RELATION OF OBESITY AND OF VOCATIONAL AND AVOCATIONAL RISK FACTORS TO OSTEOARTHRITIS

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Given the recent advances in our understanding of risk factors for OA, an updated review of the relationship between obesity and vocational and avocational risk factors for OA is needed. After undertaking a MEDLINE search encompassing articles published in 2002–2004 we selected and review here articles that have filled gaps in our knowledge or changed our understanding of how loading factors, transmitted through occupational or avocational activities and by obesity, influence the risk of OA.

Avocation, vocation, and OA. In our original review of this topic[1] we argued that the effect of sports activity on OA risk depended upon whether the activity was undertaken by a person with an already damaged joint or a normal joint. Because the protective mechanisms of the damaged joint are impaired, it is vulnerable to the transarticular loading that occurs with sports activity. In contrast, a normal joint, especially in a younger person, is relatively resistant to damage. An exception to this observation exists, however, among professional athletes, in whom overuse may be so great that it may gradually or acutely injure a joint that is otherwise normal.

Two studies evaluating the risk of OA in professional athletes have been published in the last 2 years. In one, 92 former football players who were now managers of teams of premier football clubs in England and a larger number of non-footballer controls were surveyed. The outcome examined was "proven degenerative disease of the hip, defined as arthritis diagnosed by a doctor using an x-ray." Control subjects were individuals who had undergone a barium enema and thus had had a radiograph that permitted incidental visualization of the hip joints. Thirteen percent of the ex-football players, but only 2% of the controls, reported having OA of the hip, i.e., the risk of hip OA markedly and significantly increased among the professional football players[2].

In a smaller study of elite former javelin throwers and high jumpers, performed 10 years or more after their retirement, hip radiographs of the athletes were compared to those of age- and sex-matched controls[3]. Hip OA was far more prevalent in the retired elite athletes. However, despite the higher prevalence of OA, no increased risk of functional loss was apparent. The above 2 studies corroborate previous studies, suggesting that participation in professional athletics predisposes to development of OA in a joint that is overused.

Occupational activities constitute a different model of loading. It is assumed that persons undertaking jobs that demand physical labor have normal joints at the outset but that these jobs require overuse beyond the point at which joint protective mechanisms are effective. In a national survey undertaken in Canada, Rossignol and colleagues[4] further confirmed that blue collar workers have a higher risk than office workers of knee, hip, and hand OA, and polyarticular OA. Notably, this risk was present in both men and women who were unskilled laborers. This study is unique in providing new data on occupational activities in women, among whom housekeepers were at especially high risk of disease.

Obesity and OA. Whereas research findings in the past couple of years have filled gaps in our understanding of the relationship of vocation and avocation to OA, our comprehension of the relation of obesity and OA has genuinely taken a leap forward, based on several important new findings.

First, it has been thought that obesity increases the risk of OA in the hip and knee by increasing load on these weight-bearing joints. Alternatively, because obesity and OA are both associated with genetic predispositions, the 2 conditions could be linked if the predispositions were themselves shared (i.e., genes that cause obesity also predispose to OA). By radiographic assessment of OA in a large group of mono- and dizygotic twins from England, Manek and colleagues[5] confirmed the strong association of obesity with knee OA and their previous finding that heritability for knee OA was high. However, they could not detect a shared genetic pathway between body mass index (BMI) and knee OA and concluded that such a pathway was probably not the explanation for the strong association between obesity and knee OA.

Given that mechanical effects of obesity are likely to predominate as an explanation for the association of obesity with knee and hip OA, 2 important recent studies provide additional insights into this relationship: In a cohort of persons who had undergone meniscal resection 15–22 years earlier, Englund and Lohmander[6] noted that those with a BMI $\leq$ 30 were especially likely to develop symptomatic and radiographic knee OA. It is noteworthy that these men and women were primarily in their mid-50s at the time of followup and that 66% of those with BMI $\leq$ 30 had radiographic tibiofemoral OA (vs 44% of those with BMI $<$ 25). More important, 43% of persons with BMI $\leq$ 30 at time of followup, but only 18% with BMI $<$ 25 at that time, had developed symptomatic knee OA ($p = 0.001$ by test for trend). Those with a BMI of 25–29 were at intermediate risk. These data suggest that persons who have undergone even partial meniscectomy should control their weight to avoid developing symptomatic knee OA later in life.

