# Disk Degeneration and Low Back Pain: Are They Fat-Related Conditions?

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## Abstract

Low back pain (LBP) is the world's most debilitating condition. Disk degeneration has been regarded as a strong determinant associated with LBP. Overweight and obesity are public health concerns that affect every population worldwide and whose prevalence continues to rise. Studies have indicated strong associations between overweight/obesity and disk degeneration as well as with LBP. This broad narrative review article addresses the various mechanisms that may be involved leading to disk degeneration and/or LBP in the setting of overweight/obesity. In particular, our goal is to raise awareness of the role of fat cells and their involvement via altered metabolism or the release of adipokines as well as other pathways that may lead to the development of disk degeneration and LBP. Understanding the role of fat in this process may aid in the development of novel biological therapies and technologies to halt the progression or regenerate the disk. Moreover, with genetic advancements and the appreciation of genetic epidemiology, a more personalized approach to spine care may have to consider the role of fat in any preventative, therapeutic, and/or prognosis modalities toward the disk and LBP.

**Keywords**
- spine
- disk degeneration
- low back pain
- obesity
- fat
- adipokines
- metabolism

Low back pain (LBP) is a serious debilitating condition that presents detrimental socioeconomic implications, affecting 80% of the general population at some point in time.[1,2] In the United States, direct and indirect costs to treat LBP have been estimated to be ~90 billion USD annually and similar high costs have been documented in other countries as well.[3] Overall, LBP affects daily function, diminishes quality of life, and increases work disability and health care costs.[4]

Overweight and obesity (traditionally as a measure of body mass index [BMI] or waist circumference) are public health concerns that affect many populations worldwide and whose prevalence continues to rise.[5,6] Approximately, 23 and 10% of the world's adult population are overweight and obese, respectively.[6] In fact, such prevalence rates are expected to increase exponentially by the year 2030 if preventative measures are not employed. For example, in the United States it has been estimated that a third of children are obese, which is distressing because childhood obesity increases the risk of adulthood obesity.[7] In Europe, several countries (e.g., United Kingdom, Germany, Croatia) have noted that over 60% of their populations to be at least overweight. Even in parts of Asia (e.g., China), the prevalence of overweight and obesity has increased due to the rise of the fast food culture, adoption of more Westernized lifestyles, and financial affluence.[8] As a result, epidemiologic trends have noted that society has entered the obesity phase.[5]

A principal underlying determinant for LBP incidence is intervertebral disk degeneration,[9–19] the risk of which has

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been attributed to genetic, environmental, and lifestyle factors.[17,20–24] Among these, overweight and obesity, or rather body fat, have been associated with increased LBP rates.[17,22,24] Body weight has also been implicated as a prognostic factor in spine surgery patients undergoing surgical intervention to address discogenic back pain and other spinal disorders.[25–27] Although it has been a long-standing belief that body weight exerts its deleterious effects on the spine due to altered biomechanics (e.g., loading), mounting evidence suggests that biochemical and metabolic changes brought upon by fat may also play a role in the development of disk degeneration and with that LBP. In lieu of these concerns, the goal of this review is to present the potential pathomechanisms involved in the obesity/LBP association, to discuss of the role of fat in the development of disk degeneration and LBP, and, to a lesser degree, describe the implications of obesity in spine surgery patients.

## Anatomy and Physiology of the Intervertebral Disk

The intervertebral disks separate the vertebral bodies to facilitate load transmission and multiaxial flexibility while playing the role of "shock absorber" in response to dynamic spinal compression. Moreover, the disk acts as a "spacer" by providing height to the spinal column, allowing passage of nerves through the intervertebral foramen and facilitates biomechanical synergy with the posterior facet joints.

The intervertebral disk consists of an inner gelatinous core (nucleus pulposus) and a thick outer ring of fibrous cartilage (annulus fibrosus; ►**Fig. 1**). The nucleus pulposus is mainly composed of a proteoglycan and type II collagen in a ratio of 20:1. The proteoglycans are hydrophilic in nature, thereby creating a swelling pressure that provides compressive stiffness to the disk.[28,29] The annulus fibrosus serves as an intervertebral ligament composed of up to 25 concentric collagen lamellae that provide bending and shear stiffness/strength.[28] The nucleus is separated from the adjacent vertebra by the end plate, which is a thin bilayer of cartilage and porous subchondral bone. The end plate balances two conflicting requirements of being porous to facilitate transport between nucleus cells and vertebral capillaries and being stiff to resist axial compressive loads.[30]

Early degenerative processes include enzymatic degradation of nucleus proteoglycans that leads to decreased swelling and reduced disk water. These changes are brought upon by age progression and excessive physical loading,[31] which adversely affect disk biomechanics leading to altered tissue stress distributions and biological activities that in turn cause nuclear fibrosis and disorganization of the annular architecture (►**Fig. 2**).[19–22,31–33] Biochemical changes of the extracellular matrix and damage accumulation at the disk periphery trigger inflammatory cellular responses that promote a cascade of further structural modifications that progressively compromise disk biomechanics.[31,34,35] Furthermore, progression of disk degeneration may also be associated with end plate and

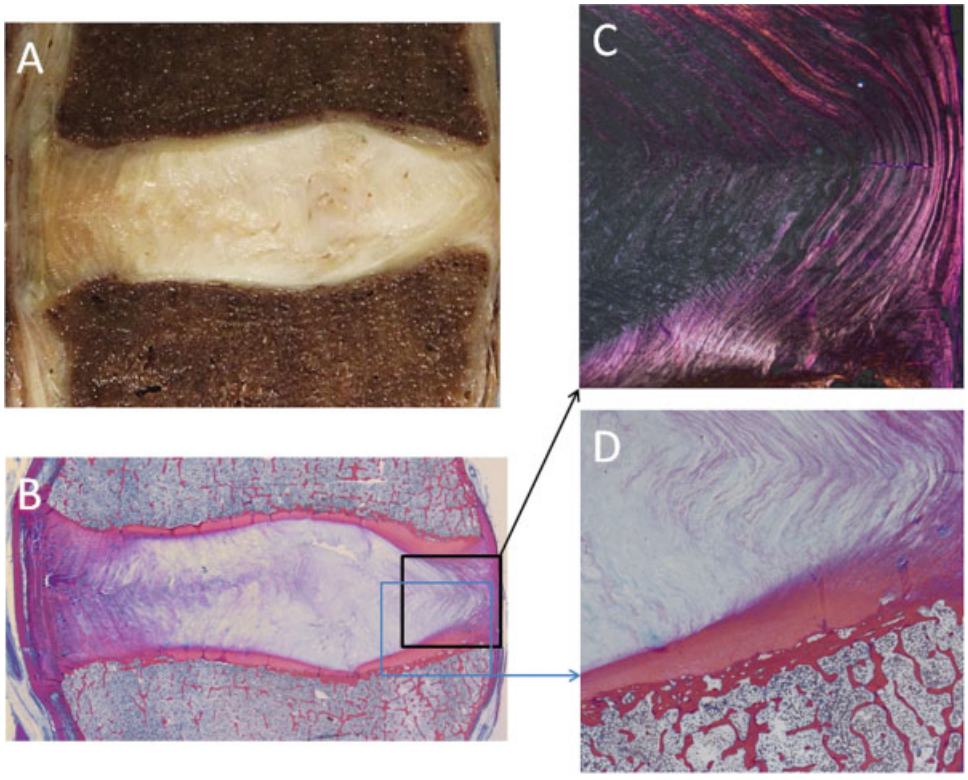


**Fig. 1** (A) Midsagittal section of a human lumbar disk with intermediate degeneration (Thompson grade III), showing fibrous consolidation of the nucleus pulposus and lack of nucleus/annulus distinction. (B) Midsagittal histologic section stained with Heidenhain connective tissue stain that clearly demonstrates the cartilaginous end plates. (C) Histologic sections of annulus fibrosus viewed with polarized light that highlights the distinct outer annular collagen lamellae that are birefringent. (D) High-magnification image of the annulus/end plate junction demonstrating annulus lamellae integration with cartilage end plate.

