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Weight Loss and Obesity in the Treatment and Prevention of Osteoarthritis

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Introduction

Obesity is a global health issue, with 315 million adults are classified as obese, defined as a body mass index (BMI) of $\geq 30 \text{ kg/m}^2$.^{1, 2} Both children³ and the elderly⁴ are susceptible to obesity. Significant progress in the medical management of the metabolic symptoms related with obesity, has increased the lifespan of the obese individual.⁵ There is a tradeoff with longevity in the aging obese person, as the musculoskeletal system must bear the burden of carrying excessive weight over the person's lifespan. As BMI values increase, joint pain symptoms and severity increase.⁶ Joint pain may reflect the underlying pathological process of osteoarthritis (OA). For every 5kg weight gain, there is a commensurate 36% increased risk for developing OA.¹ In obese individuals, pain is most prevalent in the load-bearing joints including the lower limb and the low back,^{6, 7} but can manifest in upper extremity joints, hand and digits,⁸ thoracic spine and neck. In addition, cadaveric studies have revealed that obesity is related to greater knee OA severity than in normal weight individuals.⁹ Also, obesity is associated with faster OA progression than normal weight. Pain-related physical incapacitation worsens obesity, subsequent gait abnormalities and muscle weakness.¹⁰ Importantly, pain may mediate obesity-induced impairment of physical functioning and deterioration of health-related quality of life.^{11, 12} Weight loss sets in motion a cascade of events that can prevent OA onset or combat existing OA symptoms and disability. These events include reduction of mechanical and biological stressors. This article will review the newest evidence of the relationship between obesity and OA, and the effect of weight loss on the prevention and treatment of OA.

Obesity-Specific Mechanisms of OA Pathophysiology

While there are numerous pathways that contribute to OA onset, obesity-specific mechanisms include relative loss of muscle mass and strength over time, mechanical stress and systemic inflammation. Excessive adipose tissue compresses load-bearing joints and creates an inflammatory environment within tissues and joints. Figure 1 briefly summarizes the proposed obesity-related mechanisms underlying OA. Obesity induces abnormal joint

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loads and leads to adverse changes in the composition, structure and properties of articular cartilage. With increased body weight, both muscle mass and fat mass increase; yet the volume of muscle mass remains relatively low and inadequate to match the loads placed upon it. When strength is normalized for body mass, obese persons have lower muscle strength than normal weight counterparts, including the quadriceps¹³ and lumbar¹⁴ muscle groups. Obese people attempt to compensate for muscle weakness and instability by altering gait patterns and adopting different body transfer patterns to move excessive weight. With inadequate lower limb strength, less absorption of the impact forces on weight bearing joints occurs. Repetitive forces damage articular cartilage. Joint misalignment in the load bearing joints may occur with increased body segment girths, altered posture, skeletal muscle strength imbalance or weakness of muscles that control joint motion.¹⁵ In obesity, skeletal muscle becomes laden with intramuscular fat, and this fat is associated with elevated systemic levels of proinflammatory biomarkers. As obesity worsens, these biomarkers induce a feed-forward process of muscle catabolism and loss of strength.¹⁶ Over time, the cumulative effects of excessive body fat, and mechanical loading and aberrant joint motion, contribute to the OA pathophysiology and onset of inflammation and pain.¹⁷

Low grade systemic inflammation is now considered a hallmark of obesity and manifests as elevations in interleukins (IL) 1 β , IL-6, tumor necrosis factor (TNF- α) and the acute phase reactant C-reactive protein (CRP).¹⁶ These biomarkers might link obesity with the onset and progression of OA. In severe obesity, levels of these proteins are as much as 10-fold higher than those in normal weight.^{18, 19} Similar to adults, high body mass is related to increased CRP levels and decreased adiponectin levels in children.²⁰ The local inflammation response in the synovial fluid of joints afflicted by OA includes elevations of IL-1 β , and skeletal muscle. Systemic levels of IL-1 β , IL-6, TNF- α and CRP also rise with the presence of hip or knee OA. Five-year prospective evidence indicates that elevated levels of TNF- α or CRP can predict the progression OA.^{21, 22} Chronically high IL-6 levels are predictive of knee OA over a ten year period.²³ IL-1 protein content of the vastus lateralis is 34% higher while quadriceps strength is 40% lower in obese persons with OA compared to those without.²⁴