While obesity clearly increases loading across the knee, a given level of obesity does not cause a similar level of loading across all knees. Because varus or valgus malalignment of the limb determines whether loading of the knee is focal or more diffuse, it stands to reason that obese persons with malalignment will have an especially high absolute level of loading in a knee that might already be at risk for OA because of their obesity. Indeed, an obese person with a neutrally aligned limb and OA may distribute their obesity

throughout the knee and not be at increased risk of progression of joint damage, whereas a severely malaligned knee would distribute any loading focally, and any level of loading might be injurious. Therefore, the knees that are especially vulnerable to the effects of obesity may be those in limbs that are only moderately malaligned. In such knees, the absolute amount of focal loading in a thin person might be below a level that is injurious, whereas in an obese person, loading with normal usage might exceed this threshold.

Among 227 persons with symptomatic knee OA who were followed for 30 months, considering all knees, Felson and colleagues[7] found that obese subjects had a significantly increased risk of radiographic progression of OA (defined as joint space loss), although the increase was not impressive (odds ratio = 1.08 per 2 unit increase in BMI). Among limbs with neutral alignment, obesity had no effect on radiographic progression (OR = 1.0). Similarly, subjects with severely malaligned limbs exhibited, in general, a high risk of OA progression, but in this subgroup progression was no more likely to occur in obese subjects than in the nonobese (OR = 0.93). Only in those subjects with moderately malaligned limbs did obesity have an effect on progression of OA (OR per 2 unit increase in BMI = 1.23, $p \leq 0.01$; Figure 1).

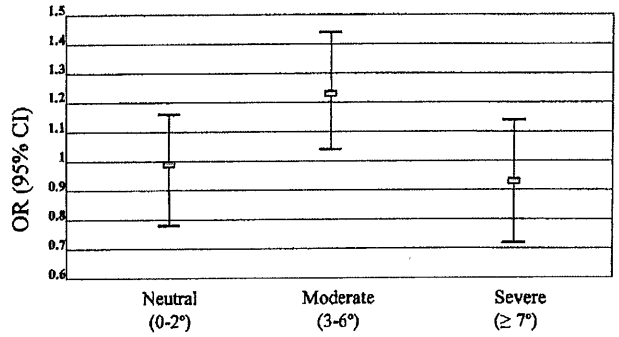

Figure 1. Effect of a 2-unit increase in body mass index on the risk of OA progression by stratum of knee-limb alignment. Absolute values are shown for limb malalignment. With permission, from Felson, *et al.* Arthritis Rheum 2004;50:3904-9.

These results suggest that future trials of weight loss in OA should restrict entry to subjects with moderate malalignment. The results also may suggest why some patients with knee OA who lose weight do not experience symptomatic improvement. Lastly, they suggest that some limbs are so severely malaligned that the unloading that results from substantial weight loss may not be very effective in relieving symptoms.

The past 2 years have also seen the first published study of a large-scale randomized trial of a dietary intervention in knee OA. This pivotal trial, reported by Messier and colleagues[8], tested 2 interventions, exercise and diet focused on weight loss, in 316 overweight and obese adults 60 years of age and older who had symptomatic knee OA. Subjects were randomized to 1 of 4 groups: the control group received a healthy lifestyle education intervention; a second group received only dietary intervention, with a goal of 5% weight loss to be achieved by intensive dietary training accomplished through group and individual sessions; a third group received a multifaceted aerobic and resistance training intervention 3 times weekly; and a fourth group received