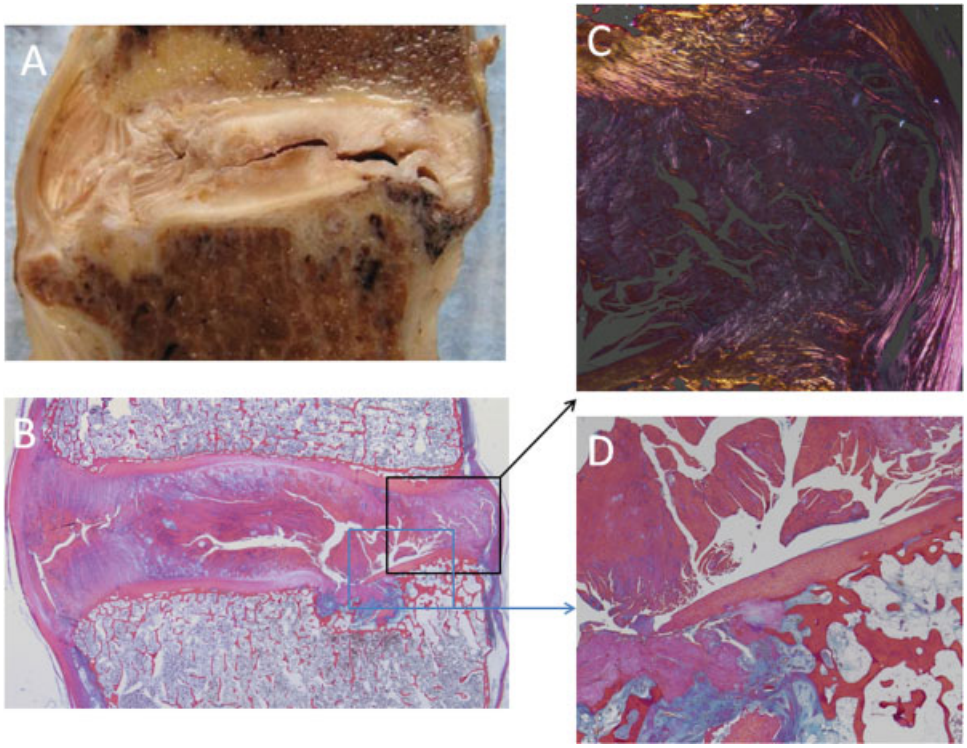


**Fig. 2** (A) Midsagittal section of human lumbar disk with advanced degeneration (Thompson grade V), showing horizontal fissures within the nucleus, radial, and circumferential fissures in the annulus, and defects within the cartilage end plate and subchondral bone. (B) Heidenhain-stained section highlighting extensive tissue damage and fibrovascular subchondral bone marrow in the region of cartilage defect. (C) Histologic sections of annulus fibrosus viewed with polarized light showing loss of normal birefringence (see Fig. 1C for comparison), indicating denatured and disorganized annular collagen lamellae. (D) High-magnification view of damage to end plate cartilage and subchondral bone.

subchondral bone edema (e.g., Modic changes) that can further contribute to the development of pain.[36–38] In fact, overweight/obesity has also been implicated with end plate and Modic changes of the lumbar spine.[39–41]

## Disk Degeneration and Low Back Pain

For the past two decades, magnetic resonance imaging (MRI) has been the gold standard for assessing intervertebral disk degeneration in vivo.[42–44] Although there have been numerous classification schemes proposed to assess disk degeneration on MRI, many investigators have traditionally referred to the Pfirrmann or the Schneiderman criteria,[42,43] both of which rely on signal intensity of the disk on imaging to denote grades of degeneration severity. In one of the earliest spine degeneration MRI studies, Boden et al noted in 67 subjects that disk degeneration is quite common, even in asymptomatic individuals.[45] These and other observations raised questions regarding associations between disk degeneration assessed by anatomic imaging and clinical symptoms. However, more recent studies based on large populations (over 2,500 Southern Chinese subjects) have shown that disk degeneration on MRI is significantly associated with LBP history in adults, and such an association increases according to the global severity of disk degeneration (i.e., degenerative disk disease score).[46] Samartzis et al have also noted that disk degeneration severity in asymptomatic individuals is predictive for future first-time LBP episodes.[47] These trends appear generalizable as Takatalo et al have noted for the Northern Finnish Birth Cohort that the severity of disk degeneration on MRI is associated with the severity of low back symptoms over a 3-year period in young adults.[18] What's more, a systematic review by Chou et al, addressing the association of disk degeneration on MRI and symptoms in various populations throughout the world, observed a significant association between disk degeneration and chronic LBP.[11]

## Body Mass Index and Lumbar Disk Degeneration

Although body weight has been noted to be associated with the development of cardiovascular disease, diabetes, and malignancies among other conditions, its effects upon disk degeneration have remained elusive. The nature of this is largely attributed to the lack of large epidemiologic studies with a proper study design, patient-based studies, insufficient statistical analyses, mode of radiographic/imaging assessment in defining the phenotype of disk degeneration, and/or conjecture arising from limited radiographic interpretation of additional spinal findings (e.g., Schmorl nodes) that may contribute to the degenerative process.[12,48–52] Furthermore, the association of overweight and obesity with the extent (i.e., levels with disk degeneration) and severity of disk degeneration of the lumbar spine remain unknown because previous studies have failed to quantitatively assess such parameters on advanced imaging. However, because overweight and particularly obesity have been associated with LBP,[23] and because disk degeneration on MRI is an etiologic factor related to LBP,[14,16,17] it would appear reasonable that elevated BMI may be instrumental in the development of disk

degeneration. It should be noted that BMI cutoff values denoting overweight or obesity do vary between ethnic populations.[53]

According to a meta-analysis by Shiri et al, obesity, as measured by BMI, is significantly associated with LBP.[23] However, to date, the relationship between body weight and disk degeneration has been contentious. In a study of 270 elderly Japanese individuals, Hangai et al noted that high BMI values presented a risk in developing disk degeneration based on MRI.[48] According to Liuke et al in their study of 129 middle-aged Finn males, obesity was associated with the development of disk degeneration.[51] Conversely, according to the Rotterdam Study, which is a population-based study entailing Dutch subjects, a cross-sectional analysis of 2,819 individuals 55 years and older who underwent X-ray assessment did not note any association between elevated BMI and disk space narrowing.[12] Similarly, based on the findings of the Chingford Study population of 1,003 elderly women from the United Kingdom, a prospective longitudinal assessment noted only a potential trend between elevated BMI values and the development of disk space narrowing on plain radiographs.[49] According to the Framingham Study, a cross-sectional analysis of 187 North American subjects who underwent computed tomography to assess spinal degenerative changes noted in obese subjects a higher prevalence of facet joint osteoarthritis but without disk space narrowing.[50] According to Videman et al in their assessment of 44 pairs of male monozygotic twins from the Finnish Twin Cohort who had 8-kg or greater discordance in body weight between siblings, disk degeneration (based on quantitative signal variation in MRI) was not associated with overweight or obesity.[52] In fact, the authors concluded that greater body mass "is not harmful to the disk" and that it may "delay" disk degeneration. However, due to the 8-kg discordance in body weight and small sample size, this may not be an effective manner in assessing the effects of overweight or obesity upon disk degeneration because there may be incomparable groups comparing various BMI categories.