Inflammation is mediated by the activities of several adipokines such as adiponectin and leptin.²⁵ Leptin modulates food intake by acting on neural pathways in the hypothalamus and brainstem. While the specific mechanisms underlying adipokine action in OA are not fully known, recent evidence suggests that excessive leptin levels may activate cellular pathways that contribute to cartilage breakdown.²⁵ Normally, leptin activates expression of growth factors and production of extracellular matrix in cartilage, and can up-regulate matrix metalloproteinases and IL-1 both of which contribute to nitric oxide production and subsequent chondrocyte apoptosis and cartilage breakdown.²⁶ Leptin is also found in cartilage and osteophytes in persons with OA. Hyperleptinemia occurs locally in the human osteoarthritic joint. The combined influence of pain and worsening inflammation in untreated obesity likely contributes to an elevated risk for functional impairment in the obese, older adult. Adiponectin is a hormone secreted by adipocytes. Although produced in relatively low concentrations compared to that found in plasma, this hormone could be found in the synovial fluid of osteoarthritic joints likely derived from the infrapatellar fat pad and synovium. Conflicting evidence indicates that adiponectin can be pro-inflammatory (triggering IL-6 and nitric oxide production) or anti-inflammatory (upregulating inhibitors of metalloproteinases).²⁷ But what is clear is that there is a link between dysregulation of adiponectin and OA.

Therefore, the collective and interrelated effects of relatively low muscle mass and accumulation of adipose tissue in obesity, contribute to joint degeneration and OA onset via joint compressive forces and aberrant biomechanics, hyperleptinemia and inflammation.

Functional Disability, Obesity and OA

Obesity and OA collectively increase the incidence of mobility disability.^{28–40} Activities such as walking, chair rise and stair climb, and timed up-and-go tasks are performed at slower speeds and are more challenging for the obese individual. Cross-sectional data support that as BMI increases by one standard deviation, the times to complete timed-up and go and chair rise tests increase by 5.0% and 6.4%, respectively.³⁰ There is a progressive worsening of function and mobility with an increase in BMI. Gait parameters such as stride length and the average daily number of steps taken decreases by 55% when BMI exceeds 30 kg/m².⁴⁰ Of note, lower limb physical function and disability are not affected by adiposity distribution (assessed by 20 meter walk, knee flexion/ extension strength and chair rise time), as demonstrated by a cross sectional study of a group of older adults with either central or gynoid obesity.⁴¹

Prospective studies consistently show obesity-related deterioration of walking ability, chair rise and stair climb ability.⁴² Mechanisms for disability include muscle weakness, increased stiffness and pain. The severity of cartilage defects in obese people with knee OA is moderately associated with stiffness, pain and subjective and objective assessments of disability.⁴³

Kinesiophobia Due to Pain

The definition of OA includes the presence of pain symptoms. As such, pain may be a significant factor contributing to mobility impairment in obese individuals.^{32, 44} The combined effects of obesity and degenerative joints may induce fear of movement (kinesiophobia), because weight-bearing activities such as walking, climbing stairs, body transfers and activities of daily living cause pain.⁴⁵ As OA pain worsens over the long term, obese persons disengage from regular weight bearing activities and weight gain is exacerbated. We have recently found that obese persons with low back pain and knee pain rate kinesiophobia higher than non-obese individuals.^{46, 47} While higher kinesiophobia scores corresponded to higher perceived disability for tasks such as body transfers (chair rise), climbing stairs, jumping and running, these higher scores were surprisingly not associated with worse performance during functional tests such as flexibility, range of motion and muscle strength. These findings suggest that functional impairment in OA may be partly regulated by fear and perceived inability to perform certain tasks. Catastrophizing about pain is associated with severity of pain in obese patients with knee OA.^{48, 49} Both catastrophic thought patterns and somatization may foster hypervigilance to OA pain, and lead to avoidance of physical activity.⁵⁰ This psychosocial component is commonly overlooked when developing plans of care for the obese patient with OA pain.

