 70 years (cohort 1), 75 years (cohort 2) and 79 years (cohort 3).	Radiographic (K&L)	Age and gender	DIP, PIP, MCP II-V, MCPI, 1st CMC joints were assessed: ♂: 'BMI was correlated to MCP I and IP I (p< 0.05) but not with other joints' ♀: 'BMI was correlated with DIP (p<0.01) but not with other joints'	62
Kalichman, 2005[27]	General population of Chuvasa, Russia, (Chuvasha Skeletal Aging). Agricultural. n = 663 males and 605 females. Age males: 18 to 89 years, mean 46.3 years and females 18 to 90 years, mean 48.2.	Radiographic (K&L)	Age and gender	Correlation between overweight and OA: 0.11	62
Grotle, 2008[19]	General population of Ullensaker, near Oslo, Norway. Rural. n = 1470 males and 1796 females. Mean age 45 years	Self-reported	Age and gender	Self-reported OA: BMI < 20, OR 0.70 (0.24 to1.99) BMI 20 to 25, OR 1 (index) BMI 26 to 30 OR 1.00 (0.69 to1.48) BMI > 30, OR 1.57 (0.93 to 2.64)	46

Hochberg, 1993[23]	Female volunteers in Baltimore (Baltimore Longitudinal Study of Aging). Middle class. n = 317. Mean age 55 years.	Radiographic (K&L)	Age and gender	'all independent variables (age, WHR, % fat) were significantly different across grade of hand OA except BMI'	46
Hochberg, 1991[22]	Male volunteers in Baltimore (Baltimore Longitudinal Study of Aging). Middle class. n = 888. Mean age 56 years.	Radiographic (K&L)	Age and gender	'the distribution of these residual values were not significantly different by grade of hand osteoarthritis for any of these independent variables (like BMI)'.	46
Sonne-Holm, 2006[33]	General population of Osterbro, Copenhagen, Denmark (Copenhagen City Health Study). n = 1295 males and 2060 females.	Radiographic (K&L)	Not adjusted	'OA is associated with K&L grade 2 to 3 (p<0.0000)'	38
Acheson, 1975[37]	General population New Haven, Connecticut, USA. n = 300 males and 385 females. Age older than 21 years.	Radiographic (K&L)	Gender	Difference on the average weight between subjects with OA and without OA. ♂: 172.13 vs. 171.58 lbs, not significant ♀: 143.96 vs. 134.48, p<0.01	31
Kellgren, 1958[40]	Random sample of general population in Leigh, UK. Urban. n = 204 males and 277 females. Age 55 to 64 years.	Radiographic features	Not adjusted	'DIP OA is associated with overweight males (p <0.01) but no significant association on PIP, 1st CMC, MP and wrists in both sexes.'	31
Engel, 1968[38]	General population in USA. (Health Examination Survey I). n=6672. Age 18 to 79 years.	Radiographic features	Age, gender	Association between Ponderal index (height divided by the cubed root of weight) and hand OA for age groups: ♂: 45 to 54 yr: p 0.01, 55 to 64 yr: -, 65 to 74 yr: p 0.05 ♀: 45 to 54 yr: p 0.0005, 55 to 64 yr: -, 65 to 74 yr: -	23

[1] in parentheses: 95% confidence interval, [2] quality score in per cent (%)
1st CMC, carpometacarpal joints of the thumb; ACR, American College of Rheumatology; BMI, body mass index; CMC: carpometacarpal joints; DIP, distal interphalangeal joints; K&L, Kellgren and Lawrence radiographs scoring system; MCP, metacarpophalangeal joints; OARSI, Osteoarthritis Research Society International scoring system; PIP, proximal interphalangeal joints.

5.3.3. Study quality assessment

The two reviewers agreed on 305 (90%) of 340 criteria. The disagreements were solved in a single meeting and mostly concerned the assessment of hand osteoarthritis (criteria 9 and 10). The mean of quality scores was 63%.

The participation rates in most studies were lower than 80% (criterion 5). One cohort study had limitations in the assessment of hand osteoarthritis (criteria 9 and 10) and the follow-up (criteria 14 and 15). Two case–control studies had limitations in the assessment of hand osteoarthritis (criterion 10). Moreover, two of three case–control studies had potential selection bias, being sampling bias (items 2 and 5). This bias was also commonly seen in cross-sectional studies.