Based on a study by Samartzis et al, which was composed of 2,599 Southern Chinese subjects ranging in age from 21 to 63 years, the authors noted a significant association between elevated BMI values, in particular obesity, and the overall presence of lumbar disk degeneration and number of degenerative levels, global severity of degeneration, and end-stage disk degeneration with disk space narrowing in MRI.[22] In a particular seminal finding, the authors noted a significantly positive linear trend association between BMI and disk degeneration of the lumbar spine, where individuals who were overweight and obese presented with an increased likelihood of having disk degeneration (30 and 80%, respectively) in comparison with normal-weight individuals. End-stage disk degeneration with disk space narrowing is often coupled with degenerative changes throughout the vertebral motion segment (e.g., canal and neuroforaminal stenosis, ligamentous thickening) and altered lumbar kinematics that increase the risk of LBP.[12] Such severity of disk degeneration may help explain the increased prevalence of prolonged and chronic LBP in overweight and obese individuals concluded in the recent meta-analysis.[23]

Even though overweight and, in particular, obesity are influential factors related to disk degeneration, the exact mechanism of this association remains speculative. For numerous years, it has been postulated that overweight and obesity contribute to disk degeneration by excessive compressive loading. However, recent studies have noted a linear association between hand osteoarthritis and atherosclerosis in elderly females.[54,55] Such findings are independent of increased loading effects that could be brought upon by body weight and contradict that overweight and obesity contributes to osteoarthritis only via altered biomechanics. The explanation for this phenomenon may be mediated by an inflammatory response by secondary mediators secreted by adipocytes, such as adipocytokines (e.g., adiponectin, leptin, resistin), macrophage-derived factors (e.g., interleukin [IL]-1β), or proinflammatory cytokines and chemokines (e.g., C-reactive protein, tumor necrosis factor-α [TNF-α], IL-6).[56] Another potential mechanism may be attributed to vascular insufficiency to the vertebrae and subsequently to the disk brought upon by atherosclerosis or high serum lipids that can diminish nutrient and metabolite transport into the disk.[48,57] Other possible mechanisms can be attributed to a metabolic disorder or gene-environmental interaction effects.[58,59]

## Adipokines and Disease

Adipose tissue is a loose connective tissue that is composed of adipocytes or fat cells that store energy in the form of lipids as well as aid in cushioning and insulating the body. Two types of adipose tissue exist, white and brown. Although brown adipose tissue is mainly thought to exist in infants, it can also be found in regions of the neck and the thorax surrounding large blood vessels. As such, the majority of fat cells are white adipose tissue, commonly noted in the abdominal region, thighs, buttocks, and other body parts. The distribution of adipose tissue throughout the body is determined by sex hormones, which explains the predominance of fat distribution in the buttocks and breast regions in females and abdominal fat in males. Nonetheless, small blood vessels, fibroblasts, and macrophages also exist between adipocytes.

Besides being a great reservoir for the production of energy, adipose tissue has been recognized as a major endocrine organ that secretes various proteins and hormones that have a direct role in the development of various obesity-related diseases, such as diabetes type 2 and cardiovascular pathology. With weight gain, macrophages infiltrate the adipose tissue, representing ~60% of adipose tissue.[60,61] Adipocytes have numerous receptors, which sense the presence of pathogens and inflammation. Upon receptor stimulation and cross talk with macrophages, the adipocytes activate cascades of inflammatory signal transduction, secreting numerous proinflammatory cytokines (►**Fig. 3**). These cytokines are key metabolism mediators known as "adipokines."[60] Adipokines have also been implicated as playing a role in the development of numerous conditions, ranging from cerebral (e.g., Alzheimer disease, dementia) to musculoskeletal disorders.[62–64]

In 1995, leptin, a key adipokine, was discovered. Since then, research focusing upon adipokines has gained

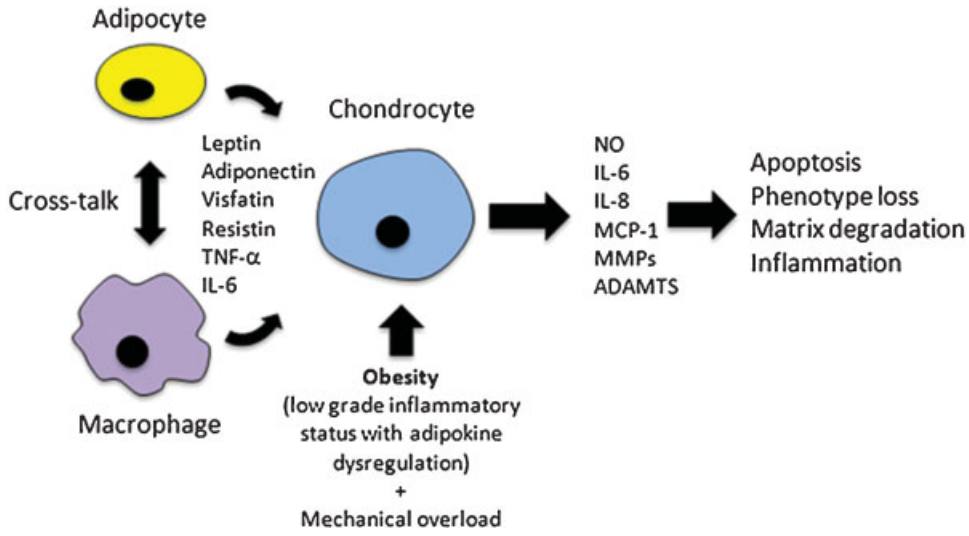


**Fig. 3** The production of adipokines in obesity and their effects upon disk cells. Abbreviations: ADAMTS, a disintegrin and metalloproteinase with thrombospondin motifs; IL, interleukin; MCP-1, monocyte chemotactic protein-1; MMPs, matrix metalloproteinases; NO, nitric oxide; TNF-α, tumor necrosis factor-α.

tremendous momentum. To date, over 50 adipokines have been identified, such as adipsin, cathepsin, IL-6, IL-8, leptin, nerve growth factor, retinol binding protein-4 (RBP-4), TNF-α, and thrombopoietin. Assessment of adipokines has been done by high-sensitivity immunoassays either via uniplex or high-throughput multiplex approaches utilizing serum.[65–67] The more common ones, such as leptin, adiponectin, resistin, and RBP-4, have been thoroughly addressed in the literature with respect to their role with obesity-related diseases.[60] These adipokines have been noted to be markers for glucose homeostasis, to regulate adipose tissue and body weight, to cause immune dysfunction, to affect metabolism, to stimulate energy expenditure, and to play a role in bone formation/function and local/systemic inflammatory states.[68] Increased serum level of leptin is directly associated with obesity and is suspected to be involved in reorganizing the cytoskeleton of nucleus pulposus cells; thus, altering the disk organization and structure.[69,70] This leads us to believe that leptin is involved in the pathogenesis of disk degeneration.

