2 Understanding the relationship between body weight and osteoarthritis

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Overweight people are at high risk of developing knee osteoarthritis (OA) and may also be at increased risk of hand and hip OA. Furthermore, being overweight accelerates disease progression in knee OA. While the increased joint stress accompanying obesity may explain the strong linkage between obesity and knee OA risk, it does not necessarily explain why obese people have a high risk of disease in the hand nor why obese women are at higher comparative risk of knee disease than obese men. Unfortunately, studies of metabolic factors linked to obesity have not provided an explanation for these findings. There are a paucity of data on weight loss as a treatment for OA, but preliminary information suggests it is especially effective in knee disease and that even small amounts of weight reduction may have favourable effects.

Key words: osteoarthritis; obesity; epidemiology; risk factors.

Osteoarthritis (OA), the most common form of arthritis, is a slowly evolving, degenerative disease affecting cartilage and bone. Like other chronic non-infectious diseases, its aetiology appears multifactorial, and the disease may be preventable by risk factor modification. One of the best studied potentially modifiable risk factors is obesity. Obesity represents two biologically different factors. On the one hand, there is adiposity, an increase in the body’s reservoir of fatty tissue while on the other hand, there is obesity, with its associated increase in stress on weightbearing joints. Both of these factors may come into play as causes of OA (see below).

Risk factors for OA vary by joint (Felson, 1988). Knee injuries, like those sustained in football, predispose to knee OA but obviously not to hand OA. Some factors may have purely local effects, whereas others may have systemic effects. The effects of weight (or adiposity) may be both local and systemic.
Excess weight and the risk of knee OA

Population-based studies of OA have consistently shown that overweight people are at higher risk of developing knee OA than non-overweight controls. Estimates of risk vary and depend, to some degree, on both the criteria for obesity and the definition of OA. In data from the first National Health and Nutrition Examination Survey, conducted throughout the USA from 1971 to 1975 (Anderson and Felson, 1988), obese women (body mass index (BMI) > 30 yet ≤ 35) had almost four times the risk of OA as women whose BMI was under 25. For men in the same weight category (BMI > 30 yet ≤ 35), the risk was increased 4.8-fold over men who were of normal weight. These risk estimates are similar to those found in other studies.

While studies have shown a cross-sectional association between obesity and knee OA, people who were overweight could have gained weight after developing OA because of their knee pain and sedentary level of activity. Recent studies, however, have proved that obesity precedes knee OA occurrence. In one study, for example, people who were overweight at an average age of 37 years, an age when OA of the knee is extremely uncommon, were at increased risk of developing knee OA when they reached their 70s (Felson et al, 1988). Also, repeated X-rays in population studies of people without OA, have shown that a person’s weight at baseline is directly correlated with their risk of developing knee OA later (Schouten et al, 1992; Felson et al, 1997).

One report of the association between obesity and knee OA suggested that it occurred only in tibiofemoral, and not patellofemoral, OA (Cooper et al, 1994), but two subsequent investigations, both from larger studies than the first, reported that obese people are at higher than expected risk of both tibiofemoral and patellofemoral OA (Cicuttini et al, 1996; McAlindon et al, 1996). In fact, obese people may be at especially high risk of getting OA in both tibiofemoral and patellofemoral knee compartments (McAlindon et al, 1996).

Several other features of the association between obesity and knee OA are noteworthy. Firstly, obese people appear to be at an especially high risk of bilateral as opposed to unilateral knee OA, the latter of which may be more often associated with knee injury. Secondly, this strong association is not attenuated by adjustment for other factors correlated with obesity (Davis et al, 1988) such as hyperlipidaemia, hyperuricaemia and diabetes, and it is unexplained by distribution of adipose tissue in the body. Finally, in some studies the relationship between obesity and knee OA has been stronger in women than in men (Felson et al, 1988, 1997; Schouten et al, 1992). Obese women have an especially high risk of knee OA, whereas obese men have a marginally higher risk than non-obese men. Some of the sex difference may be explained by the tendency for thin men to have a history of an OA-inducing knee injury.

Not only are obese people at high risk of developing knee OA, increasingly, longitudinal studies suggest that obese people with knee OA have a higher risk of experiencing disease progression than thinner people.
(Dougados et al., 1992). Furthermore, women with unilateral disease who are overweight may be at a much higher risk of developing bilateral knee OA than their non-obese counterparts (Spector et al., 1994).

**Excess weight and the risk of hip OA**

Obese people have a higher than expected risk of developing hip OA, although the association of weight with hip OA in most studies is not as strong as with knee OA. Studies (Table 1) have been inconsistent, with some reporting no association (Kellgren, 1961; Saville and Dickson, 1968; van Saase et al., 1988; Tepper and Hochberg, 1993).

