FEATURE ARTICLE

Obesity-related pain: Time for a new approach that targets systemic inflammation

We may be able to reduce pain, disability, and related comorbidities in obese patients by implementing modest weight loss and fitness interventions to address systemic inflammation.

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Illustration: Dave Cutler

Pain with obesity is an increasingly common problem in the patients who walk into our clinics. Unfortunately, the overlap of these 2 conditions can seem like too much for us to address in one office visit. If the patient is in pain, we start there. I would argue, however, that we need to begin viewing obesity in our patients as an opportunity to improve their pain.

People with obesity-related pain represent 2 epidemics: the 100 million Americans with chronic pain and the 150 million who are overweight or obese.[1,2] In June 2013, the American Medical Association declared obesity a disease.[3] Similarly, the Institute of Medicine has called for a "cultural transformation" to better assess and treat pain.[4]

With those calls for action in mind, this article explores the idea of a negative association

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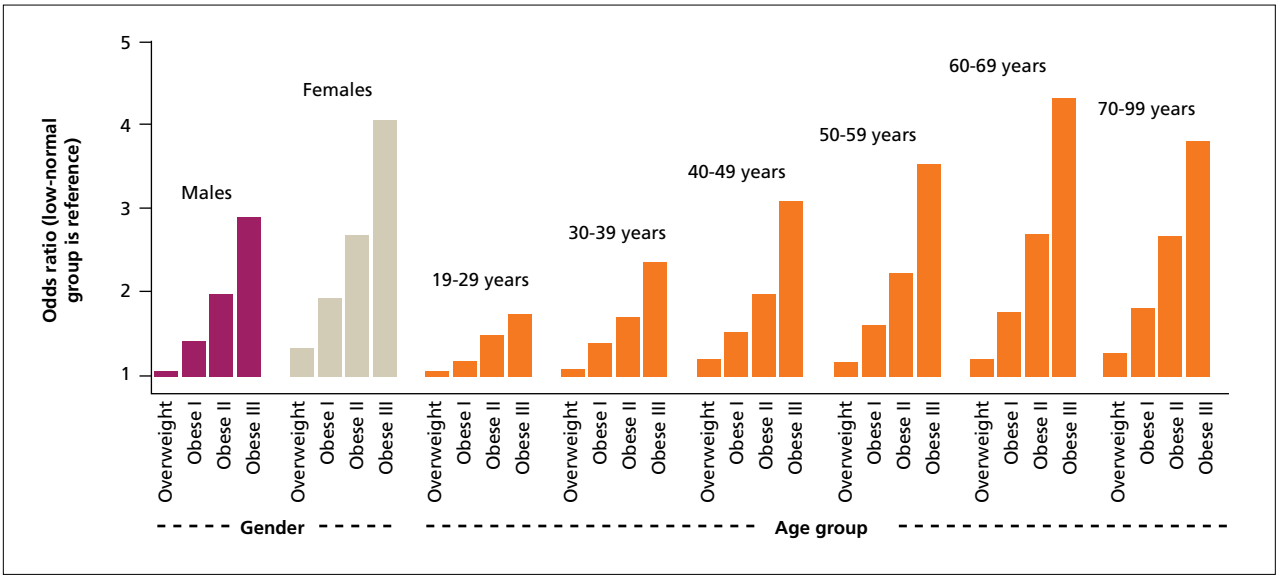
FIGURE 1: Odds ratios for "pain yesterday" for BMI classifications* by gender and age group†[6]



*Body mass index (BMI) classifications: low through normal, <25; overweight = 25 to <30; obese I = 30 to <35; obese II = 35 to <40; obese III, ≥40.

†Based on a survey of >1 million Americans.

Source: Reprinted with permission from Stone AA, Broderick JE. Obesity and pain are associated in the United States. *Obesity (Silver Spring).* 2012;20:1491-1495.[6]

between pain and obesity that goes beyond mechanical overload. The emerging evidence reviewed here elucidates potential connections between these conditions, including systemic inflammation. It suggests that we can reduce pain, disability, and related comorbidities for our patients with even modest weight loss and fitness interventions.