Based on a study by Dumond et al, high leptin levels, independent of BMI, have been associated with the development of knee osteoarthritis in humans.[71] Increased levels of leptin have been found in knee cartilage destruction, suggesting that adipokines may play a critical role in the pathophysiology of osteoarthritis. Leptin has been noted to increase production of matrix metalloproteinase (MMP)-1, MMP-3, and MMP-13 in knee cartilage, contributing to the catabolic effects of osteoarthritis.[72] Other adipokines (e.g., adiponectin) have also been implicated in the development and severity of knee osteoarthritis.[73,74]

In a study by Yusuf et al assessing the role of serum leptin, resistin, and adiponectin in the radiographic progression of hand osteoarthritis during a 6-year follow-up, the authors noted that adiponectin had an independent role from other risk factors in the progression and pathophysiology of disease.[75] Recent studies have also noted that adipokine levels (e.g., leptin, visfatin, resistin, adiponectin, TNF-α, IL-6), independently of BMI, were predictive for the radiographic progression of rheumatoid arthritis over a 4-year period.[76] In fact, studies have also noted that ratios of various adipokines (e.g., adiponectin/leptin) may predict knee pain severity in subjects with osteoarthritis.[77]

Studies have shown the adipokines, such as leptin, may be associated with cardiometabolic risk and may predict metabolic syndrome; as such, early identification of adipokines may lead to an early diagnosis or prevention of the metabolic syndrome.[78] The effects upon disease of these adipokines may also be synergistic with the presence of altered metabolism (e.g., metabolic syndrome), which may propagate or hinder their effect. For example, according to a study by Shah et al assessing adipokines and fat compositions in South Asian subjects, the authors noted that leptin levels may increase with an increase in adiposity, whereas adiponectin may also be mediated by metabolic factors (i.e., high-density lipoprotein, triglycerides, and glucose).[79]

## Adiposity, Adipokines, Lumbar Disk Degeneration, and Low Back Pain

Recently, numerous studies have surfaced that provide a firm foundation connecting the association between adipose tissue activity, or rather adipokine secretions, to that of disk degeneration and LBP. Urquhart et al conducted a study in 135 individuals assessing body composition via dual radiograph absorptiometry and the association with LBP intensity and disability.[80] The authors concluded that body fat and not lean tissue mass was significantly correlated with a higher LBP intensity and worse disability. Although some may argue that an increase in fat mass or adiposity, in particular at the abdominal region, may increase the stress and strain upon the lower spine thereby contributing to degenerative changes of the disk, one may argue against this notion. For one, Urquhart et al have noted a significant independent relationship between an increase in body fat of the extremities in relation to LBP.[80] Second, studies have noted that obesity is a

risk factor for osteoarthritis of the hand, which is a non-weight-bearing region.[81,82]

Macrophage-secreted proinflammatory cytokines are found in disk degeneration, which contribute to the degradation of the disk's matrix. Furthermore, in discogenic LBP individuals, such cytokines are found in the disk affecting the ingrowth of nerve fibers, a process that contributes to pain generation. Studies by Zhao et al and Gruber et al assessing human disk tissue have noted leptin receptors in the disk, concluding that leptin can lead to cell clustering and disk degeneration.[83,84] Studies have also noted that increasing leptin levels may increase bone mineral density of the vertebral bodies, which may affect the adaptive response by the disk to accommodate the increased stress stemming from the altered bone mineral density state of the adjacent vertebrae. Cadaveric disk tissue assessment has also found the presence of cathepsin, an adipokine, in the disk and noted its role in degradation of the matrix and disk degeneration.[85,86] Moreover, cathepsin expression has been noted in vertebral end plate cartilage destruction and sclerosis in mice.[87] Studies have also noted inflammatory cytokines (e.g., TNF-α, IL-6) in degenerated facet joints.[88] As such, it is extremely plausible that systemic metabolic and/or inflammatory mediators released from adipokines may play a role in the development of disk degeneration and subsequently LBP (►**Fig. 3**).

Based on the population-based cohort study of Southern Chinese subjects reported by Samartzis et al, following adjustment for age, gender, work load, and other factors, overweight and obesity based on BMI were significantly associated with the development and severity of lumbar disk degeneration.[22] Furthermore, based on this cohort, males presented with a higher risk of disk degeneration than females. It is worth noting that adiposity deposition is greater in the abdominal region for males than it is for females, which may elaborate as to the propensity of disk degeneration prevalence among males. Moreover, based on this study, there were individuals who were regarded on BMI as overweight and obese who did not have disk degeneration. In a population-based study assessing a Finnish cohort of young adults, Takatalo et al noted that an increase in abdominal obesity measured on sagittal MRIs was associated with a severity of disk degeneration in young males (►**Fig. 4**).[24] Being mindful that abdominal obesity is a significant factor associated with increased adipokine levels, such a study presents seminal findings that adipokines may play a role in lumbar disk degeneration. As such, it may be plausible that an increase in abdominal fat may lead to an increase in adipokine secretion of proinflammatory cytokines and metabolic mediators that may contribute to spinal degeneration by introducing inflammatory changes or increasing their expression in the disk.

## Altered Metabolism and Endothelial Compromise in Disk Degeneration

The role of improper vascular supply or metabolism in the mechanistic pathway of disk degeneration has been under heated debate and interest. Although the intervertebral disk in adults is one of the largest avascular structures in the human body, it receives nutrients and metabolites from diffusion from the end plate and the vascular plexuses surrounding the disk (►**Fig. 5**). The end plate is semipermeable and controls diffusion into the disk by moderating the transport of small solutes, such as oxygen, glucose, and sulfate, and prevents loss of macromolecules.[89,90] Aging, disk geometry, and disk loading have also been implicated in affecting nutrient transport to the disk.[32,91–93] In recent years, there has been strong evidence suggesting that if the nutritional supply of the end plate is altered by targeting its microcirculation, the risk of developing intervertebral disk degeneration increases. Studies have noted that altered metabolism may affect the normal integrity of the disk by affecting proteoglycan synthesis, thereby contributing to

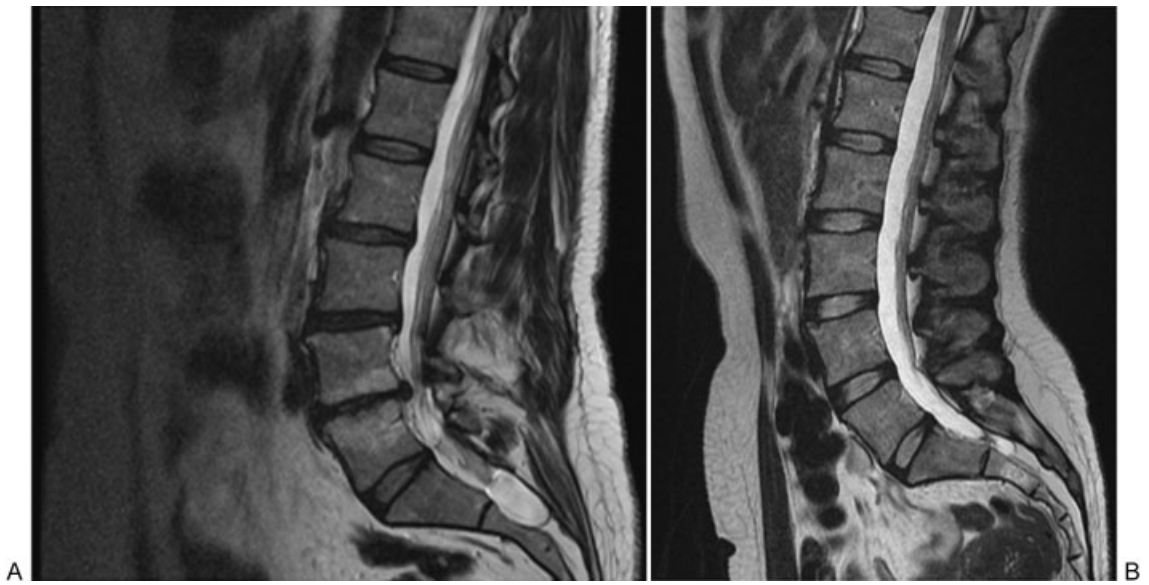


**Fig. 4** Sagittal T2-weighted magnetic resonance imaging of the lumbar spine. (A) Obese subject with disk degeneration and bulging of L2–L5, with disk space narrowing, end plate irregularities, and Modic changes at L4–L5. Also note the presence of a sacral cyst. (B) A normal-weight individual with nondegenerated lumbar disks.