5.3.4. Associations shown in included studies

Hand osteoarthritis in at least one joint showed a statistically significant positive association with weight in 16 of 25 (64%) studies.[12-16,18,20,26,30,31,33,34,37,38,40,42] The other nine studies showed a non-significant or no association. Fourteen of 25 studies [10,13,14,16,18-20,24,28,30,31,34,36,39] presented association sizes as OR and RR values (figure 5.2) giving an estimated pooled risk ratio of 1.9 for the positive association between (over)weight and the development of hand osteoarthritis. Three [15,31,37] of these 16 studies showed a significant positive association in one gender, but a non-significant or no association in the other gender.

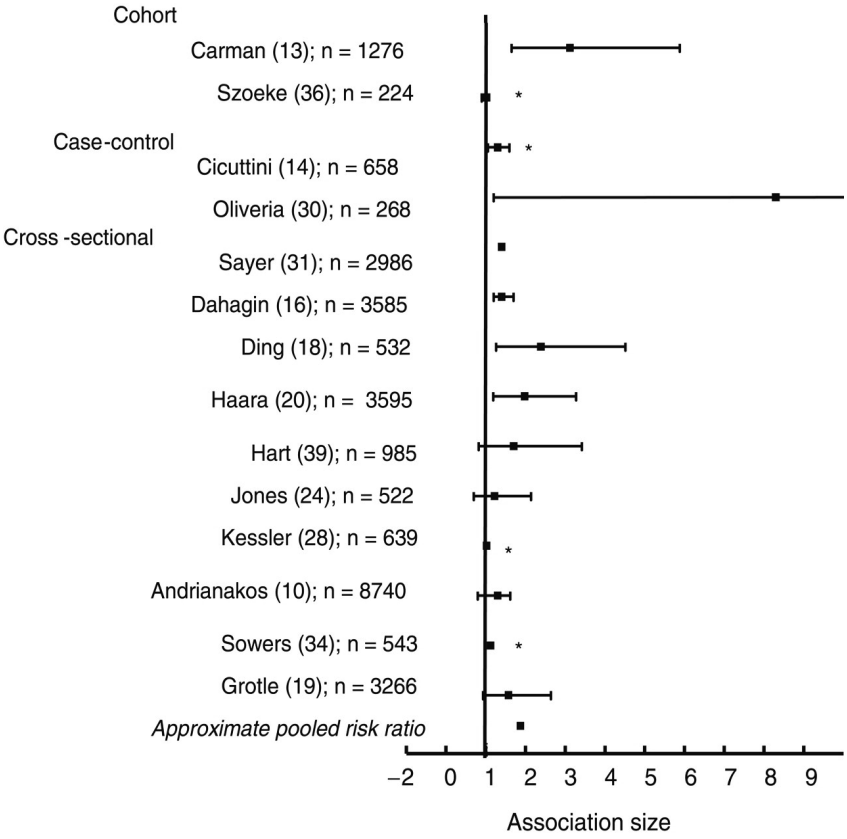

Figure 5.2 Forest plot showing the association sizes (odds ratios (OR) or relative risks (RR)) between (over)weight or body mass index (BMI) with hand osteoarthritis of the studies included, arranged by study design and quality scores (from high to low). The numbers in parentheses represent the references. n represents number of study population. For information on the actual association sizes concerning used hand osteoarthritis phenotype and BMI category see table 5.3. Studies labeled with an asterisk are those that presented OR or RR as an increase per unit BMI.

Six of nine studies [12,14-16,18,24,39,40,42] investigating distal interphalangeal joints, two of eight [12,14-16,36,39,40,42] studies investigating proximal interphalangeal joints, one of four studies [12,22,40,42] investigating metacarpophalangeal joints and four of 12 studies [12,14-16,20,24,28,33,36,39,40,42] investigating first carpometacarpal joints showed a positive significant association with weight or BMI.

5.3.5. Levels of evidence

The level of evidence for a positive association between weight or BMI and hand osteoarthritis is moderate. Fifteen of 25 included studies [10,13-16,18,20,24,28,30,31,34,36,39,42] were considered to be of high quality. Of two high-quality cohort studies [13,36] one [13] showed an RR of 3.12 (1.65 to 5.88); the second showed no association.