Weight loss reduces joint pain and increases physical function. Randomized controlled trials show that knee OA pain reduction is associated with increased mobility and physical function.^{51–54} As weight loss occurs, the compressive forces through the loading bearing joints such as the knee are dramatically reduced by almost fourfold.⁵⁵ A reduction of body weight can attenuate the painful symptoms and likely reduces the fear of movement. In obese adults, achieving ~5% loss of body weight will relieve some joint pain, but a loss of at least 10% of body weight is associated with moderate to large clinical improvements in joint pain.⁵⁶ The management of OA pain with weight loss extends past pain reduction, and has powerfully positive ramifications for increased physical capability and independence, increased participation in home and community activities, and overall quality of life.

Weight Loss and Treatment of OA in the Obese Adult

Several options for weight loss exist, ranging from medications, to exercise and dietary modification, and bariatric surgery. The “right choice” of treatment for the obese patient should be tailored to meet the individual needs. Depending on the severity of obesity and OA, creative staging of interventions for progressive weight loss in OA may be implemented to minimize pain symptoms and kinesiophobia.

Weight Loss Medications

Medications may be used alone or in concert with other interventions to induce weight loss. Two FDA approved medications to treat obesity are Orlistat (Xenical; Hoffman LaRoche Pharmaceuticals Company) and Sibutramine (Meridia; Abbott Laboratories). Orlistat is a gastric and pancreatic lipase inhibitor which decreases fat absorption in intestines by roughly 30%.⁵⁷ Meta analysis revealed that 120 mg of Orlistat (three times daily) elicits 5% weight loss in 33% of patients.⁵⁸ Numerous studies have supported the efficacy of Sibutramine when administered for 6–24 months.⁵⁹ Thirty four % of patients achieved a minimum of 5% loss of body weight, and 15% of patients lost 10% or more of body weight over the course of one year. An important finding is that medications may be more effective when coupled with exercise and diet. For example, when Sibutramine is used in conjunction with a lifestyle modification intervention (ie, exercise and diet), weight loss is greater than that achieved with medication or the intervention alone.⁶⁰

Exercise and Diet

This review will focus on the randomized controlled trials (RCT) of exercise interventions in the older demographic. Published RCTs have examined weight loss and functional effects after aerobic exercise and resistance exercise programs, multimodal exercise programs, and multimodal training with or without caloric restriction. Several RCTs were identified that included resistance exercise (RX) and/or aerobic exercise (AX) (Table 1). RX features the use resistance exercise machines, strengthening exercise using body weight and home-based strengthening exercise. AX typically involves sustained large muscle activity such as walking, climbing stairs, stationary cycling, or aquatic aerobic exercise,^{61, 62, 63–65, 66} Multimodal training consists of a variety of aerobic, resistive and flexibility components during a single session. Multimodal activity programs have been implemented for durations lasting three months to one year.^{67–69} Often, the multimodal activity programs are coupled with dietary changes as part of a comprehensive lifestyle overhaul.

Among these RCTs, several have focused on the obese knee OA population and are presented in Table 1.^{51, 54, 66, 69–71} Training periods ranged from 2 to 6 months with a frequency of 2 to 3 times a week, and follow-ups up to 18 months. AX intensities required to elicit favorable functional changes included an intensity of 50–85% heart rate reserve for land based exercise^{54, 70, 71} or 65% of maximal heart rate in aquatic exercise.⁶⁶ The intensity of performing RX exercises varied among studies, ranging from using own the weight of the limb segment, body weight or cuff weight as the resistance,⁷¹ or use of dumbbells.⁵¹ Even simple home-based exercise studies indicate efficacy in reducing OA pain in this population; studies have featured quadricep contractions and functional tasks (e.g., rising from a chair) for up to 24 months.⁷² Compared with education control and diet groups, the exercise group achieved a 30% reduction in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scores and improvement in WOMAC functional scores.