Obesity complicates pain management

Obesity is associated with increased pain and reduced benefit from pain treatments. More than one-third of adult Americans (35.7%) are obese (body mass index [BMI] ≥30).[5] Individuals with obesity experience daily pain at much higher rates than those of low to normal weight. A survey of >1 million Americans found that pain rates were 68% to 254% higher in individuals classified as obese compared with nonobese groups.[6] The association held for both men and women, became stronger in older age groups, and persisted in higher-weight groups even when controlled for other pain conditions (FIGURE 1).[6]

Broader definitions of obesity. BMI calculations based on weight and height (kg/m^2) are the traditional definition of obesity recognized by the World Health Organization and Centers for Disease Control and Prevention (TABLE 1). In addition, obesity is now recognized in normal-weight individuals with elevated body fat percentage (normal-weight obesity [NWO])[7] and in individuals with signs of metabolic syndrome (ie, metabolic obesity), characterized by elevated waist circumference, fasting blood glucose, triglycerides, and blood pressure, as well as reduced HDL cholesterol.[8]

Visceral fat is an independent risk factor for cardiovascular disease. Individuals with central abdominal obesity appear to be at higher risk of atherogenesis than those with peripheral obesity. Insulin resistance, a sequela of intra-abdominal fat accumulation, increases the risk of stroke, type 2 diabetes, and heart disease.[8]

Adding waist circumference to the BMI calculation can help you identify abdominal distribution of obesity.[8] Waist circumference

TABLE 1
World Health Organization definition of obesity based on body mass index (BMI)

Weight status	BMI (kg/m^2)
Underweight	<18.5
Normal	18.5 to 24.9
Overweight (pre-obese)	25.0 to 29.9
Obese class I	30.0 to 34.9
Obese class II	35 to 39.9
Obese class III (morbid obesity)	≥40

Online BMI calculators are available from the Centers for Disease Control and Prevention at: http://www.cdc.gov/healthyweight/assessing/bmi.

Source: World Health Organization. BMI classification. Available at: http://apps.who.int/bmi/index.jsp?introPage=intro_3.html.

>40 inches for men and >35 inches for women substantially increases the risk of metabolic complications.[9]

A clinical tool developed by Sharma and Kushner (TABLE 2)[10] identifies 5 stages of disability from obesity-related medical conditions and recommends a management approach at each stage. This Edmonton Obesity Staging System is complementary to the BMI classifications of obesity. It recognizes that patients—whatever their BMI—may have no apparent risk factors or functional impairments (stage 0); subclinical disease, with mild impairment such as mild aches, pain, and fatigue (stage 1); or moderate to severe organ damage and disability (stages 2 to 4).

A predictor of reduced pain relief. Pain clinicians feel frustration when interventions that generally have a good chance of working fall short. Evidence supports the observa-

TABLE 2
The Edmonton Obesity Staging System for managing metabolic and functional risk[10]

Stage	Patient characteristics	Management approaches
0	No apparent obesity-related risk factors, eg, blood pressure, serum lipids, fasting glucose levels are within normal range No physical symptoms No psychopathology No functional limitations and/or impairment of well-being	Identify factors contributing to increased body weight. Counsel patient on lifestyle measures, including healthy eating and increased physical activity, to prevent further weight gain.
1	Obesity-related subclinical risk factor(s), eg, borderline hypertension, impaired fasting glucose, elevated liver enzymes Mild physical symptoms, eg, dyspnea on moderate exertion, occasional aches and pains, fatigue Mild psychopathology Mild functional limitations and/or mild impairment of well-being	Investigate for other (non–weight-related) contributors to risk factors. Institute more intense lifestyle interventions, including diet and exercise, to prevent further weight gain. Monitor risk factors and health status.
2	Established obesity-related chronic disease(s), eg, hypertension, type 2 diabetes, sleep apnea, osteoarthritis, reflux disease, polycystic ovary syndrome, anxiety disorder Moderate limitations in activities of daily living and/or well-being	Initiate obesity treatments, including considerations of all behavioral, pharmacologic, and surgical treatment options. Maintain close monitoring and management of comorbidities as indicated.
3	Established end-organ damage, eg, myocardial infarction, heart failure, diabetic complications, incapacitating osteoarthritis Significant psychopathology Significant functional limitation(s) and/or impairment of well-being	Initiate more intensive obesity treatment, including consideration of all behavioral, pharmacologic, and surgical treatment options. Aggressively manage comorbidities as indicated.
4	Severe (potentially end-stage) disability/ies from obesity-related chronic diseases Severe disabling psychopathology Severe functional limitation(s) and/or severe impairment of well-being	Institute aggressive obesity management as deemed feasible. Prescribe palliative measures, including pain management, occupational therapy, and psychosocial support.