Both high-quality case–control studies [14,30] reported a positive significant association, with an OR of 1.30 (1.06 to 1.59)[14] and 8.3 (1.2 to 56.5).[30] Of 11 [10,15,16,18,20,24,28,31,34,39,42] high-quality cross-sectional studies, seven studies [15,16,18,20,31,34,42] reported a positive association.

In a subgroup of studies that used radiographic criteria with or without clinical criteria for hand osteoarthritis, 13 of 21 studies were deemed to be high quality. Ten [13-16,18,20,30,31,34,42] of these 13 studies showed a positive association and the level of evidence remained moderate. In the subgroup of studies using radiographic criteria only (18 studies; of which 10 were high quality), seven [13-16,20,34,42] studies showed a positive association, but because of the lack of a sufficient number of high-quality cohort (only one study) and case–control (only one study) studies, the level was limited. The subgroup of clinical studies [10,31] showed conflicting levels of evidence.

Using alternative cut-offs for methodological quality assessment (median or 25th percentile) did not change the results. When using the 75th percentile as the cut-off, few studies were retained, leading to limited level of evidence.

5.3.6. Publication bias

We plotted the association sizes (OR and RR) against the sample sizes of 14 studies to investigate publication bias (figure 5.3). Visually, the plot was asymmetric.

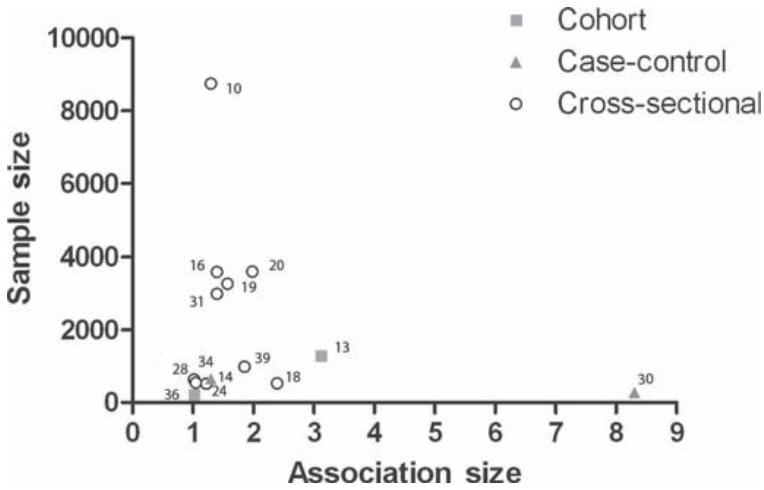

Figure 5.3 Funnel plot showing the relationship between association sizes (odds ratios (OR) or relative risks (RR)) and sample size. The numbers represent the references of the studies. When studies presented multiple association sizes, the largest RR or OR concerning a cut-off at body mass index (BMI) 25 kg/m^2 was denoted. If this information was not available, the association size of a cut-off at a higher BMI level was used. Preferentially, association sizes for radiographic hand osteoarthritis and for men and women combined were presented.

5.4. DISCUSSION

This systematic review showed that the evidence for a positive association between weight or BMI and hand osteoarthritis is moderate. This conclusion is based on three high-quality studies with preferred study designs. A moderate level of evidence did not change for the subgroup of studies investigating hand osteoarthritis using radiographic criteria. When no best-evidence synthesis was performed, a pooled risk ratio was approximately 1.9, in which 64% of published studies showed a positive association between (over)weight and hand osteoarthritis.

The strength of a systematic review is the use of a focused research question, an extended search strategy and a predefined system to evaluate the quality of evidence. Here, we also use qualitative levels of evidence to give a conclusion when a summary of quantity statistic was not appropriate. Yet, this systematic review has some possible limitations, which also reflect the limitations of the published studies.