<table>
<thead>
<tr>
<th>Reference</th>
<th>Total (cases)</th>
<th>Sex</th>
<th>Disease definition</th>
<th>General findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kellgren (1961)</td>
<td>379 (46)</td>
<td>Both</td>
<td>Radiographical</td>
<td>Obese and non-obese with equal prevalence of OA</td>
</tr>
<tr>
<td>Saville and Dickson (1968)</td>
<td>121 (121)</td>
<td>Both</td>
<td>Clinical</td>
<td>Mean weight OA = mean weight in population</td>
</tr>
<tr>
<td>Kraus et al. (1978)</td>
<td>200 (100)</td>
<td>Both</td>
<td>Severe clinical</td>
<td>Increased risk of OA in obese (RR = 2.7, P&lt;0.005)</td>
</tr>
<tr>
<td>Hartz et al. (1986)</td>
<td>4225 (59)</td>
<td>Both</td>
<td>Radiographical</td>
<td>Increased relative weight in those with OA</td>
</tr>
<tr>
<td>Tepper and Hochberg (1993)</td>
<td>2490 (73)</td>
<td>Both</td>
<td>Radiographical</td>
<td>Overweight (by BMI) unassociated with OA (OR = 1.02)</td>
</tr>
<tr>
<td>van Saase et al. (1988)</td>
<td>2168 (122)</td>
<td>Both</td>
<td>Radiographical</td>
<td>In obese men OR for OA=2.59; for obese women, OR for OA=0.40</td>
</tr>
<tr>
<td>Vingard (1991)</td>
<td>569 (247)</td>
<td>Male</td>
<td>THR patients (clinical)</td>
<td>For obese at age 40 OA risk increased (OR = 3.5 (1.4, 4.5))</td>
</tr>
<tr>
<td>Heliövaara et al. (1993)</td>
<td>7217 (369)</td>
<td>Both</td>
<td>Clinical</td>
<td>Heaviest persons with increased risk of hip OA (OR = 2.0)</td>
</tr>
<tr>
<td>Roach et al. (1994)</td>
<td>332 (99)</td>
<td>Male</td>
<td>Clinical</td>
<td>Obese with higher risk of hip OA (OA = 2.0 (1.0, 4.0))</td>
</tr>
</tbody>
</table>

BMI, body mass index; OR, odds ratio; RR, relative risk; THR, total hip replacement.

Two published studies (Heliövaara et al., 1993; Tepper and Hochberg, 1993) and a third, presented in abstract form (Nevitt et al., 1993) have suggested that obese people have an especially high risk of bilateral, but not unilateral, hip OA (Table 2). In approximately 5000 women who had hip X-rays for the Study of Osteoporotic Fractures, obesity was associated with an 80% increase in the odds of bilateral hip OA (OA = 1.8) but only a 40% increase in unilateral OA (OA = 1.4).

Differences in disease definition may explain study differences. Those studies focusing on only radiographical disease have not consistently
Table 2. Association of obesity with bilateral and unilateral hip osteoarthritis (OA).

<table>
<thead>
<tr>
<th>Reference</th>
<th>Disease definition</th>
<th>Odds ratio (95% CI) for association of obesity with bilateral OA</th>
<th>Odds ratio for association with unilateral OA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tepper and Hochberg (1993)</td>
<td>Radiographical</td>
<td>2.0 (0.97, 4.2)</td>
<td>0.5 (0.3, 1.2)</td>
</tr>
<tr>
<td>(NHANES-I)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heliövaara et al (1993)</td>
<td>Clinical</td>
<td>For BMI 30–35 1.6 (1.0, 2.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>For BMI &gt;35 2.8 (1.4, 5.7)</td>
<td></td>
</tr>
<tr>
<td>Nevitt et al (1993)</td>
<td>Radiographical</td>
<td>For heaviest quintile 1.8 (1.1, 2.8)</td>
<td>1.4 (0.9, 2.1)</td>
</tr>
</tbody>
</table>

BMI, body mass index; CI, confidence interval.

reported that those with hip OA were heavier than non-hip OA subjects, whereas studies using symptomatic hip OA, or clinical disease, as a case definition have, in general, reported an association (Vingard, 1991; Heliövaara et al, 1993; Roach et al, 1994). The association of obesity with symptomatic hip OA could be explained by obesity inducing hip symptoms in those with structural disease. Alternatively, the failure to detect an association of obesity with radiographical OA could reflect imprecision of radiographical diagnoses of hip OA and suggest that clinical hip OA more validly reflects disease pathology.

