A Review Paper

Obesity and Osteoarthritis

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Abstract

Osteoarthritis (OA) has become one of the leading causes of disability in the United States. Mechanical forces exerted on the joints are a significant cause of OA and one of the most modifiable risk factors. As determined by body mass index (BMI), 34 million US adults are obese, and 13 million of these are morbidly obese. Female sex, lower educational levels, obesity, and poor muscular strength are associated with symptomatic disease and subsequent disability. Recently, genetics has been shown to be a significant factor in the disease process. March and Bagga (*Med J Aust.* 2004; 180 (5 suppl): S6-S10) showed that the risk for knee OA increased by 36% for every 2 units of BMI (5 kg) of weight gain. Bariatric surgery results in a mean weight loss of 44 kg (97 lb). Eighty-nine percent of patients had complete relief of pain caused by OA in at least one joint after undergoing bariatric surgery.

Osteoarthritis (OA) is a painful degenerative condition that can affect one or more of the joints. Weight-bearing joints (eg, spine, hip, knee, ankle) are often involved in the disease process. Mechanical forces exerted on the joints are a significant cause of OA and one of the most modifiable risk factors with respect to weight loss and activity modification.

The obesity problem is reaching epidemic proportions in the United States, and increased weight translates to increased force on the weight-bearing joints. As the population has aged and become heavier, OA has become one of the leading causes of disability. Losing weight, though not always easy, is of paramount importance in slowing OA progression.

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Epidemiology

The World Health Organization[1] stated that the "epidemic of obesity" affects an estimated 1 billion people worldwide. Based on recent body mass index (BMI) data, 34 million US adults are obese, and 13 million of these are morbidly obese.[2] In a 1999–2002 study of US adults 20 years old or older, 65.1% were overweight, 30.4% were obese (BMI, 30-39), and 4.9% were extremely obese (BMI, >40).[3] Even more important, the incidence of overweight US children has quadrupled over the past 25 years,[4] and, among children 6 to 19 years old, 16% were overweight, and 31% were at risk for being overweight.[3] Ten percent of the European population over age 65 shows radiographic evidence of OA, and half of this group is symptomatic.[5] Of the US population that is over age 55, 2.4% has disabling pain from knee OA, and by age 65 twice as many women as men in the same age range are affected.[6] Known causes of hip OA include primary inflammatory arthridities, ankylosing spondylitis, rheumatoid arthritis, metabolic diseases, developmental dysplasia of the hip, Legg–Calvé–Perthes disease, and slipped capital femoral epiphysis. However, this list accounts for only a minority of hip OA cases. Fixed risk factors for OA are age, sex, family history, and race.[7] On the other hand, modifiable risk factors include obesity, activity, exercise, muscle weakness, and joint injury.[7] The mortality rate of morbidly obese people is 12 times that of the overall population.[2] Female sex, lower educational levels, obesity, and poor muscular strength are associated with symptomatic disease and subsequent disability.[8]

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OA is one of the leading causes of disability. In Australia, OA is the third leading cause of life-years lost to disability.[8] OA has a substantial disease burden and affects quality of life on many levels. "People with OA have more difficulty and take longer to perform activities of daily living, having less time available for leisure activities, depend significantly more on family and friends for assistance, and spend more money on healthcare than age-matched and sex-matched peers in the general population."[8] For patients with symptomatic OA, March and Bagga[8] found lower scores in 6 of the 8 Short Form-36 (SF-36) functional outcome questionnaire domains that deal with quality of life. Last, OA is the leading indica-

tion for hip and knee replacement surgeries, with more than 250,000 performed annually in the United States. In England, approximately 1.5% of the population will have a total knee arthroplasty (TKA) performed in their lifetime.[9]

Etiology

OA is a chronic degenerative joint disease caused by mechanical factors (creating increased force across the joint) and systemic factors. During the single-leg stance in the gait cycle, a force of 3 to 6 times that of body weight is transmitted across the knee joint. Likewise, the force exerted across the hip is 3 times that of body weight. These forces are increased several times over during high-impact activities. "Therefore, any increase in weight may be roughly multiplied by these factors to reveal the excess force across the knee when an overweight person walks."[10] This increase in force elevates stress on articular cartilage and causes its eventual breakdown, which in turn causes proliferation of periarticular bone (to distribute the increased forces) and culminates in decreased joint space. If unchecked, this vicious cycle continues until the joint space is obliterated.