tion that pain treatments are less effective in patients with obesity compared with those who are not obese.

This pattern has been noted with behavioral pain interventions[11] and in clinical trials. For example, the Spine Patient Outcomes Research Trial (SPORT) for the treatment of lumbar disc herniation examined the benefit of operative and nonoperative treatments in more than 1000 participants. At 4-year follow-up, individuals who were obese had improved significantly less in both treatment groups than did their nonobese counterparts.[12]

Obesity-related pain as systemic inflammation

Obesity causes mechanical disruption, including joint compression and alignment changes that can lead to pain.[13] The association of obesity to pain is often related to areas with mechanical overload (eg, symptomatic knee osteoarthritis [OA] and chronic back pain), and is evidenced by the fact that the rate of early retirement, disability, and risk of requiring surgical treatment are several times higher among people who are overweight or obese.[14]

Pain that occurs with obesity is not exclusively mechanical, however. Increased rates of pain in locations above the knees and low back also have been associated with obesity, including the thoracic spine, neck, upper extremities (rotator cuff tendinitis and carpal tunnel syndrome), as well as with conditions including fibromyalgia, migraine, and headache (TABLE 3).[13,15-17]

Obesity-related pain is a conceptual framework to describe pain and related disability in individuals with obesity and metabolic dysregulation.[7] This concept suggests that systemic inflammation is likely additive in individuals with pain and obesity. Thus, interventions such as exercise that target systemic inflammation and obesity could be important in relieving pain as well.[18]

A number of adipocyte-derived cytokines and markers of systemic inflammation have been associated with obesity and metabolic syndrome.[19] Interestingly, C-reactive protein (CRP) and tumor necrosis factor α (TNF-α) are related both to inflammation and to the progression of OA and low back pain.[20,21] (See FIGURE 2.)

Briggs et al showed increased reporting of low back pain among individuals with elevated CRP, particularly those classified as obese.[18]

TABLE 3
Pain conditions associated with obesity[13,15-17]

- Carpal tunnel syndrome
- Connective tissue disorders (eg, rheumatoid arthritis)
- Fibromyalgia
- Gastrointestinal disorders*
- Gout
- Low back pain
- Migraine and headache
- Neuropathy*
- Osteoarthritis: multiple sites (eg, knee, hip, hand)
- Plantar fasciitis
- Rotator cuff tendonitis

*Refers to subtypes of the condition.

Hormones traditionally viewed as playing a role in obesity, such as leptin and adiponectin, have been linked with upregulation of matrix metalloproteinase and joint degeneration.[22]

A 20-year study by Schett and colleagues[23] found type 2 diabetes to be an independent predictor of severe OA progressing to joint replacement in a group of >900 patients. These authors noted that evidence linking type 2 diabetes with joint degeneration supports the concept that OA is part of the metabolic syndrome. Their data suggest that glucose metabolism directly affects joint integrity, independent of body weight.