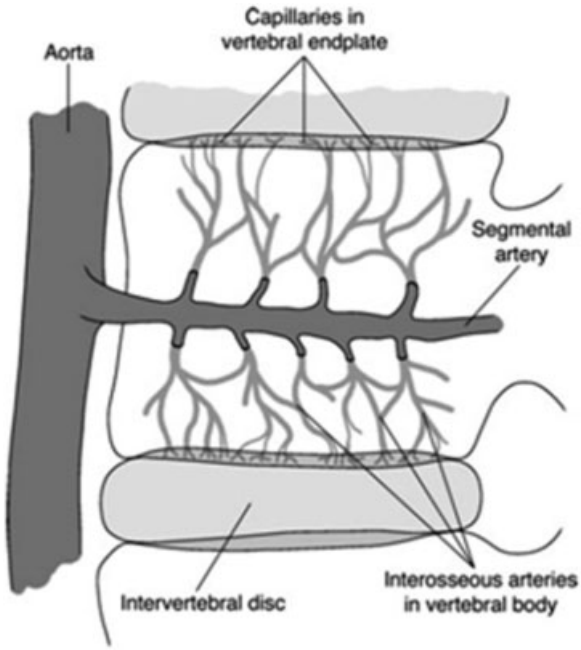


**Fig. 5** The organization of the blood vessels branching from the segmental artery entering the vertebral body and end as capillaries.

degenerative changes.[94,95] Implementing nuclear magnetic resonance spectroscopy, studies have noted that the metabolic marker of lactate production by the disk is associated with discogenic back pain.[96] Other authors have noted that increased serum level of apolipoprotein E is associated with chronic LBP.[97,98] In addition, occlusion or insufficient arterial blood supply to the lumbar spine due to improper end plate permeability or vascular disorder (e.g., atherosclerotic plaque occlusion) may have direct implications upon the integrity of the intervertebral disk, leading to disk degeneration.[57]

### Advanced Glycation End Products

Advanced glycation end products (AGEs) are chemical compounds that cause irreversible cross-linking in mammalian proteins over time. These substances accumulate in tissues with aging, particularly when the concentration of serum glucose is high, as in diabetes.[99–101] These compounds tend to be most abundant in collagen and other connective tissue proteins that have a long half-life in vivo. Consequently, AGEs can accumulate in tissues and suppress the expression of aggrecan via acceleration in the receptor for AGEs (RAGE).[102] These factors make the intervertebral disk especially susceptible to AGE accumulation and the mechanical effects of collagen cross-linking. For example, both AGE and RAGE have been identified in the nucleus pulposus.[102] Yoshida et al used a bovine model to show that upregulation of RAGE caused a decrease in aggrecan expression at the nucleus pulposus and also the release of proinflammatory cytokines that can lead to matrix breakdown.[103] AGEs are also found to alter biochemical properties, such as the hydrophobicity of the extracellular matrix, possibly reducing hydration of the disk and affecting collagen cross-linking, thereby making the disk stiffer. Using T2-weighted MRI sequences to measure the water content in the intervertebral disks, Jazini et al found a negative correlation between the changes in disk hydration and the accumulation in AGEs.[104]

### Role of Obesity in Spine Surgery Patients

Obesity can increase the technical difficulty and complication rates of surgery due to exposure problems and associated cardiopulmonary disorders. This directly leads to an increase in health care cost with increased length of stay, consumption of resources, and in-hospital morbidity and mortality.[105] Also, obesity can further affect postoperative subjective outcome status.

Mogannam et al reviewed 476 patients who underwent anterior retroperitoneal exposure of the lumbar spine and found that more perioperative complications occurred in patients with larger BMI.[106] These included higher rates of vascular injury and overall complications, such as bowel and ureteral injuries, postoperative ileus, neurologic deficit, and cardiopulmonary and wound issues. In a cohort of 1,190 patients undergoing treatment for lumbar disk herniation, Rihn et al showed that obese patients (BMI $>$ 30) required significantly longer operation times and had more blood loss and increased length of stay.[26] Longer hospital stay was likely related to postoperative problems associated with obesity, such as risk of cardiovascular diseases,[107] thromboembolic disorders,[108] and surgical site infection.[109] Mehta et al showed that 12% of patients with surgical site infections were obese (BMI $>$ 30).[110] In addition, increased skin-to-lamina distance and thickness of subcutaneous fat, associated with obesity, were also risk factors for postoperative infections.[110] Similarly, Djurasovic et al reviewed 270 patients and found higher complication rates in the obese group due to wound-related complications.[25] In the Spine Patient Outcomes Research Trial series, patients with obesity (BMI $>$ 30) had higher rates of infection and reoperation and less improvement in symptoms for degenerative spondylolisthesis during the 4-year follow-up.[27] A Swedish study also found that a higher BMI was associated with more dissatisfaction and poorer function and quality of life.[111] For patients with lumbar disk herniation requiring surgery, obese individuals had significantly worse physical function scores on the SF-36 questionnaire and disability profile based on the Oswestry Disability Index in comparison to nonobese patients.[26] This difference was also significant for patients treated nonoperatively. Obesity also increases the risk of recurrent disk herniation ($\sim$ 10%) after surgery, hypothesized as due to increased and repetitive loading of the operated disk.[112] However, the role of adipokines and metabolic dysfunction upon spine surgery outcomes demands further investigation.

## Summary

Because overweight/obesity continues to rise in many populations, this could theoretically also increase the prevalence of disk degeneration and LBP. Although evidence is mounting to suggest that lumbar disk degeneration is also part of the spectrum of "obesity-related diseases" as is diabetes and cardiovascular disease, understanding the interaction between genetics, metabolism, environmental factors, and

adipokines will broaden the pathophysiologic understanding of disk degeneration. In addition, such an understanding may also aid in predicting the progression of disk degeneration and the development of LBP. As such, preventative measures or targeted therapies for disk degeneration can be developed. Because body fat and its consequences (i.e., altered metabolism) may affect the disk and its disk degeneration profile, potential biological therapies, tissue repair technologies, and even genetic assessment should take into consideration this ongoing risk factor that may contribute to the viability of any new intervention, its efficacy, and outcomes. As such, a more personalized approach to understanding disk degeneration and its treatments considering body fat may be a practical platform that requires further future investigation.

