AlterG Enabled Exercise:
Breaking the Obesity-Osteoarthritis Cycle

Introduction
Obesity and knee osteoarthritis (OA) are among the most common comorbid chronic illnesses in the United States. Large population studies have revealed obesity to be a strong risk factor for OA (1) and weight loss can lead to a reduction in symptoms. A review of four randomized, controlled trials involving 454 overweight patients with knee OA found that a weight reduction of as little as 5% resulted in significant improvements in disability caused by OA (2), while a study of overweight individuals exercising on the AlterG Anti-Gravity Treadmill has shown that an average of 12.3% body weight support can significantly reduce knee OA pain and enable comfortable exercise (3).

Exercise has long been advocated for the overweight individual desiring weight reduction, yet the ability to meaningfully perform exercise is significantly limited by OA pain during exercise.

The AlterG is the only exercise modality that allows accurate and precise real-time modulation of body weight support, speed, and inclination to enable the overweight individual to achieve high exercise levels. Furthermore, the AlterG is the only machine that allows the individual to “feel” their desired weight, which is empowering and contributes to very high levels of exercise compliance (4), and free fat loss irrespective of diet (5).

Mechanical Loading As A Causative Factor In OA
Obesity has long been recognized as a risk factor for OA (6). Common thinking suggests that excessive joint loading over time leads to damaged articular cartilage and sets in motion a cascading series of events that leads to commonly observed at the knee but can also affect the lumbar spine, hip, and ankle. Furthermore, obesity combined with varus knee alignment can accelerate medial compartment degeneration, and obesity combined with valgus knee alignment can hasten lateral compartment degeneration (6). It is believed that knee malalignment impairs cartilage nutrition (7).

With respect to articular cartilage, chondrocytes respond to mechanical changes in the local environment. Under stimulation and overloading can both lead to cartilage degradation. One explanation for this could be that the chondrocytes have recently been shown to have mechanoreceptors (8). Mechanical stimulation (compression and stretching) of these receptors causes activation of the mitogen-activated protein kinase and NF-κB pathways. Research suggests that this process results in the expression of cytokines, growth factors and metalloproteinases, and the production of mediators such as prostaglandins and nitric oxide. The end result may be inhibition of cartilage matrix formation and degradation of cartilage, both known to be triggered by overload (8). Thus there are several possible mechanisms to support the link between obesity and mechanical damage to articular cartilage.

Obesity and Adipose Tissue By Themselves Are Risk Factors For OA
There is growing evidence that fat tissue by itself is a risk factor for OA development. For example, obesity is associated with OA at sites with minimal mechanical overload such as the fingers. One study found a strong association between obesity and OA of non-weight bearing joints, particularly in the hand (9).

Further indications of a potential systemic component come from the association of OA with metabolic syndrome. One study examined a form of metabolic syndrome called “cardiometabolic clustering” (10). The knee OA prevalence in nonobese women without cardiometabolic clustering was 4.7% compared with 12.8% in obese women without clustering and 23.2% in obese women with clustering (10).

Fat tissue is now being recognized as a metabolic organ. In obese patients, white adipose tissue is known to synthesize a variety of factors, many known to promote inflammation, including cytokines, chemokines and adipokines, such as leptin, adiponectin, resistin and visfatin (8). Adipokine expression is elevated in arthritic joints, particularly in the infrapatellar fat pad and the synovium (8). It is possible then that weight loss can decrease the amount of circulating adipokines, providing an additive protective effect to mechanical unloading.

The Possible Special Role Of Leptin

The adipokine leptin is produced mainly by adipocytes. Circulating leptin levels are correlated with body fat, but are also regulated by inflammatory mediators (11). Leptin also directly affects cartilage synthesis. Normal cartilage expresses little or no leptin, but synthesis is greatly increased in osteoarthritic cartilage.

It is possible that there is a protective role for leptin in OA. However, leptin also stimulates production of a number of inflammatory molecules (11). The role of leptin likely involves a balance. Leptin is believed to have a net negative effect on cartilage metabolism. Also, leptin receptor levels are linked to increased cartilage defects and decreased levels of the bone formation biomarker osteocalcin (11).