Benefits of exercise for OA symptoms can include reduction of body weight. When exercise is coupled with diet, greater weight loss can occur. Compressive forces on the joint are

significantly reduced in proportion with the degree of weight loss.⁷³ Comparative studies show that multimodal exercise induces a 3.7% loss of body weight, whereas the diet only and diet+multimodal exercise result in 4.9% and 5.7% losses of body weight by six months.⁵⁴ Knee OA pain can be reduced with exercise or combined intervention, but the largest pain reduction (30.3%) was related with the greatest weight loss.⁵⁴ Pain improvement during the exercise intervention is the strongest contributing factor in explaining the association between exercise adherence and decreases in self-reported disability.⁷⁴

The value of exercise for OA in the obese patient is that it can be used to treat the disease and help prevent or delay the onset of the disease. Ideally, the incorporation of AX to stimulate caloric expenditure and RX to strengthen the musculature supporting the joints provides a well-rounded program to treat OA symptoms. Exercise can be applied to this population at any disease stage to help provide pain relief, strengthen muscles that surround the arthritic joint, and help control or reduce body weight, the latter being the main modifiable factor underlying OA. To help overcome kinesiophobia, exercise may need to be supervised initially and periodically thereafter to help ensure that activity is performed at the appropriate training stimulus and not compromised because of fear. Importantly, exercise interventions can be cost effective to treat knee OA in obese adults. Pain severity and functional outcomes such as walking performance and stair climb demonstrate the greatest improvements after exercise alone than after diet programs or exercise+diet interventions.⁷⁵

Bariatric Surgery

For many obese patients, meaningful weight loss is difficult as lifestyle changes are unappealing and long-term adherence is typically low. Bariatric surgery can elicit massive weight loss when post-surgical instructions are followed. Common surgical techniques include laparoscopic adjustable gastric banding, sleeve gastrectomy and vertical banded gastroplasty. Joint pain can be attenuated or abolished in morbidly obese persons with pain in the hip,^{76, 77} knee,^{77–80} ankle,^{79, 80} spine,^{77, 79–83} neck,⁷⁹ shoulder,⁷⁹ elbow wrist and hand,⁷⁹ and knee, ankle and foot pain.⁸⁴ Although there are methodological inconsistencies in the measurement follow-up times for joint pain between and within studies, the most common post-operative time point was approximately two years. Reductions in BMI values ranged from 6.2–14.7 kg/m² and this corresponded with a resolution of knee and back pain in 5–100% of patients, while pain severity was reduced in 31–94% depending on the joint and study.⁸⁵

Knee

Several studies have demonstrated that among patients with knee OA pain, bariatric procedures can predictably provide relief. Dramatic reductions in pain can occur as quickly as three months post-surgery.⁷⁷ Studies reported 9%⁸⁶ to 76%⁷⁶ less prevalence in knee pain by the final study time point as reflected by self-report surveys of joint pain and severity. Average and median WOMAC pain scores for knee pain were reduced by 51%,⁷⁹ and 66%,⁸⁶ respectively, at follow-up. Another study showed that Knee Society pain subscores are reduced by 14.8% while the function subscores improved by almost the same percent after surgery.⁷⁸ A mechanism of pain relief underlying these collective findings may be knee joint space widening with weight loss. For example, Abu-Abeid et al. found that when BMI was reduced by an average of 6.3 kg/m² after bariatric surgery, joint space widened from 4.6mm to 5.25mm.⁷⁸ These intriguing findings show that independent of physical activity level or muscle strength, knee pain related disability could be improved with weight loss alone. Relief from pain may facilitate re-engagement of the individual into regular exercise or activities that were previously unattainable.