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## References

1 Andersson GB. Epidemiological features of chronic low-back pain. Lancet 1999;354:581–585
2 Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2163–2196
3 Dagenais S, Caro J, Haldeman S. A systematic review of low back pain cost of illness studies in the United States and internationally. Spine J 2008;8:8–20
4 Deyo RA, Tsui-Wu YJ. Descriptive epidemiology of low-back pain and its related medical care in the United States. Spine (Phila Pa 1976) 1987;12:264–268
5 Gaziano JM. Fifth phase of the epidemiologic transition: the age of obesity and inactivity. JAMA 2010;303:275–276
6 Kelly T, Yang W, Chen CS, Reynolds K, He J. Global burden of obesity in 2005 and projections to 2030. Int J Obes (Lond) 2008;32:1431–1437
7 The NS, Suchindran C, North KE, Popkin BM, Gordon-Larsen P. Association of adolescent obesity with risk of severe obesity in adulthood. JAMA 2010;304:2042–2047
8 Cui Z, Huxley R, Wu Y, Dibley MJ. Temporal trends in overweight and obesity of children and adolescents from nine Provinces in China from 1991–2006. Int J Pediatr Obes 2010;5:365–374
9 MacGregor AJ, Andrew T, Sambrook PN, Spector TD. Structural, psychological, and genetic influences on low back and neck pain: a study of adult female twins. Arthritis Rheum 2004;51:160–167
10 Cheung KM, Karppinen J, Chan D, et al. Prevalence and pattern of lumbar magnetic resonance imaging changes in a population study of one thousand forty-three individuals. Spine (Phila Pa 1976) 2009;34:934–940
11 Chou D, Samartzis D, Bellabarba C, et al. Degenerative magnetic resonance imaging changes in patients with chronic low back pain: a systematic review. Spine (Phila Pa 1976) 2011;36(21, Suppl):S43–S53
12 de Schepper EI, Damen J, van Meurs JB, et al. The association between lumbar disc degeneration and low back pain: the influence of age, gender, and individual radiographic features. Spine (Phila Pa 1976) 2010;35:531–536
13 Kjaer P, Leboeuf-Yde C, Korsholm L, Sorensen JS, Bendix T. Magnetic resonance imaging and low back pain in adults: a diagnostic imaging study of 40-year-old men and women. Spine (Phila Pa 1976) 2005;30:1173–1180
14 Luoma K, Riihimäki H, Luukkonen R, Raininko R, Viikari-Juntura E, Lamminen A. Low back pain in relation to lumbar disc degeneration. Spine (Phila Pa 1976) 2000;25:487–492
15 Paajanen H, Erkintalo M, Parkkola R, Salminen J, Kormano M. Age-dependent correlation of low-back pain and lumbar disc regeneration. Arch Orthop Trauma Surg 1997;116:106–107
16 Samartzis D, Karppinen J, Luk KDK, et al. Is there a relationship between intervertebral disc degeneration based on MRI and low back pain? Paper presented at: 29th Annual Congress of the Hong Kong Orthopaedic Association; November 28–29, 2009; Hong Kong, SAR China
17 Samartzis D, Karppinen J, Mok F, Fong DY, Luk KD, Cheung KM. A population-based study of juvenile disc degeneration and its association with overweight and obesity, low back pain, and diminished functional status. J Bone Joint Surg Am 2011;93:662–670
18 Takatalo J, Karppinen J, Niinimaki J, et al. Does lumbar disc degeneration on magnetic resonance imaging associate with low back symptom severity in young Finnish adults? Spine (Phila Pa 1976) 2011;36:2180–2189
19 Visuri T, Ulaska J, Eskelin M, Pulkkinen P. Narrowing of lumbar spinal canal predicts chronic low back pain more accurately than intervertebral disc degeneration: a magnetic resonance imaging study in young Finnish male conscripts. Mil Med 2005;170:926–930
20 Battié MC, Videman T. Lumbar disc degeneration: epidemiology and genetics. J Bone Joint Surg Am 2006;88(Suppl 2):3–9
21 Eskola PJ, Lemmelä S, Kjaer P, et al. Genetic association studies in lumbar disc degeneration: a systematic review. PLoS ONE 2012;7: e49995
22 Samartzis D, Karppinen J, Chan D, Luk KD, Cheung KM. The association of lumbar intervertebral disc degeneration on magnetic resonance imaging with body mass index in overweight and obese adults: a population-based study. Arthritis Rheum 2012;64:1488–1496
23 Shiri R, Karppinen J, Leino-Arjas P, Solovieva S, Viikari-Juntura E. The association between obesity and low back pain: a meta-analysis. Am J Epidemiol 2010;171:135–154
24 Takatalo J, Karppinen J, Taimela S, et al. Association of abdominal obesity with lumbar disc degeneration—a magnetic resonance imaging study. PLoS ONE 2013;8:e56244
25 Djurasovic M, Bratcher KR, Glassman SD, Dimar JR, Carreon LY. The effect of obesity on clinical outcomes after lumbar fusion. Spine (Phila Pa 1976) 2008;33:1789–1792
26 Rihn JA, Kurd M, Hilibrand AS, et al. The influence of obesity on the outcome of treatment of lumbar disc herniation: analysis of the Spine Patient Outcomes Research Trial (SPORT). J Bone Joint Surg Am 2013;95:1–8
27 Rihn JA, Radcliff K, Hilibrand AS, et al. Does obesity affect outcomes of treatment for lumbar stenosis and degenerative spondylolisthesis? Analysis of the Spine Patient Outcomes Research Trial (SPORT). Spine (Phila Pa 1976) 2012;37:1933–1946
28 Cassinelli EH, Hall RA, Kang JD. Biochemistry of intervertebral disc degeneration and the potential for gene therapy applications. Spine J 2001;1:205–214