The first caveat is the heterogeneities in multiple aspects of the studies, such as the definition of BMI, hand osteoarthritis and study population. Studies categorised BMI in various ways, mainly based on the distribution of the study population, such as tertiles and median or BMI as a continuous variable. Preferentially, the cutoff of BMI is 25 kg/m^2, as the World Health Organization definition for overweight could be used.[43] However, this was the case in only a minority of studies. Included studies also defined hand osteoarthritis in various ways, using radiographic and clinical criteria. Subgroup analysis of studies that used radiography to make a diagnosis of hand osteoarthritis, however, did not change the level of evidence. The level of evidence became conflicting when we performed a subgroup analysis in only two studies defining hand osteoarthritis using clinical criteria. The lack of clinical studies might reflect the available evidence, which suggests that radiography is a better method of defining hand osteoarthritis in epidemiology studies.[4] Another heterogeneity that should be mentioned here is the study population. Although most studies used a mixed sex population, a third of the included studies concerned only women. These heterogeneities lead to difficulties in comparing studies and in summarizing studies quantitatively. The second caveat of this review is the possibility of publication bias. However, when we examine the funnel plot carefully, the asymmetry is caused by one study with a large effect.[30] That study also differs from other studies in that it used hand osteoarthritis based on clinical criteria supported by radiographic findings. The third caveat of this review is that theoretically the criteria we used can influence the outcomes of the review. We used and modified criteria that were previously used in systematic reviews of the musculoskeletal field, because no generally accepted set of criteria exist for methodological quality assessment in observational studies.

The consequence of the moderate level of evidence of an association is that further research is likely to have an important impact.[44] Therefore, future studies, especially well-designed prospective cohort or case–control studies, are called for, which should also investigate the aetiological mechanisms of the association and temporal relationship between overweight or obesity and hand osteoarthritis.

The pathogenesis of osteoarthritis is largely unknown and no disease-modifying treatment exists, therefore knowledge of the role of overweight in hand osteoarthritis is of importance for understanding and treating (hand) osteoarthritis. The association between overweight and hand osteoarthritis suggests that factors other than mechanical forces also play a role. Some possible links between overweight and osteoarthritis have been proposed, such as metabolic alteration, atherosclerosis and diabetes mellitus.[45] Fat tissues secrete pro and anti-inflammatory adipo(cyto)kines, such as leptin, which was observed in synovial fluid obtained from osteoarthritic joints.[46] The concentration of leptin in advanced osteoarthritic cartilage is significantly correlated with the BMI of the patients, and its level and pattern of expression were related to the grade of cartilage destruction. Obesity-associated atherosclerosis can also accelerated the osteoarthritis process by vascular disease in subchondral bone.[47] Finally, in diabetes mellitus, advanced glycation end-products (AGE) are formed and accumulated. AGE cross-links the damaged collagen network and leads to cartilage changes associated with osteoarthritis. This AGE formation is initiated by sugars and by lipids.[48]

In summary, this is the first systematic review to investigate the association between weight and BMI and hand osteoarthritis. The association is positive and the level of evidence is moderate. This calls for well-designed studies that further estimate the association as well as its underlying mechanisms.

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References

(1) Felson DT, Chaisson CE. Understanding the relationship between body weight and osteoarthritis. Baillieres Clin Rheumatol 1997 Nov;11(4):671-81.

(2) Hunter DJ, Felson DT. Osteoarthritis. BMJ 2006 Mar 18;332(7542):639-42.

(3) Zhang W, Doherty M, Leeb BF, Alekseeva L, Arden NK, Bijlsma JW, et al. EULAR evidence based recommendations for the diagnosis of hand osteoarthritis - report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis 2008 Feb 4.

(4) Hart DJ, Spector TD. Definition and epidemiology of osteoarthritis of the hand: a review. Osteoarthritis Cartilage 2000;8 Suppl A:S2-S7.

(5) Cook DJ, Mulrow CD, Haynes RB. Systematic reviews: synthesis of best evidence for clinical decisions. Ann Intern Med 1997 Mar 1;126(5):376-80.

(6) Borghouts JA, Koes BW, Bouter LM. The clinical course and prognostic factors of non-specific neck pain: a systematic review. Pain 1998 Jul;77(1):1-13.

(7) Lievense AM, Bierma-Zeinstra SM, Verhagen AP, van Baar ME, Verhaar JA, Koes BW. Influence of obesity on the development of osteoarthritis of the hip: a systematic review. Rheumatology (Oxford) 2002 Oct;41(10):1155-62.

(8) van Tulder, Furlan A, Bombardier C, Bouter L. Updated method guidelines for systematic reviews in the cochrane collaboration back review group. Spine 2003 Jun 15;28(12):1290-9.

(9) Egger M, Davey SG, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997 Sep 13;315(7109):629-34.

(10) Andrianakos AA, Kontelis LK, Karamitsos DG, Aslanidis SI, Georgountzos AI, Kaziolas GO, et al. Prevalence of symptomatic knee, hand, and hip osteoarthritis in Greece. The ESORDIG study. J Rheumatol 2006 Dec;33(12):2507-13.