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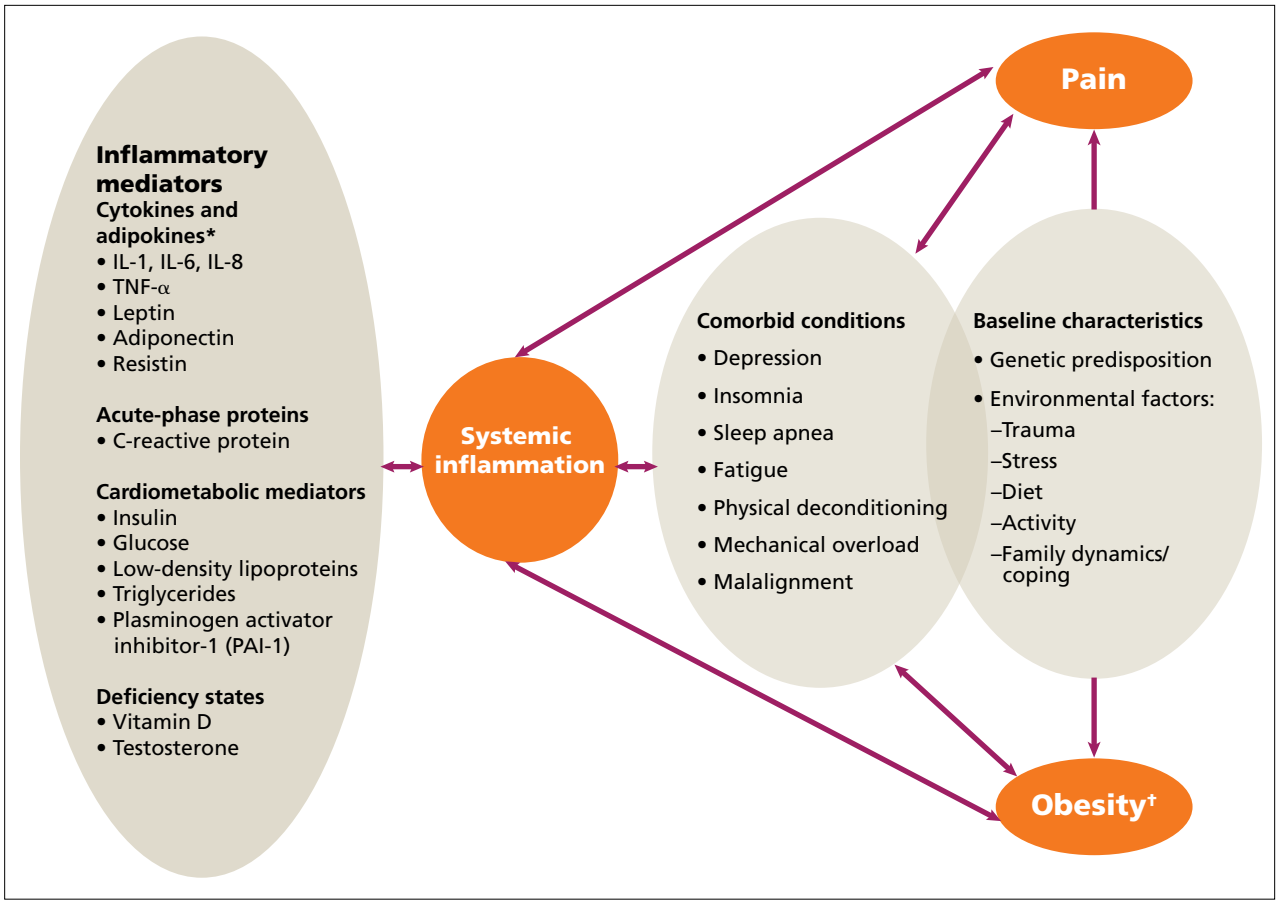
Opportunity: Weight loss, pain, and function

Weight loss provides important and often overlooked potential in reducing pain. Although the additive burden of pain and obesity can seem overwhelming to patients and clinicians, even modest weight loss can produce positive results.[24]

In the Framingham study, an 11-pound weight loss was associated with a 50% reduction in the risk of symptomatic knee arthritis.[25] In another study of knee OA, an 11% loss of body weight from diet alone resulted in a 50% decrease in pain across 8 weeks in patients with a mean BMI of 35.9.[26]

An integrative approach that combines nutrition, activity, and behavioral strategies appears to provide maximum benefit. In the

FIGURE 2: Obesity-related pain: A proposed framework related to systemic inflammation



*Adipokines are cytokines secreted by adipose tissue.