29 Urban JP, McMullin JF. Swelling pressure of the lumbar intervertebral discs: influence of age, spinal level, composition, and degeneration. Spine (Phila Pa 1976) 1988;13:179–187
30 Fields AJ, Sahli F, Rodriguez AG, Lotz JC. Seeing double: a comparison of microstructure, biomechanical function, and adjacent disc health between double- and single-layer vertebral endplates. Spine (Phila Pa 1976) 2012;37:E1310–E1317
31 Adams MA, Freeman BJ, Morrison HP, Nelson IW, Dolan P. Mechanical initiation of intervertebral disc degeneration. Spine (Phila Pa 1976) 2000;25:1625–1636
32 Adams MA, Dolan P, Hutton WC. The stages of disc degeneration as revealed by discograms. J Bone Joint Surg Br 1986;68: 36–41
33 Adams MA, Roughley PJ. What is intervertebral disc degeneration, and what causes it? Spine (Phila Pa 1976) 2006;31: 2151–2161
34 Fujiwara A, Lim TH, An HS, et al. The effect of disc degeneration and facet joint osteoarthritis on the segmental flexibility of the lumbar spine. Spine (Phila Pa 1976) 2000;25:3036–3044
35 Fujiwara A, Tamai K, An HS, et al. The relationship between disc degeneration, facet joint osteoarthritis, and stability of the degenerative lumbar spine. J Spinal Disord 2000;13:444–450
36 Jensen RK, Leboeuf-Yde C, Wedderkopp N, Sorensen JS, Jensen TS, Manniche C. Is the development of Modic changes associated with clinical symptoms? A 14-month cohort study with MRI. Eur Spine J 2012;21:2271–2279
37 Kuisma M, Karppinen J, Niinimäki J, et al. Modic changes in endplates of lumbar vertebral bodies: prevalence and association with low back and sciatic pain among middle-aged male workers. Spine (Phila Pa 1976) 2007;32:1116–1122
38 Wang Y, Videman T, Battié MC. ISSLS prize winner: Lumbar vertebral endplate lesions: associations with disc degeneration and back pain history. Spine (Phila Pa 1976) 2012;37:1490–1496
39 Mok FP, Samartzis D, Karppinen J, Luk KD, Fong DY, Cheung KM. ISSLS prize winner: prevalence, determinants, and association of Schmorl nodes of the lumbar spine with disc degeneration: a population-based study of 2449 individuals. Spine (Phila Pa 1976) 2010;35:1944–1952
40 Mok F, Samartzis D, Karppinen J, et al. Modic changes of the lumbar spine in Southern Chinese. Presented at: World Forum for Spine Research: Intervertebral Disc; July 5–8, 2010; Montreal, Canada
41 Law T, Anthony MP, Chan Q, et al. Ultrashort time-to-echo MRI of the cartilaginous endplate: technique and association with intervertebral disc degeneration. Presented at: World Forum for Spine Research: the Intervertebral Disc—from Degeneration to Pain; June 18–21, 2012; Helsinki, Finland
42 Pfirrmann CW, Metzdorf A, Zanetti M, Hodler J, Boos N. Magnetic resonance classification of lumbar intervertebral disc degeneration. Spine (Phila Pa 1976) 2001;26:1873–1878
43 Schneiderman G, Flannigan B, Kingston S, Thomas J, Dillin WH, Watkins RG. Magnetic resonance imaging in the diagnosis of disc degeneration: correlation with discography. Spine (Phila Pa 1976) 1987;12:276–281
44 Thompson JP, Pearce RH, Schechter MT, Adams ME, Tsang IK, Bishop PB. Preliminary evaluation of a scheme for grading the gross morphology of the human intervertebral disc. Spine (Phila Pa 1976) 1990;15:411–415
45 Boden SD, Davis DO, Dina TS, Patronas NJ, Wiesel SW. Abnormal magnetic-resonance scans of the lumbar spine in asymptomatic subjects. A prospective investigation. J Bone Joint Surg Am 1990;72:403–408
46 Samartzis D, Karppinen J, Chan D, et al. The association of disc degeneration based on magnetic resonance imaging and the presence of low back pain. Presented at: World Forum for Spine Research: Intervertebral Disc; July 5–8, 2010; Montreal, Canada
47 Samartzis D, Karppinen J, Luk KDK, et al. Baseline MRI characteristics in asymptomatic subjects as predictors for future first-time LBP episode. Spineweek. Amsterdam, The Netherlands; May 28–June 1, 2012
48 Hangai M, Kaneoka K, Kuno S, et al. Factors associated with lumbar intervertebral disc degeneration in the elderly. Spine J 2008;8:732–740
49 Hassett G, Hart DJ, Manek NJ, Doyle DV, Spector TD. Risk factors for progression of lumbar spine disc degeneration: the Chingford Study. Arthritis Rheum 2003;48:3112–3117
50 Kalichman L, Guermazi A, Li L, Hunter DJ. Association between age, sex, BMI and CT-evaluated spinal degeneration features. J Back Musculoskeletal Rehabil 2009;22:189–195
51 Liuke M, Solovieva S, Lamminen A, et al. Disc degeneration of the lumbar spine in relation to overweight. Int J Obes (Lond) 2005;29:903–908
52 Videman T, Gibbons LE, Kaprio J, Battié MC. Challenging the cumulative injury model: positive effects of greater body mass on disc degeneration. Spine J 2010;10:26–31
53 Consultation WHOE; WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363: 157–163
54 Jonsson H, Helgadottir GP, Aspelund T, et al. Hand osteoarthritis in older women is associated with carotid and coronary atherosclerosis: the AGES Reykjavik study. Ann Rheum Dis 2009;68: 1696–1700
55 Haara MM, Manninen P, Kröger H, et al. Osteoarthritis of finger joints in Finns aged 30 or over: prevalence, determinants, and association with mortality. Ann Rheum Dis 2003;62:151–158
56 Das UN. Is obesity an inflammatory condition? Nutrition 2001;17:953–966
57 Kauppila LI. Atherosclerosis and disc degeneration/low-back pain—a systematic review. Eur J Vasc Endovasc Surg 2009;37: 661–670
58 Katz JD, Agrawal S, Velasquez M. Getting to the heart of the matter: osteoarthritis takes its place as part of the metabolic syndrome. Curr Opin Rheumatol 2010;22:512–519
59 Solovieva S, Lohiniva J, Leino-Arjas P, et al. COL9A3 gene polymorphism and obesity in intervertebral disc degeneration of the lumbar spine: evidence of gene-environment interaction. Spine (Phila Pa 1976) 2002;27:2691–2696
60 Balistreri CR, Caruso C, Candore G. The role of adipose tissue and adipokines in obesity-related inflammatory diseases. Mediators Inflamm 2010;2010:802078
61 Luciani A, Dechoux S, Deveaux V, et al. Adipose tissue macrophages: MR tracking to monitor obesity-associated inflammation. Radiology 2012;263:786–793
62 Hui W, Litherland GJ, Elias MS, et al. Leptin produced by joint white adipose tissue induces cartilage degradation via upregulation and activation of matrix metalloproteinases. Ann Rheum Dis 2012;71:455–462
63 Massengale M, Lu B, Pan JJ, Katz JN, Solomon DH. Adipokine hormones and hand osteoarthritis: radiographic severity and pain. PLoS ONE 2012;7:e47860
64 Theodoropoulou A, Metallinos IC, Psyrogiannis A, Vagenakis GA, Kyriazopoulou V. Ghrelin and leptin secretion in patients with moderate Alzheimer's disease. J Nutr Health Aging 2012;16: 472–477
65 Schipper HS, de Jager W, van Dijk ME, et al. A multiplex immunoassay for human adipokine profiling. Clin Chem 2010;56: 1320–1328
66 Luc G, Empana JP, Morange P, et al. Adipocytokines and the risk of coronary heart disease in healthy middle aged men: the PRIME Study. Int J Obes (Lond) 2010;34:118–126
67 Liu MY, Xydakis AM, Hoogeveen RC, et al. Multiplexed analysis of biomarkers related to obesity and the metabolic syndrome in