Low Back

The lumbar spine is the most researched “joint area” in bariatric populations. In one study, back pain was followed in morbidly obese patients undergoing vertical banded gastroplasty and non-obese counterparts for two years⁸². BMI was reduced by 14.3 kg/m², and improvements occurred in all pain and disability assessments (Visual analogue scale for pain, Oswestry Disability Index, Roland-Morris Disability Questionnaire and the Waddell Disability Index). Uncontrolled studies have revealed that the frequency of back pain was reduced in 83% of patients,⁷⁹ and lumbar back pain symptoms were reduced in 82–90% patients after 6–22 months.^{76, 79} In obese persons with chronic debilitating axial back pain the severity of back pain symptoms was reduced by 44% after bariatric surgery.⁸¹ Pain relief was also associated with lower ODI scores.

Other Joint Pain

Weight loss after bariatric surgery may not impact hip OA pain as much as that experienced by other load-bearing joints. While some data indicate that hip pain can improve,⁷⁶ most studies do not support favorable changes in hip pain after surgery. Lateral and medial hip pain symptoms were not significantly reduced by one year,⁷⁹ and the presence of hip OA pain was not different in bariatric patients at two or six years after surgery.⁸⁰ Even if obesity increases the vertical loading stressors and compressive forces with weight bearing activity, the positioning of the femoral head in the acetabulum may not be affected with increased weight as much as other load bearing joints.⁸⁷ Limited data indicate that the frequency of foot pain is reduced by 42% to 95% after a bariatric surgery procedure.^{76, 79} While hand OA pain symptoms moderately decreased after bariatric surgery, shoulder pain did not decrease with palpation or range of motion.⁷⁹ The lack of OA pain relief in the shoulder may be due to the low baseline prevalence of shoulder OA or high error within the small sample sizes to detect a surgery related change.

Potential Mechanisms Underlying Relief from OA Symptoms

Weight loss with medications, exercise (with or without diet) and bariatric surgery can favorably alter the mechanical and biochemical profiles of obese adults with OA. Mechanical stress can be reduced as shown by a lowering of maximal knee compressive forces relative to magnitude of weight loss.⁷³ Surgical weight loss can also substantially lower joint compressive forces, which may increase the joint space width.⁷⁸ Reductions in the central deposition of fat on the abdomen and in the girths of lower limb segments may facilitate normalization of joint alignment. The collective benefits of lower joint loading and joint realignment would attenuate cartilage stress and silence one trigger of local joint inflammation. Weight loss reduces the synthesis of IL-6⁸⁸⁸⁹ and TNF- α and increases the production of anti-inflammatory cytokines (IL-10) by subcutaneous adipose. A loss of body fat attenuates systemic levels of inflammatory cytokines such as IL-6 by 25–30%.¹⁸ Leptin and CRP levels also decrease with weight loss.⁸⁸⁸⁹ Irrespective of the method of weight loss, suppression of the proinflammatory cytokines can occur. These biochemical changes would complement the mechanical benefits of weight loss to reduce OA symptoms.

Prevention

Identification of effective treatments to prevent OA in obese younger populations is lacking. This is partly due to the challenges of long-term prospective research, and the lack of control in documenting processes that may influence OA onset. However, we surmise that the participation in regular physical activity and weight management may be critical in avoiding early onset of OA or increased risk of the disease. Some advocates suggest a screening process that begins in adolescence, in which family history is reviewed. If there is a positive family history, the individual can be counseled by the health care team on prevention

techniques including strengthening exercise, (eg, leg raises, weight bearing exercise, strengthening exercise [quadriceps, hamstrings]), endurance exercise and judicious use of resistance exercise.⁹⁰ Guidelines to achieve or maintain a healthy weight can include dietary recommendations, healthful living and management of musculoskeletal pain. Successful disease prevention programs include the family, and therefore OA risk may be decreased if the entire family adopts healthy behaviors and loses excessive weight. From the physiological perspective, the OA related states of chronic inflammation and elevated mechanical stress on the joints may be curtailed or avoided if preventative measures are put into place during adolescence. Inflammation is improved with interventions that induce a 5% weight loss, regardless of the type or duration of the intervention.²⁰ The adage ‘an ounce of prevention is worth a pound of cure’ may be directly applicable to the obese person at risk for OA; for every reduction in weight, there is a decrease in the risk of OA onset.