Excess weight and the risk of hand OA

Because hand joints are non-weightbearing, the association between hand OA and weight is critical to an understanding of how obesity acts to cause OA. Surprisingly, people who are overweight may also be at higher risk of hand OA than those who are not overweight. A recent longitudinal study over 23 years, showed that those who were overweight had a higher risk of developing hand OA than those who were not (Carman et al, 1994). However, cross-sectional studies of the relationship between obesity and hand OA have not all been positive (Table 3), although a few suggest an association. Reports of an association of weight with hand OA have been inconsistent across studies, but have been seen in men and women and for distal interphalangeal joint (DIP) OA, proximal interphalangeal joint (PIP) OA and carpometacarpal (CMC) joint OA. As in studies of hip OA, discrepant definitions of disease may underlie study differences, but there are also substantial differences between studies in subject ages, OA prevalence and definitions of weight. The scattered positive associations seen in many studies are noteworthy, yet the impressive number of null findings can not be dismissed either. Most of the epidemiological studies summarized in Table 3 were large enough to detect moderate associations between obesity and hand OA, so that small sample size is not necessarily the best explanation of the null findings.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Number of subjects</th>
<th>Sex</th>
<th>Disease definition/joints</th>
<th>General findings†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keligren and Lawrence (1958)</td>
<td>379</td>
<td>Both</td>
<td>Radiographical OA</td>
<td>Obese men with more DIP OA than non-obese. No association in other joints or in women</td>
</tr>
<tr>
<td>Acheson and Collart (1975)</td>
<td>2207</td>
<td>Both</td>
<td>Radiographical OA in Index finger (sum of DIP, PIP, MCP)</td>
<td>Weight/height associated with OA in women, but not men</td>
</tr>
<tr>
<td>van Saase et al (1988)</td>
<td>2168</td>
<td>Both</td>
<td>Radiographical OA Joint groups: DIP, PIP, MCP, CMC</td>
<td>In men, BMI associated with DIP, PIP and MCP OA, but not CMC OA; in women BMI associated with DIP, PIP OA but not MCP, CMC OA</td>
</tr>
<tr>
<td>Begge et al (1991)</td>
<td>340</td>
<td>Both</td>
<td>Radiographical OA Joint groups: DIP, PIP, IP, MCP, CMC</td>
<td>OA of hand joints correlated with BMI in men, but not women</td>
</tr>
<tr>
<td>Hochberg et al (1991)</td>
<td>888</td>
<td>Male</td>
<td>Radiographical OA Highest grade for most severely affected DIP joint</td>
<td>No association between OA and any of 3 measures of obesity</td>
</tr>
<tr>
<td>Hochberg et al (1993)</td>
<td>317</td>
<td>Female</td>
<td>Radiographical OA Highest grade for most severely affected of the DIP, PIP or CMC joint</td>
<td>No association between radiographical hand OA and any of 3 measures of obesity</td>
</tr>
<tr>
<td>Hart and Spector (1993)</td>
<td>1003</td>
<td>Female</td>
<td>Radiographical OA Joint groups: CMC, 2 or more DIP or PIP</td>
<td>For highest tertile of BMI (versus lowest) OR of OA 1.2 = (NS) at PIP, 1.5 (NS) at DIP and 1.7 (P &lt; 0.05)* at CMC</td>
</tr>
<tr>
<td>Carman et al (1994)*</td>
<td>1275</td>
<td>Both</td>
<td>Radiographical OA Develop OA in one or more hand joints</td>
<td>Obesity at baseline was associated with more incident OA at 23-year follow up</td>
</tr>
<tr>
<td>Cicutti et al (1996)</td>
<td>658 twin</td>
<td>Female</td>
<td>Radiographical OA (Any OA in DIP, PIP, CMC)</td>
<td>Twin difference in weight correlated with CMC osteophytes, but not OA in DIP, PIP</td>
</tr>
</tbody>
</table>

* Only longitudinal study. All others cross-sectional.
† Positive associations are so characterized based on whether they were statistically significant.
BMI, body mass index; CMC, carpometacarpal; DIP, distal interphalangeal; IP, interphalangeal; MCP, metacarpophalangeal; NS, not significant; OR, odds ratio; PIP, proximal interphalangeal.
In studies in which weight is assessed as a risk factor for both knee and hand OA, weight has a stronger association with knee OA (Van Saase et al., 1988; Spector et al., 1994). Since obese people do not necessarily have greater force across their joints than those who are not overweight, the relationship between obesity and hand OA remains enigmatic.