human plasma, using the Luminex-100 system. Clin Chem 2005;51:1102–1109
68 Inadera H. The usefulness of circulating adipokine levels for the assessment of obesity-related health problems. Int J Med Sci 2008;5:248–262
69 Li Z, Shen J, Wu WK, et al. Leptin induces cyclin D1 expression and proliferation of human nucleus pulposus cells via JAK/STAT, PI3K/Akt and MEK/ERK pathways. PLoS ONE 2012;7:e53176
70 Li Z, Shen J, Wu WK, et al. The role of leptin on the organization and expression of cytoskeleton elements in nucleus pulposus cells. J Orthop Res 2013;31:847–857
71 Dumond H, Presle N, Terlain B, et al. Evidence for a key role of leptin in osteoarthritis. Arthritis Rheum 2003;48:3118–3129
72 Koskinen A, Vuolteenaho K, Nieminen R, Moilanen T, Moilanen E. Leptin enhances MMP-1, MMP-3 and MMP-13 production in human osteoarthritic cartilage and correlates with MMP-1 and MMP-3 in synovial fluid from OA patients. Clin Exp Rheumatol 2011;29:57–64
73 Staikos C, Ververidis A, Drosos G, Manolopoulos VG, Verettas DA, Tavridou A. The association of adipokine levels in plasma and synovial fluid with the severity of knee osteoarthritis. Rheumatology (Oxford) 2013;52:1077–1083
74 de Boer TN, van Spil WE, Huisman AM, et al. Serum adipokines in osteoarthritis; comparison with controls and relationship with local parameters of synovial inflammation and cartilage damage. Osteoarthritis Cartilage 2012;20:846–853
75 Yusuf E, Ioan-Facsinay A, Bijsterbosch J, et al. Association between leptin, adiponectin and resistin and long-term progression of hand osteoarthritis. Ann Rheum Dis 2011;70:1282–1284
76 Klein-Wieringa IR, van der Linden MP, Knevel R, et al. Baseline serum adipokine levels predict radiographic progression in early rheumatoid arthritis. Arthritis Rheum 2011;63:2567–2574
77 Gandhi R, Takahashi M, Smith H, Rizek R, Mahomed NN. The synovial fluid adiponectin-leptin ratio predicts pain with knee osteoarthritis. Clin Rheumatol 2010;29:1223–1228
78 Li WC, Hsiao KY, Chen IC, Chang YC, Wang SH, Wu KH. Serum leptin is associated with cardiometabolic risk and predicts metabolic syndrome in Taiwanese adults. Cardiovasc Diabetol 2011;10:36
79 Shah A, Hernandez A, Mathur D, et al. Adipokines and body fat composition in South Asians: results of the Metabolic Syndrome and Atherosclerosis in South Asians Living in America (MASALA) study. Int J Obes (Lond) 2012;36:810–816
80 Urquhart DM, Berry P, Wluka AE, et al. 2011 Young Investigator Award winner: Increased fat mass is associated with high levels of low back pain intensity and disability. Spine (Phila Pa 1976) 2011;36:1320–1325
81 Cicuttini FM, Baker JR, Spector TD. The association of obesity with osteoarthritis of the hand and knee in women: a twin study. J Rheumatol 1996;23:1221–1226
82 Oliveria SA, Felson DT, Cirillo PA, Reed JI, Walker AM. Body weight, body mass index, and incident symptomatic osteoarthritis of the hand, hip, and knee. Epidemiology 1999;10:161–166
83 Zhao CQ, Liu D, Li H, Jiang LS, Dai LY. Expression of leptin and its functional receptor on disc cells: contribution to cell proliferation. Spine (Phila Pa 1976) 2008;33:E858–E864
84 Gruber HE, Ingram JA, Hoelscher GL, Hanley EN Jr. Leptin expression by annulus cells in the human intervertebral disc. Spine J 2007;7:437–443
85 Ariga K, Yonenobu K, Nakase T, et al. Localization of cathepsins D, K, and L in degenerated human intervertebral discs. Spine (Phila Pa 1976) 2001;26:2666–2672
86 Konttinen YT, Kääpä E, Hukkanen M, et al. Cathepsin G in degenerating and healthy discal tissue. Clin Exp Rheumatol 1999;17:197–204
87 Liang QQ, Li XF, Zhou Q, et al. The expression of osteoprotegerin is required for maintaining the intervertebral disc endplate of aged mice. Bone 2011;48:1362–1369
88 Igarashi A, Kikuchi S, Konno S, Olmarker K. Inflammatory cytokines released from the facet joint tissue in degenerative lumbar spinal disorders. Spine (Phila Pa 1976) 2004;29:2091–2095
89 Katz MM, Hargens AR, Garfin SR. Intervertebral disc nutrition. Diffusion versus convection. Clin Orthop Relat Res 1986;(210):243–245
90 Urban JP, Holm S, Maroudas A, Nachemson A. Nutrition of the intervertebral disc: effect of fluid flow on solute transport. Clin Orthop Relat Res 1982;(170):296–302
91 Holm S, Nachemson A. Nutrition of the intervertebral disc: acute effects of cigarette smoking. An experimental animal study. Ups J Med Sci 1988;93:91–99
92 Rajasekaran S, Babu JN, Arun R, Armstrong BR, Shetty AP, Murugan S. ISSLS prize winner: a study of diffusion in human lumbar discs: a serial magnetic resonance imaging study documenting the influence of the endplate on diffusion in normal and degenerate discs. Spine (Phila Pa 1976) 2004;29:2654–2667
93 Terahata N, Ishihara H, Ohshima H, Hirano N, Tsuji H. Effects of axial traction stress on solute transport and proteoglycan synthesis in the porcine intervertebral disc in vitro. Eur Spine J 1994;3:325–330
94 Bibby RL, Webster-Brown JG. Characterisation of urban catchment suspended particulate matter (Auckland region, New Zealand); a comparison with non-urban SPM. Sci Total Environ 2005;343:177–197
95 Ohshima H, Urban JP. The effect of lactate and pH on proteoglycan and protein synthesis rates in the intervertebral disc. Spine (Phila Pa 1976) 1992;17:1079–1082
96 Keshari KR, Lotz JC, Link TM, Hu S, Majumdar S, Kurhanewicz J. Lactic acid and proteoglycans as metabolic markers for discogenic back pain. Spine (Phila Pa 1976) 2008;33:312–317
97 Cameron BM, VanderPutten DM, Merril CR. Preliminary study of an increase of a plasma apolipoprotein E variant associated with peripheral nerve damage. A finding in patients with chronic spinal pain. Spine (Phila Pa 1976) 1995;20:581–589, discussion 589–590
98 VanderPutten DM, Cameron BM, Merril CR. Increased apolipoprotein-E concentrations in individuals suffering chronic low back syndrome identified by two-dimensional gel electrophoresis. Appl Theor Electrophor 1993;3:247–252
99 Monnier VM, Kohn RR, Cerami A. Accelerated age-related browning of human collagen in diabetes mellitus. Proc Natl Acad Sci U S A 1984;81:583–587
100 Kohn RR, Cerami A, Monnier VM. Collagen aging in vitro by nonenzymatic glycosylation and browning. Diabetes 1984;33:57–59
101 Monnier LH, Chaintreuil JS, Colette C, et al. Plasma lipid fatty acids and platelet function in insulin-dependent diabetic patients. Diabete Metab 1983;9:283–287
102 Yokosuka K, Park JS, Jimbo K, et al. Advanced glycation end-products downregulating intervertebral disc cell production of proteoglycans in vitro. J Neurosurg Spine 2006;5:324–329
103 Yoshida T, Park JS, Yokosuka K, et al. Up-regulation in receptor for advanced glycation end-products in inflammatory circumstances in bovine coccygeal intervertebral disc specimens in vitro. Spine (Phila Pa 1976) 2009;34:1544–1548
104 Jazini E, Sharan AD, Morse LJ, et al. Alterations in T2 relaxation magnetic resonance imaging of the ovine intervertebral disc due to nonenzymatic glycation. Spine (Phila Pa 1976) 2012;37:E209–E215
105 Kalanithi PA, Arrigo R, Boakye M. Morbid obesity increases cost and complication rates in spinal arthrodesis. Spine (Phila Pa 1976) 2012;37:982–988

106 Mogannam A, Bianchi C, Chiriano J, et al. Effects of prior abdominal surgery, obesity, and lumbar spine level on anterior retroperitoneal exposure of the lumbar spine. Arch Surg 2012;147: 1130–1134
107 Memtsoudis SG, Kirksey M, Ma Y, et al. Metabolic syndrome and lumbar spine fusion surgery: epidemiology and perioperative outcomes. Spine (Phila Pa 1976) 2012;37:989–995
108 Fineberg SJ, Oglesby M, Patel AA, Pelton MA, Singh K. The incidence and mortality of thromboembolic events in lumbar spine surgery. Spine (Phila Pa 1976) 2013;38:1154–1159
109 Koutsoumbelis S, Hughes AP, Girardi FP, et al. Risk factors for postoperative infection following posterior lumbar instrumented arthrodesis. J Bone Joint Surg Am 2011;93: 1627–1633
110 Mehta AI, Babu R, Karikari IO, et al. 2012 Young Investigator Award winner: The distribution of body mass as a significant risk factor for lumbar spinal fusion postoperative infections. Spine (Phila Pa 1976) 2012;37:1652–1656
111 Knutsson B, Michaelsson K, Sanden B. Obesity is associated with inferior results after surgery for lumbar spinal stenosis: a study of 2633 patients from the Swedish Spine Register. Spine (Phila Pa 1976) 2013;38:435–441
112 Meredith DS, Huang RC, Nguyen J, Lyman S. Obesity increases the risk of recurrent herniated nucleus pulposus after lumbar microdiscectomy. Spine J 2010;10:575–580