(11) Bagge E, Bjelle A, Eden S, Svanborg A. Factors associated with radiographic osteoarthritis: results from the population study 70-year-old people in Goteborg. J Rheumatol 1991 Aug;18(8):1218-22.

(12) Bergstrom G, Bjelle A, Sundh V, Svanborg A. Joint disorders at ages 70, 75 and 79 years--a cross-sectional comparison. Br J Rheumatol 1986 Nov;25(4):333-41.

(13) Carman WJ, Sowers M, Hawthorne VM, Weissfeld LA. Obesity as a risk factor for osteoarthritis of the hand and wrist: a prospective study. Am J Epidemiol 1994 Jan 15;139(2):119-29.

(14) Cicuttini FM, Baker JR, Spector TD. The association of obesity with osteoarthritis of the hand and knee in women: a twin study. J Rheumatol 1996 Jul;23(7):1221-6.

(15) Cvijetic S, Campbell L, Cooper C, Kirwan J, Potocki K. Radiographic osteoarthritis in the elderly population of Zagreb: distribution, correlates, and the pattern of joint involvement. Croat Med J 2000 Mar;41(1):58-63.

(16) Dahaghin S, Bierma-Zeinstra SM, Koes BW, Hazes JM, Pols HA. Do metabolic factors add to the effect of overweight on hand osteoarthritis? The Rotterdam Study. Ann Rheum Dis 2007 Jul;66(7):916-20.

(17) Davis MA, Neuhaus JM, Ettinger WH, Mueller WH. Body fat distribution and osteoarthritis. Am J Epidemiol 1990 Oct;132(4):701-7.

(18) Ding H. Association between overweight and dip osteoarthritis among middle-aged Finnish female dentists and teachers. Obesity Research and Clinical Practice 2008;2(1):61-8.

(19) Grotle M, Hagen KB, Natvig B, Dahl FA, Kvien TK. Prevalence and burden of osteoarthritis: results from a population survey in norway. J Rheumatol 2008 Apr;35(4):677-84.

(20) Haara MM, Manninen P, Kroger H, Arokoski JP, Karkkainen A, Knekt P, et al. Osteoarthritis of finger joints in Finns aged 30 or over: prevalence, determinants, and association with mortality. Ann Rheum Dis 2003 Feb;62(2):151-8.

(21) Haara MM, Heliovaara M, Kroger H, Arokoski JP, Manninen P, Karkkainen A, et al. Osteoarthritis in the carpometacarpal joint of the thumb. Prevalence and associations with disability and mortality. J Bone Joint Surg Am 2004 Jul;86-A(7):1452-7.

(22) Hochberg MC, Lethbridge-Cejku M, Plato CC, Wigley FM, Tobin JD. Factors associated with osteoarthritis of the hand in males: data from the Baltimore Longitudinal Study of Aging. Am J Epidemiol 1991 Nov 15;134(10):1121-7.

(23) Hochberg MC, Lethbridge-Cejku M, Scott WW, Jr., Plato CC, Tobin JD. Obesity and osteoarthritis of the hands in women. Osteoarthritis Cartilage 1993 Apr;1(2):129-35.

(24) Jones G, Cooley HM, Stankovich JM. A cross sectional study of the association between sex, smoking, and other lifestyle factors and osteoarthritis of the hand. Journal of Rheumatology 2002;29(8):1719-24.

(25) Kalichman L, Cohen Z, Kobyliansky E, Livshits G. Interrelationship between bone aging traits and basic anthropometric characteristics. American Journal of Human Biology 2002;14(3):380-90.

(26) Kalichman L, Malkin I, Kobyliansky E. Association between physique characteristics and hand skeletal aging status. Am J Phys Anthropol 2005 Dec;128(4):889-95.

(27) Kalichman L, Kobyliansky E. Age, body composition, and reproductive indices as predictors of radiographic hand osteoarthritis in Chuvashian women. Scand J Rheumatol 2007 Jan;36(1):53-7.

(28) Kessler S, Stove J, Puhl W, Sturmer T. First carpometacarpal and interphalangeal osteoarthritis of the hand in patients with advanced hip or knee OA. Are there differences in the aetiology? Clin Rheumatol 2003 Dec;22(6):409-13.