†Includes various definitions of obesity as discussed in the article, including normal-weight obesity (NWO) and metabolic obesity.

IL, interleukin; TNF-α, tumor necrosis factor α.

Sources: Briggs MS, Givens DL, Schmitt LC, et al. Relations of C-reactive protein and obesity to the prevalence and the odds of reporting low back pain. *Arch Phys Med Rehabil.* 2013;94:745-752. Gregor MF, Hotamisligil GS. Inflammatory mechanisms in obesity. *Annu Rev Immunol*. 2011;29:415-445. Vodo S, Bechi N, Petroni A, et al. Testosterone-induced effects on lipids and inflammation. *Mediators Inflamm*. 2013;2013:183041.

18-month Arthritis, Diet, and Activity Promotion Trial (ADAPT), weight loss plus moderate exercise provided greater improvement in function and pain in overweight and obese adults with knee OA, compared with either intervention alone. A 5% weight loss resulted in a 24% improvement in function and a 30% reduction in pain.[27]

Weight loss can reduce pain in patients with obesity and knee OA regardless of the degree of joint damage (as assessed by magnetic resonance imaging [MRI]), muscle strength, or knee-joint alignment, reported Gudbergsen et al.[28] Some aspects of structural deformity may stabilize or reverse with weight loss.[29]

Effective for knee pain and more. Although most trials have evaluated weight loss in people with symptomatic OA, several trials have found benefit in other common pain conditions, such as fibromyalgia and low back pain.

Dietary weight loss resulted in reduced tender points and significantly improved quality of life in obese patients with fibromyalgia, as assessed by the Fibromyalgia Impact Questionnaire in a 6-month controlled trial by Senna et al.[30] Patients who lost weight also slept better and were less depressed than those without weight loss. The investigators also observed an association between weight loss and reduced levels of proinflammatory mediators interleukin 6 (IL-6) and CRP.

Other studies also note that weight loss appears to improve depression and sleep dysfunction, which may contribute to obesity's symptomatic burden. IL-6, linked to these common comorbidities, also is associated with the progression of OA and degree of obesity.[31,32]

A 52-week program of diet and exercise, along with regular group and educational meetings, was effective in reducing BMI in obese patients with low back pain, reported Roffey et al.[33] The interventions also were asso-

ciated with a trend toward improved pain and clinically significant improvements in function.

Exercise does not worsen pain conditions. Patients with pain and obesity may feel discomfort as they begin an exercise program, but postexertional soreness does not represent long-term worsening of a pain condition. Longitudinal data from the 30,000-patient Norwegian HUNT study confirm that exercise overall does not appear to increase the risk of osteoarthritis at any level of BMI.[34] An exhaustive literature review suggested that moderate exercise did not cause progression of osteoarthritis.[35]

A better way to assess and treat pain

Comorbid obesity and pain conditions may be related to subtle processes that start early in life, including genetics, environmental stress, and trauma. Cultural and familial coping patterns, fear avoidance, maladaptive stress coping, and autonomic dysfunction can influence motivation and behavior.[36]

In interviewing primary care patients with coexisting pain and obesity, Janke and Kozak[37] found 5 major behavioral themes:

- Depression can magnify comorbid physical symptoms and complicate treatment.
- Physical pain may trigger hedonic hunger (eating for pleasure rather than to satisfy a biological need), associated with depression and shame.
- Pain may lead to emotional or "binge" eating.
- Pain may result in altered dietary choices.
- Pain may lead to feelings of low self-efficacy for physical activity.

Pain clinicians know the obstacles faced by patients with chronic pain and obesity. We realize how hard it is for them to move, that exercise can flare their pain, and that they may not make the best food choices.

The next logical step is to routinely include weight reduction as a component of pain treatment for our patients with comorbid obesity or metabolic dysregulation. The evidence points to the potential for increased benefit from pain treatments and reduction in obesity-related comorbidities. This would represent what the Institute of Medicine calls a "cultural transformation" in our understanding of pain states and our approach to the clinical encounter.

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