Several studies have directly examined the obesity-caused mechanical changes occurring in the knee and in the articular cartilage in general. Gushue and colleagues[11] conducted a gait study and wrote that their "overweight group of children showed a significantly higher peak internal knee abduction moment in early stance" and that "these data suggest that overweight children may not be able to compensate for alterations in the frontal plane during gait, which may lead to increased medial compartment joint loads." A separate study found a statistically significant direct association between body mass and peak values of compressive forces, resultant forces, the abduction moment, and the medial moment of the knee; each pound of weight loss results in a 4-fold reduction in load per step during daily activities.[12] Two other studies also showed that increased weight increases activation of the mechanoreceptors within the cartilage (stretch-activated channels, α-5B1 integrin, CD44 on chondrocytes).[13,14] This activation may cause the expression and production of cytokines, growth factors, metalloproteinases, and mediators such as prostaglandins and nitric oxide.[13] These overload conditions may be speculated to trigger both inhibition of matrix synthesis and onset of cartilage degradation.[14]

Interestingly, mechanical factors cannot fully explain the higher incidence of OA in the non–weight-bearing joints (eg, hands) of obese patients versus nonobese patients.[15-17] However, results from newer studies are shedding light on the fact that OA may have both genetic and systemic factors. More than 600 genes, markers, and regions of chromosomes have been linked to obesity.[18,19] Some examples include a specific β-2 adrenergic receptor that has been linked with changes in body composition, a MC4R gene mutation that has been linked with binge eating, and leptin, which regulates short- and long-term control of hunger.[18] Some families in which OA is prevalent have a genetic defect in type 2 collagen caused by a single amino acid substitution (Cys substitution for Arg-α1-519) that may change its molecular interactions with collagen IX, which could then destabilize the cartilage matrix.[20] Increased adiposity is associated with abnormal levels of hormones and growth factors that might accelerate cartilage breakdown, metabolically active intermediaries yet to be disclosed, dysregulation of lipid homeostasis, and increased bone mineral density.[10,21,22] Obesity has been proposed to be a chronic inflammatory state, and interleukin 1 (IL-1) encodes for susceptibility to knee OA.[23] Therefore, even in nonmechanical situations, obesity and increased adiposity have a prominent role in OA pathogenesis.

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The Role of Obesity

As reported in the literature, BMI is the parameter most often used for weight assessment. BMI is calculated as weight in kilograms divided by height in meters squared (kg/m^2). A person with a BMI of less than 20 is considered underweight, 20 to 24.9 normal, more than 30 obese,[3,9] and more than 40 morbidly obese.[2,3]

Results from multiple well-designed studies over the past 30 years have borne out a statistically significant link between obesity and OA incidence. Coggon and colleagues[9] conducted a population-based case–control study in 3 separate health districts in England. A total of 525 men and women (over age 45) on the surgical waiting list for TKAs were compared with 525 controls matched on age, sex, and primary care doctor. The odds ratio for developing OA was 0.1 (95% CI 0.0-0.5) when BMI was less than 20 versus 13.6 (95% CI 5.1-36.2) when BMI was more than 36. BMI also interacted additively with other significant risk factors, such as previous knee injury, previous meniscectomy, and presence of Heberden nodes; the odds ratio increased to 78 with all of the above risk factors. When plotted on a graph, increasing weight created an exponential rise in OA. In addition, the authors concluded that the "patterns of interaction between risk factors were similar in the two sexes, but the risks associated with obesity tended to be rather higher in women than in men."

In a population-based case–control study conducted

by Cooper and colleagues,[5] 611 patients (210 men, 401 women) were matched with case controls much the way subjects were matched by Coggon and colleagues.[9] Enlisted patients were on waiting lists for total hip arthroplasties (THAs). Hip OA was 1.7 times more likely to develop in patients with BMI of more than 28 than in patients with BMI of less than 24.5. Cooper and colleagues concluded, "Obesity and hip injury are important risk factors for OA that might be amenable to primary prevention."