(29) Kujala UM, Leppavuori J, Kaprio J, Kinnunen J, Peltonen L, Koskenvuo M. Joint-specific twin and familial aggregation of recalled physician diagnosed osteoarthritis. Twin Res 1999 Sep;2(3):196-202.

(30) Oliveria SA, Felson DT, Cirillo PA, Reed JI, Walker AM. Body weight, body mass index, and incident symptomatic osteoarthritis of the hand, hip, and knee. Epidemiology 1999 Mar;10(2):161-6.

(31) Sayer AA, Poole J, Cox V, Kuh D, Hardy R, Wadsworth M, et al. Weight from birth to 53 years: a longitudinal study of the influence on clinical hand osteoarthritis. Arthritis Rheum 2003 Apr;48(4):1030-3.

(32) Solovieva S, Vehmas T, Riihimaki H, Takala EP, Murtomaa H, Luoma K, et al. Finger osteoarthritis and differences in dental work tasks. J Dent Res 2006 Apr;85(4):344-8.

(33) Sonne-Holm S, Jacobsen S. Osteoarthritis of the first carpometacarpal joint: a study of radiology and clinical epidemiology. Results from the Copenhagen Osteoarthritis Study. Osteoarthritis Cartilage 2006 May;14(5):496-500.

(34) Sowers M, Lachance L, Hochberg M, Jamadar D. Radiographically defined osteoarthritis of the hand and knee in young and middle-aged African American and Caucasian women. Osteoarthritis and Cartilage 2000;8(2):69-77.

(35) Sowers MF, Hochberg M, Crabbe JP, Muhich A, Crutchfield M, Updike S. Association of bone mineral density and sex hormone levels with osteoarthritis of the hand and knee in premenopausal women. Am J Epidemiol 1996 Jan 1;143(1):38-47.

(36) Szoeke CE, Cicuttini FM, Guthrie JR, Clark MS, Dennerstein L. Factors affecting the prevalence of osteoarthritis in healthy middle-aged women: data from the longitudinal Melbourne Women's Midlife Health Project. Bone 2006 Nov;39(5):1149-55.

(37) Acheson RM, Collart AB. New Haven survey of joint diseases. XVII. Relationship between some systemic characteristics and osteoarthrosis in a general population. Ann Rheum Dis 1975 Oct;34(5):379-87.

(38) Engel A. Osteoarthritis and Body measurements. Vital and Health Stat 11. 1968;11:1-37

(39) Hart DJ, Spector TD. The relationship of obesity, fat distribution and osteoarthritis in women in the general population: the Chingford Study. J Rheumatol 1993 Feb;20(2):331-5.

(40) Kellgreen JH, Lawrence JS. Osteo-arthrosis and disk degeneration in an urban population. Ann Rheum Dis 1958 Dec;17(4):388-97.

(41) Sowers M, Zobel D, Weissfeld L, Hawthorne VM, Carman W. Progression of osteoarthritis of the hand and metacarpal bone loss. A twenty-year followup of incident cases. Arthritis Rheum 1991 Jan;34(1):36-42.

(42) van Saase JL, van Romunde LK, Cats A, Vandenbroucke JP, Valkenburg HA. Epidemiology of osteoarthritis: Zoetermeer survey. Comparison of radiological osteoarthritis in a Dutch population with that in 10 other populations. Ann Rheum Dis 1989 Apr;48(4):271-80.

(43) WHO. Obesity: preventing and managing the global epidemic. Report of a WHO Consultation. WHO Technical Report Series, No. 894. Geneva: World Health Organization, 2000.

(44) Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. Grading quality of evidence and strength of recommendations. BMJ 2004 Jun 19;328(7454):1490.

(45) Pottie P, Presle N, Terlain B, Netter P, Mainard D, Berenbaum F. Obesity and osteoarthritis: more complex than predicted! Ann Rheum Dis 2006 Nov;65(11):1403-5.

(46) Dumond H, Presle N, Terlain B, Mainard D, Loeuille D, Netter P, et al. Evidence for a key role of leptin in osteoarthritis. Arthritis Rheum 2003 Nov;48(11):3118-29.

(47) Conaghan PG, Vanharanta H, Dieppe PA. Is progressive osteoarthritis an atheromatous vascular disease? Ann Rheum Dis 2005 Nov;64(11):1539-41.

(48) DeGroot J. The AGE of the matrix: chemistry, consequence and cure. Curr Opin Pharmacol 2004 Jun;4(3):301-5.