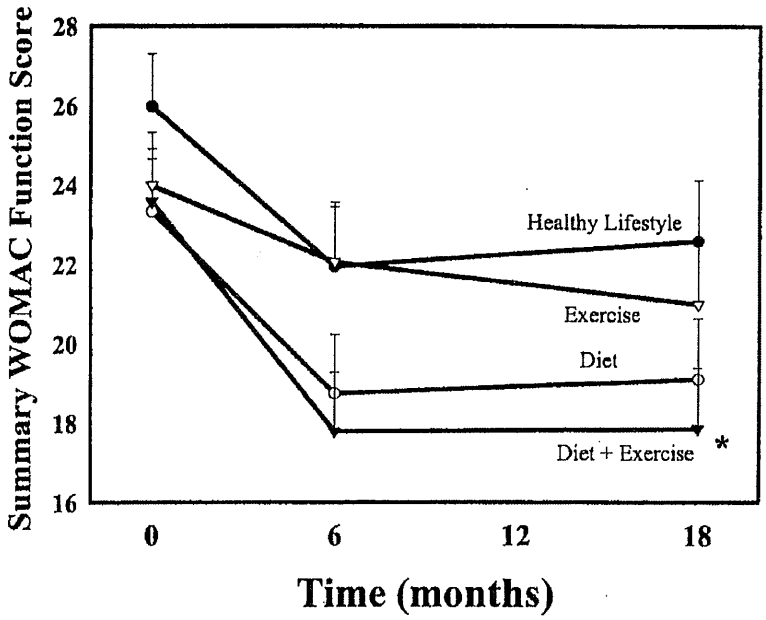

Figure 2. Mean ± SEM unadjusted Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) physical function summary scores across the 18-month intervention period. *p < 0.05 for diet plus exercise group versus healthy lifestyle group. With permission, from Messier, *et al.* Arthritis Rheum 2004;50:1501-10.

both diet and the exercise interventions. Each group was tracked for 18 months, with the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) physical function scale as the primary outcome measure (Figure 2).

Subjects in the diet group lost an average of 4.9% of their body weight (4.6 kg) and achieved significant improvement in their WOMAC physical function score, but their improvement was not significantly greater than that of the healthy lifestyle control group. Only the group randomized to diet plus exercise experienced significantly more improvement than the control healthy lifestyle group. These important results do not show an effect of weight loss as dramatic as might have been anticipated from prior uncontrolled studies and small trials. Even so, they strongly suggest the efficacy of weight loss in OA, especially if it is combined with exercise.

In summary, work in the past 2 years has led to substantial new insights into the relationship between obesity and OA, with studies suggesting for the first time that weight loss, especially if accompanied by exercise, may substantially improve symptoms.

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RISK FACTORS FOR THE DEVELOPMENT AND PROGRESSION OF HIP OSTEOARTHRITIS

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Lievense and colleagues at the Erasmus Medical Center, Rotterdam, have published several systematic reviews that nicely summarize the literature on risk factors for hip OA[1–4]. These reviews employed a common search strategy and all used the "best evidence" method of synthesizing data from observational epidemiological studies. Moderate evidence was found for a positive association between hip OA and obesity; participation in sporting activities, including running; and vocational activity, particularly involving a heavy physical workload, as characterized by farming (especially for more than 10 years) or lifting heavy loads (25 kg or more). Only limited evidence existed for a positive association between occurrence of hip OA and participation in athletics or presence of hip dysplasia in older persons.

The Rotterdam group also published a systematic review of observational studies of prognostic factors for hip OA[5], in which they divided progression of hip OA into clinical progression (e.g., progressing to total hip arthroplasty) and radiographic progression. There was strong evidence for more rapid progression in subjects with superolateral migration of the femoral head and in those with an atrophic (in comparison with a hypertrophic) bone response. Limited evidence was present for a direct association between hip dysplasia and progression, and an inverse association was noted between the joint space width (JSW) and the progression to total hip arthroplasty (i.e., the smaller the JSW, the greater the risk of progression to total hip arthroplasty). Evidence for an association between progression of OA with greater age at baseline and with female sex was not consistent across studies; some found an association while others did not. There was strong evidence that neither body weight nor BMI was associated with progression. A subsequent report[6] noted that women had significantly more rapid structural progression than men and a significantly greater relative hazard of subsequent total hip arthroplasty; however, these relationships were no longer significant after adjustment for confounding variables.

Methods of determining structural progression in hip OA were discussed at the Osteoarthritis Research Society International (OARSI) Congress in Barcelona[7]. The group determined that, at this time, conventional radiography was the only adequately validated method for assessment of structural progression in clinical and epidemiological studies of hip OA. Recommendations were published on techniques for pelvic radiography in both supine and standing positions: it was felt that separate radiographs for each hip did not provide important advantages over a single standardized radiograph of the pelvis, while they presented greater problems than the latter with respect to repositioning in longitudinal studies. The preferred outcome measure for assessing progression is JSW at the narrowest point in the hip joint. Several methods for obtaining this measurement were reviewed and it was concluded that measurement could be performed either with a calibrated eyepiece (reticule) or electronic calipers, or by computer.

Maillefert and colleagues used data from a longitudinal