**Mechanisms by which obesity could cause OA**

**Mechanical effect of excess weight**

Weight could act through two different intermediaries to cause OA. First, and most logically, being overweight, because it increases the amount of force across a weightbearing joint, could induce cartilage breakdown simply on the basis of excess force which then leads to OA. Overall force across the knee and hip are approximately 2 to 3 times body weight during walking (Schipplein and Andriacchi, 1991). Therefore, every pound of weight can be multiplied by this factor to determine its effect on knee forces. In certain positions, such as climbing stairs and getting up out of a chair, knee and hip forces are over 3 times body weight and during these activities, each pound of excess weight exerts its force according to this even higher multiplier. Furthermore, obese people have gait patterns different from thin people such as walking with increased rearfoot motion and with their forefeet abducted (Messier, 1994). This latter posture, because it can lower the adduction moment across the knee (Schipplein and Andriacchi, 1991), may ironically lower the risk of medial knee joint OA. Nonetheless, the net effect of obesity on weightbearing joint stress (force per unit area), because of the multiplier effect, is likely to be substantial.

**Metabolic concomitants of adiposity**

Explanations of the effect of obesity on OA that focus solely on the mechanical effects of weight fail to readily explain two epidemiological observations about obesity and OA. Firstly, as noted above, many studies have suggested that obese people have an elevated risk of hand OA. Secondly obese women, but perhaps not obese men, are at increased risk of knee OA; in other words, the relationship between obesity and knee OA is much stronger in women than men.

Admittedly, mechanical explanations could help to explain these observations. For example, the increased joint stress in knees of obese men could be deflected by their stronger muscles than women or force could be distributed over a greater knee area, leading to less joint stress in men than women. In hands, obese people could also have greater arm circumference and muscle mass, leading to more forceful and damaging muscle contraction across the hand joints.
Although these explanations may seem reasonable, there are others that are equally, or more, plausible, and they consist of metabolic features of adiposity. By metabolic features, we mean that persons with excess adipose tissue have abnormal levels of certain hormones or growth factors that may affect cartilage or underlying bone in such a way as to predispose to the development of OA. Following this line of reasoning, obese people may have a circulating factor, possibly a cartilage growth factor or a bone factor, that acts to accelerate cartilage breakdown and lead to OA.

As the distribution of adiposity has been linked to metabolic abnormalities, one way to investigate metabolic factors and OA is to test whether fat distribution is unique in subjects with OA compared with subjects of similar weight but without OA. Indeed, abdominal adiposity, as opposed to adiposity in thighs and the appendicular skeleton, is an independent risk factor for diabetes and ischaemic heart disease (Lapidus et al, 1984; Larsson et al, 1984). However, based on three null studies (Davis et al, 1990; Hart and Spector, 1993; Hochberg et al, 1995) evaluating the association of radiographic knee OA with different measures of fat distribution including the waist hip ratio (Spector et al, 1994; Hochberg et al, 1995), it appears that fat distribution does not affect the risk of developing knee OA.

While the risk of diabetes is markedly increased in obese people, diabetes, per se, does not appear to account for the association between obesity and OA. Indeed, the obesity–knee OA association was not attenuated by adjustment for the presence of diabetes in two studies (Davis et al, 1988; Felson et al, 1988), and further evidence (Frey et al, 1996) suggests that there is, at best, a weak correlation between the presence of diabetes and OA.

Insulin-like growth factor (IGF1) may potentiate cartilage matrix synthesis (Morales and Hascall, 1989) and, in theory, high circulating levels, if locally active in cartilage, might protect against OA. People with abdominal adiposity may have low IGF1 levels yet epidemiological studies have not confirmed that high IGF1 levels are associated with a reduced risk of OA. In fact, in the only longitudinal study so far, Schouten et al (1993) suggested the opposite—that high IGF1 levels increased the risk of developing progressive knee OA. Cross-sectional studies evaluating IGF1 levels and OA have generally been null, although one recent cross-sectional study (Lloyd et al, 1996) reported a correlation between IGF1 and severe OA.

