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Articular Cartilage Degeneration: Etiologic Association With Obesity

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Musculoskeletal joint conditions are among the most prevalent disease processes in the United States. These disease processes are second only to heart disease in causing significant disability that affects work status. Osteoarthritis, otherwise known as degenerative joint disease, is the most prevalent form of arthritis. This disease process represents a slowly evolving condition of cartilage and bone in arthrodial joints. The Centers for Disease Control and Prevention[1,2] predicted that by 2020 arthritis will gain more new patients than any other disease form in America. As in other disease processes in the body, multiple factors lead to the development of osteoarthritis.

Maintenance of normal joint homeostasis involves a balanced process of cartilage matrix degradation and repair that are performed predominantly by the resident chondrocytes. Chondrocytes respond to cytokines, growth factor signals, and physical stimuli in a complex manner to maintain joint integrity. If this balance is disrupted, cartilage matrix degradation, mediated by proteolytic enzymes that are no longer balanced by protease inhibitors, results in the release of matrix fragments into the synovial space.[3] In the latter stage of the disease, catabolism outweighs matrix repair (anabolism). Phagocytosis of cartilage matrix degradation products by the synovial macrophages is related to chronic inflammation of the synovium, which in turn results in the local synthesis of more proteases and proinflammatory cytokines. These proteases diffuse through the synovial fluid to the cartilage and induce additional cartilage matrix breakdown by direct macromolecular proteolysis. The cytokines stimulate the chondrocyte to synthesize more proteases. Cell apoptosis and necrosis can also be seen. A vicious feedback cycle occurs with matrix degradation leading to inflammation, which in turn stimulates further degradation.

Numerous causal factors can lead to this breakdown in joint homeostasis. A traumatic event is one of the most obvious initiating events. This can be in the form of a single occurrence or multiple microtraumatic events over a prolonged period. Other risk factors for the development of osteoarthritis exist, including systemic risk factors such as genetic deformities, dietary intake, estrogen use, and bone mineral density. Other issues that can affect the joints directly include muscle weakness, joint hyperlaxity, and obesity; all can predispose individuals to osteoarthritis.

According to National Institutes of Health[4] guidelines, roughly 20% of men and 25% of women are categorized as obese (body mass index [calculated as weight in kilograms divided by height in meters squared] ≥30). The number of individuals in this category has increased by 50% over the past 10 to 15 years.[5] Studies have demonstrated that obese individuals can reduce their risk of developing osteoarthritis through weight loss. In the Framingham Study,[6] an observational study, women who lost an average of 5 kg decreased their risk for knee osteoarthritis by 50%. Despite this finding, few studies demonstrate a direct correlation between weight loss and alleviation of clinical symptoms. A small randomized study[7] showed that weight loss may be associated with a reduction in clinical symptoms of osteoarthritis. This study used appetite suppressants to obtain the weight loss.

It has been harder to demonstrate a clear relationship between obesity and osteoarthritis of the hip. While bilateral hip disease has been associated with excessive weight, unilateral involvement has not. Developmental dysplasia of the hip (failure of the acetabulum in the pelvis to assume normal concavity) is associated with the development of osteoarthritis in a high percentage of affected joints.[8,9] Investigations in this patient population have demonstrated a strong correlation between greater articular surface contact stress and the development of osteoarthritis. This demonstrates a correlation between cumulative artic-

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ular surface contact stress above a critical threshold and subsequent joint degeneration.

As stated previously, an association between traumatic events and osteoarthritis exists. Experimental work assessing articular surface incongruities showed that an articular cartilage step-off of greater than 3 mm increases local contact stress.[10,11] Articular surface fractures, joint dislocations, and ligament and meniscal ruptures are associated with an increased risk for the development of osteoarthritis later in life.[12,13]

Biomechanically, each 0.5-kg increase in weight leads to an increase in force across the knee by 0.9 to 1.4 kg, an important mechanism by which obesity leads to osteoarthritic conditions. Other factors working in concert with obesity can exacerbate this mechanism, and this is the more usual scenario. I often hear an obese patient inquire ''Why is my other knee or hip feeling fine right now, doctor?'' There is probably low-level deterioration of the contralateral joint occurring at that time as well. A subacute event in the involved knee has caused a baseline cartilage flare-up that is characterized by joint effusions, stiffness, and difficulties with activities of daily living.

Our ability to consciously or unconsciously perceive joint position and movement without looking directly at the joint is termed *proprioception*. This ability is important in maintaining joint stability under dynamic conditions. Ligamentous injuries disrupt this mechanism by damaging the neurovascular supply to the ligaments. In the obese patient, there has been low-level microtrauma to the cartilage structures in the weight-bearing joints, a process that is clinically silent to the patient. During a ligamentous disruption in the knee, a direct contusion to the knee compartments typically occurs. This results from the traumatic subluxation of the femur relative to the tibia that occurs while the ligament is being torn. Typically, these individuals develop rapid deterioration in the status of the involved joint. Loss of proprioception contributes to the development of osteoarthritis in this setting. Studies have shown that proprioception at the knee declines with age[14] and is severely limited in sedentary older persons.[15] In both the involved and uninvolved knees of patients with osteoarthritis, proprioception was worse than that in age-matched control subjects.[16] This implicates proprioception or the lack thereof as an early predisposing factor that contributes to subsequent development of arthritis. The proprioceptive abilities of the joint being severed by the ligament tear adds to the progression of osteoarthritis.

The mechanical axis (the alignment of the leg when measured from the hip to the ankle) is another important factor that can exacerbate deterioration of the knee joint in particular. As stated earlier, there is a direct correlation between body weight and forces across the knee joint. In malaligned individuals (such as individuals with severe varus [bowed] or valgus [knocked] knee alignment), forces across the joint are concentrated at smaller and smaller surface areas, and (as in the case of developmental dysplasia of the hip) this increased contact stress to the cartilage leads to rapid deterioration of the joint in the overloaded knee compartment. In the obese patient, the already excessive forces across the joint are concentrated on a smaller area than in the neutrally aligned patient. One study[17] showed that the magnitude of torque adducting the knee during the stance phase of gait correlates with the severity of osteoarthritis in the knee, suggesting a correlation with the rate of disease progression and malalignment.

With this clear correlation between obesity and osteoarthritis, I always recommend weight reduction before embarking on operative treatments. This applies most directly to interventions in the knee and particularly to biologic reconstructive procedures such as microfracture, autologous chondrocyte implantation, osteochondral allograft and meniscal transplantation, tibial osteotomy, and minimally invasive arthroplasty procedures. Mithoefer et al[18] demonstrated a correlation between body mass index exceeding 30 kg/m^2 and poor clinical outcomes using the microfracture technique for treatment of articular cartilage lesions in the knee. Weight reduction has other well-known health benefits such as reduction in cardiac risk factors that lead to myocardial infarction, but there is also an association between obesity and osteoarthritis. This fact always seems less obvious to many of my patients, but I will continue to measure this objective information during their visits. When patients walk in with musculoskeletal complaints, it is important to effectively direct their attention to factors that they can control in treating or slowing the progression of the osteoarthritic condition. Weight reduction through all available means at the patient's disposal is an important treatment option to consider.

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