In a matched case–control study, Dawson and colleagues[6] used interviews to assess 50- to 70-year-old women awaiting TKAs. Contrary to previous results, "weight gain in early adult life was particularly pronounced among cases of OA." BMI of more than 25 at age 36 to 40 was statistically significantly associated with knee OA later in life. Manninen and colleagues,[24] who reviewed the social security registry of Finland and identified 6647 farmers age 40 to 64 who had applied for disability pensions, found that the "relationship between [BMI] and the incidence of disabling knee [OA] was linear, the adjusted relative risk was 1.4 (95% CI, 1.2-1.5) per standard deviation of the index (3.8 kg/m^2)." The relative risk was highest for bilateral knee OA, and the positive association between relative weight and OA was similar in men and women. March and Bagga[8] showed that the risk for knee OA increased by 36% for every 2 units of BMI (5 kg) of weight gain. BMI of more than 30 increased the risk for knee OA approximately 20-fold. In an editorial, Nevitt and Lane[21] cited the Johns Hopkins Precursor Study, in which men in their 20s who had a BMI of more than 25 were at 3 times the risk for developing knee OA in their 60s as compared with thin age-matched men with a BMI of less than 25. Last, Felson[10] cited the First National Health and Nutrition Examination Survey, conducted in the United States from 1971 to 1975, in which risk for developing knee OA was 4 times higher for women with a BMI of more than 30 than for women with a BMI of less than 25. Men in the same categories had a 4.8-fold increased risk for OA. "Persons in the upper 20% of weight have 7-10 times the risk of disease of those in the lowest 20% of weight."

The Role of Weight Loss

Given that weight gain is associated with increased OA incidence (as already described), weight loss should be associated with decreased OA incidence. Coggon and colleagues,[9] pointing to their research results, indicated that lowering BMI to the normal range (20-24.9) would reduce the number of OA cases by more than 50%. In addition, "if all overweight and obese people reduced their weight by 5 kg or until BMI was within the recommended normal range, 24% of surgical cases of knee OA might be avoided." Felson[10] cited the Framingham Osteoarthritis Study, which concluded that a loss of 5 kg (11 lb) reduced OA risk by more than 50%; also in that study, a weight loss of 1 reference BMI range reduced male symptomatic knee OA by 21.4% and overall female knee OA by 33%. Messier and colleagues[25] found that a weight loss of 5% over 18 months in obese adults with knee OA resulted in an 18% improvement in function alone and in a 24% improvement in function when exercise was added. Last, according to a review by Gelber,[7] hip OA would decrease by 25% if obesity were eliminated.

When Morbidly Obese Patients Are Unsuitable Candidates for Arthroplasty

Parvizi and colleagues[2] studied 20 TKAs and THAs in morbidly obese patients who underwent bariatric surgery before their orthopedic procedures. BMI decreased from a mean of 49 to a mean of 29. Mean time until arthroplasty was performed was 23 months. The authors concluded that "morbidly obese individuals, with severe degenerative joint disease, who are considered unsuitable for arthroplasty because of excess weight, should be considered for bariatric surgery. Total joint arthroplasty after surgical treatment of obesity has an excellent outcome with an acceptable complication rate."

The Role of Bariatric Surgery

Bariatric surgeries, most commonly gastric stapling, are abdominal procedures performed to help morbidly obese patients lose weight. Given the role of obesity and OA and the role of weight loss and OA, bariatric procedures not only might decrease obesity but also might decrease OA incidence and symptoms. McGoey and colleagues[26] performed vertical-banded gastroplasties (gastric stapling procedures) on 105 morbidly obese patients (at least 45 kg or 100 lb overweight at time of surgery). Eighty-eight percent of these patients had chronic musculoskeletal pain that interfered with activities of daily living. Mean weight loss was 44 kg (97 lb). After this large weight loss, 89% of patients had complete relief of pain in one or more joints. Pain incidence decreased from 57% to 14% in the knee, from 62% to 11% in the spine, from 11% to 2% in the hip, from 34% to 2% in the ankles, and from 21% to 1% in the feet. In a study by Peltonen and colleagues,[27] the "recovery rate for pain in the knee and ankle joints in men and pain in the neck and back and in the hip, knee and ankle joints in women improved in the surgical group after 2 years"; in addition, obese women who underwent surgery had a lower incidence of work-restricting pain in the knee and ankle joints over 2 and 6 years.

Parvizi and colleagues[2] studied outcomes of total joint arthroplasty in patients who had been surgically treated for morbid obesity—see the Box above.

Conclusions

Obesity is a major risk factor for OA, but it is a modifiable risk factor. As the epidemic of obesity continues to grow, OA incidence will follow. From 1960 to 1988, 20- to 29-year-old men with a BMI of more than 30 had a 1.4-fold increase in OA, and this increase was even larger in women.[21] Between 1988 and 1994, 43% of the 20- to 39-year-old men had a

BMI of more than 25.[21] "Primary and secondary prevention programs aimed at reducing obesity, preventing injury, and improving rehabilitation and physical activity are urgently needed."[8] In addition, clearly we need programs aimed at decreasing childhood obesity and therefore preventing obese children from becoming obese adults. Ultimately, if all other attempts at weight loss have failed, bariatric surgery is a consideration in the morbidly obese patient population.

Authors' Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

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This paper will be judged for the Resident Writer's Award.