In post-menopausal women, the main source of circulating oestrogens is fat. Androstenedione produced by the adrenal glands undergoes conversion to oestrone, a biologically active oestrogen, in adipose tissue. Obese post-menopausal women have higher circulating oestrogen levels than thin women. While it is possible that high circulating oestrogens predispose obese women to OA, there is little evidence to support this. Firstly, Cauley et al (1993) evaluated oestradiol and oestrone levels in over 200 post-menopausal women drawn from a community sample and found no association between oestrogen levels and the amount of radiographic hand OA. Secondly, a series of epidemiological studies examining the rate of OA in post-menopausal oestrogen users versus non-users (Nevitt and Felson, 1996) strongly suggest that oestrogen replacement therapy lowers the risk of OA rather than increases it.
A factor related to oestrogen levels, bone density, however could explain how obesity causes OA. Women with high bone density are at high risk of getting OA (Hannan et al, 1992), and obese post-menopausal women, because of their high circulating levels of oestrogen, have higher bone densities on average than thin post-menopausal women. This possible explanation has not been directly tested, but studies have reported persistent strong associations between knee OA and obesity, even after adjusting for bone density (Felson et al, 1997), suggesting that the high bone density of obese women does not fully explain the causal association between obesity and knee OA.

It should be noted that, in epidemiological terms, ‘explanatory’ metabolic factors would have to be intervening variables (obesity acts through them) or confounders (obesity is associated with them but not causally) of the association between obesity and OA. According to Walker (1991) to qualify as the ‘explanatory factor’ for the association between obesity and OA, a metabolic factor must be a stronger risk factor for disease than the associated factor (obesity) and must also be highly correlated with the associated factor (i.e. must be strongly correlated with obesity). Since the odds ratio for the association between knee OA and obesity ranges up to 7 in some studies, it is unlikely that any explanatory factor can account for this strong relationship. Therefore, at least for knee OA, mechanically-based obesity-induced joint stress plays a role in its causation.

**Weight loss to prevent or treat OA**

In the Framingham study where subjects have been studied biennially for 40 years including serial weight measurements, Felson et al (1992) evaluated whether weight loss or weight gain affected the risk of incident symptomatic knee OA in women. For women whose baseline body mass index values were at least 25 (over the median), weight loss lowered the rate of knee OA. The adjusted odds ratio per two units of body mass index (approximately 11 pounds for a women of normal height) was 0.41, a reduction of more than 50% in the risk of developing knee OA ($P = 0.02$). Weight gain was associated with a slightly increased rate of later knee OA (odds ratio 1.28 for a two-unit weight gain). For women whose baseline weight was under the median, neither weight gain nor weight loss significantly affected their risk of later disease.

How much disease might be prevented if obese people lost weight? Using data from the Framingham OA Study (Felson, 1995), OA was defined by the presence of symptoms and radiographs showing OA. For women, if those in the highest weight group (for women, BMI ≥ 29) dropped into the overweight group (BMI of 25–28.9) and those in the overweight category dropped into the reference group (BMI < 25), the total rate of knee OA would decrease by 33%. For women, weight accounts for more OA than any other known factor; for men, in which obesity is less consistently linked to the risk knee OA, obesity is second to major knee injury as a preventable cause of knee OA.

In a recent report (Felson et al, 1997) from the Framingham Study, in
which serial radiographs were obtained, weight change over an 8-year period between radiographs directly affected the risk of developing radiographic knee OA. Specifically, for every 10 lb increase in weight, the odds of developing radiographic OA increased by 40% with a commensurate decrease for a 10 lb weight loss. This effect of weight change was seen in women and not in men.

There is an unfortunate paucity of data on weight loss as a treatment for OA. One uncontrolled natural experiment occurred when a large group of morbidly obese patients underwent gastric stapling operations and were assessed before and after the operation (Mc Goey et al, 1990). It should be noted that these patients did not necessarily have OA, although many had joint pain in the knees and back. At one year after surgery, with a weight loss of 100 lb on average, symptoms in the knees, hips and other joints were much less frequent than before. For example, 57% of subjects had knee pain before surgery versus a 14% prevalence of knee pain after. This impressive result suggests that patients with OA who are overweight will experience symptomatic relief with weight loss, although the amount of weight loss needed to alleviate symptoms and prevent disease progression is unknown. In a small, randomized trial (Williams and Foulsham, 1981), persons with clinical knee or hip OA were randomized to an appetite suppressant, phentermine or placebo and all patients participated in weight reduction sessions. While most patients in both groups lost weight and there were no significant differences in joint symptoms at the end of the trial, weight loss (3–6 kg on average) correlated strongly with a reduction in OA clinical score; a correlation that was stronger for knee than for hip OA. Finally, people with OA who are overweight are often ineligible for total knee and total hip surgeries; procedures that effectively alleviate pain.

Summary

Being overweight is an important modifiable risk factor for OA in the knees, hips and hands. The biological mechanism, while likely related to joint force, is not entirely clear. Weight loss may prevent OA, especially in the knees, and those who are overweight are at high risk of disease progression.

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Practice point

- a modest amount of weight loss (10–15 lb) is likely to alleviate symptoms and delay disease progression in patients with knee OA
References