The importance of leptin in OA etiology associated with obesity was observed in leptin-deficient and leptin receptor-deficient mice. Despite severe obesity (a 10-fold increase in adipose tissue), the levels of inflammatory cytokines in the mice were mostly unchanged, and the incidence of knee OA did not increase, although reduced subchondral bone thickness and increased relative trabecular bone volume were observed in the tibial epiphysis (12). These results suggest a role for leptin in cartilage and bone metabolism as well as in immune response.

Other Adipokines Are Also Related To Cartilage Metabolism

There are many other adipokines produced by body fat tissue, all of which can play a role in the increased risk of osteoarthritis with obesity (13, 14, 15, 16, 17, 18). The key take-away is that a reduction of body fat mass- regardless of weight loss- has the potential to decrease OA risk.

Studies Investigating The Effects Of Weight Loss On OA

A subset analysis of the Arthritis, Diet, and Activity Promotion Trial (ADAPT) evaluated the effects of high weight loss on knee loads during walking in

individuals with knee OA (19). The study included 76 sedentary participants who performed gait analysis at baseline and 18 months. The cohort was stratified into weight loss categories as follows: high (>5% weight loss), low (<5% weight loss), and none (0% or weight gain). High weight loss reduced knee joint compressive loads during walking primarily due to lower hamstring forces. Another study specifically investigating weight loss effects on knee joint forces showed a positive correlation with even small amounts of weight reduction (20).

In contrast to those studies, which demonstrated the favorable biomechanical effects of weight loss, another investigation found evidence for additional metabolic benefits (21). Investigators recruited 44 greatly obese patients with knee OA (mean age 44, BMI 50.7 kg/m^2) and collected clinical data and blood samples before and 6 months after bariatric surgery. The gastric surgery led to a considerable decrease in body weight (approximately 20%), a marked reduction in knee pain (approximately 50% on visual analogue scale), and improvement on all WOMAC subscales. Measures of insulin, insulin resistance, total cholesterol, leptin, interleukin-6, and high-sensitivity C-reactive protein all decreased.

The Specific Role Of AlterG Enabled Exercise

The studies outlined above show a potential causal link between obesity and the development of osteoarthritis. There appears to be a mechanical component as well as a metabolic component. Furthermore, weight loss has been shown to positively improve the mechanical and metabolic components. However, from a practical standpoint many individuals with osteoarthritis desiring weight loss are unable to lose weight. One important factor is that meaningful exercise is difficult or even impossible because exercise increases pain.

Many exercise formats are proposed for obese individuals, including overland walking, bicycling, swimming, or aquatic exercise, but only the AlterG offers specific advantages that enable comfortable exercise for all people.

The e-Knee study from Scripps Clinic, La Jolla, California has provided an equation that accurately and precisely correlates knee joint forces as a function of body weight support, treadmill speed, and inclination on the AlterG (22). Thus, the mechanical forces causing osteoarthritis pain can be quantified during exercise, and only the AlterG allows real-time modulation of the variables to achieve pain relief.

Christensen et al (2) showed that as little as 5% body weight reduction is needed to start producing pain relief, and Takacs and Leiter (3) have shown that 12.3% is the average amount of body weight reduction needed for comfortable exercise on the AlterG. The advantage of the AlterG in this setting is that it allows the individual to titrate body weight support for pain relief in 1% increments, effectively allowing them to set a target for weight reduction. This ability to “feel their desired weight” is empowering, and leads to very high compliance rates with exercise. An unpublished study from the UK (4) showed a 91% compliance with a 16-week obesity exercise program, well in excess of industry-standard compliance rates (typically around 45%).

And finally, the AlterG has been proven to have a statistically significant reduction in free fat mass, irrespective of diet (5). As noted above, reducing free fat mass is expected to have positive effects on the metabolic factors linking obesity to osteoarthritis.

Conclusion

Further definitive studies are required to prove the link between weight loss, fat loss, and decreased osteoarthritis pain but the mechanical and metabolic early evidence is compelling.

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