Conclusion

Obesity induces several pathways that predispose an individual to symptomatic OA. Growing evidence indicates that irrespective of weight loss method, reduction of body fat can reduce the mechanical and biochemical stressors that contribute to joint degeneration. A variety of methods can be used treat OA including medications, exercise (with or without diet) and bariatric surgery. Prevention of OA may be achieved in part through screening of children at risk for OA, and education of the whole family to increase the chance of long-term success of disease prevention.

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Figure 1.
Potential obesity related pathways that contribute to osteoarthritis.

Randomized controlled trials (RCTs) of exercise interventions to treat osteoarthritis (OA) symptoms in obese adults.

Table 1

Author	Population	Exercise Program	Weight change	OA related Outcomes
Focht et al. ⁷¹ (N=316)	60 years	ADAPT; 18 months Four study groups		Exercise + Diet had greatest ↓ in OA pain and greatest ↓ stair climb time and 6 min walk distance compared with the remaining groups at 18 months (p<0.05)
		1. Exercise (3 days/ wk RX 2 sets, 12 reps of leg exercises, 15 min AX at 50–75% Heart rate reserve)	NR	
		2. Diet (5% loss of body weight using group sessions)	NR	
		3. Exercise + Diet	NR	
Lim et al. ⁶⁶ (N=75)	50 years	4. Control group	NR	
		2 months Three study groups		WOMAC scores ↓ by 13.8 and 9.9 points in the aquatic and conditioning groups compared to 2.7 in the control group (p<0.05). Knee pain intensity ↓ by 25% and 14% in the aquatic and land based exercise groups; pain interference ↓ by 33% and 19%, but ↑ by 6% in the control group (p<0.05).
		1. Aquatic exercise (40 min/ 3 × wk; 65% max HR)	1.1 kg	
		2. Land based conditioning exercise Leg extensor exercise (40 min/ 3 × wk; at 60% 1 RM)	0.96 kg	
Messier et al. ⁵¹ (N=24)	60 years	3. Control (home based exercise for legs)	0.47 kg	
		6 months Two study groups Exercise vs Diet+Exercise		The exercise and Diet+Exercise groups had 32–40% and 15–46% ↓ ambulation and transfer knee pain, respectively.
		1. Exercise (3X/wk, 20min walking, 20–30 min RX; 10–12 reps of 7 exercises)	1.8 kg	
		2. Exercise + Diet (group sessions met 1 hr/wk)	8.5 kg	
Messier et al. ⁵⁴ (N=316)	60 years	ADAPT; 18 months Four study groups		WOMAC pain scores ↓ the most in the Exercise + Diet group compared to all remaining groups (–2.2 points vs. –0.40 to –1.23 points; p<0.05). WOMAC physical function scores ↑ most in the Exercise+Diet and Diet only groups compared with Exercise and control groups (24% and 18% vs. 12% and 13%; p<0.05). No significant changes were observed in lateral and medial knee joint space width.
		1. Exercise (3 days/ wk RX 2 sets, 12 reps of leg exercises, 15 min AX at 50–75% Heart rate reserve)	3.5 kg	
		2. Diet (5% loss of body weight using group sessions)	4.6 kg	
		3. Exercise + Diet	5.2 kg	
		4. Healthy lifestyle (control)	1.1 kg	

NR = not reported; AX = aerobic exercise; RX = resistance exercise
WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index
ADAPT = Arthritis, Diet, and Activity Promotion Trial; PAIBCT = Physical activity, Inflammation and Body Composition Trial