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The Gravity of Weight

A Bone of Contention: Osteoporosis and Weight

"Down to the bone" may have some new connotations: the bone-fat connection



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"Thy bones are marrowless..." (Act III, Scene IV) says Shakespeare's frightened Macbeth as he tries to reassure himself there is no danger upon seeing the ghost of Banquo, the Scottish general he had ordered to be killed. How does bone marrow, though, relate to body weight and even to osteoporosis? "Is osteoporosis the obesity of bone?" That is the provocative question that researchers Rosen and Bouxsein, in an article appearing several years ago in the journal *Nature Clinical Practice (Rheumatology)*, asked.

Osteoporosis is a serious condition that affects both men and women and can occur at any age. Rosen and Bouxsein note that signs and symptoms include back pain, fractures (most commonly at the spine, hip, distal radius, and

proximal humerus) without accompanying significant trauma, and low bone mineral density, a measure of bone mass. A bone's quality is a function of bone geometry and bone strength, as well as its mineral density. When bone mineral density is low, though, bones are fragile and prone to fracture. One of the best ways to measure it is by dual-energy X-ray absorptiometry (DXA),



Glams Castle, home of Shakespeare's Macbeth.

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particularly of the spine, hip, and wrist. DXA, incidentally, is also one of the most accurate ways to measure body composition and specifically our percentage of our body fat. Osteoporosis typically occurs in the elderly (and especially women after menopause). It can also occur in the context of nutritional deprivation (i.e. severe food restriction) as seen in those with anorexia nervosa, as well as secondary to organ transplantation, chronic liver or kidney disease, Cushing's Disease (with its increased production of glucocorticoids), rheumatoid arthritis, lymphoma, and types 1 and II diabetes. Further, both excessive alcohol

consumption and cigarette smoking have been associated with increased risks of osteoporosis.

Rosen and Bouxsein note that both obesity and osteoporosis have some features in common: both are "disorders of body composition that are growing in prevalence;" both may have a genetic basis as well as influences from the environment; both diseases tend to develop over time and are associated with "significant morbidity and mortality;" and perhaps most importantly, both "can be traced to dysregulation of a common precursor cell," i.e., both fat cells (adipocytes) and bone cells (osteoblasts) derive from the same embryonic mesenchymal cells. These researchers describe how what are called pluripotential bone-marrow mesenchymal stem cells can differentiate into osteoblasts (cells that form bone) or adipocytes (fat cells), depending on a complex process involving "switches" within the cells "suggesting significant plasticity" between the two cell types. Shapses and Sukumar, writing in the *Annual Review of Nutrition* (2012) note one important obvious difference: osteoporosis is often considered a "silent disease" (i.e. its first sign can be a fracture) in contrast to obesity which has "high visibility."

Originally it was thought that those with excessive weight (i.e. who have an "increased mechanical load" due to their weight) were less likely to develop osteoporosis. Sharma et al in a recent article (2014) in the *Journal of Midlife Health*, report that large population-based studies now call into question the notion that increased weight is protective of bone health. The situation, though, is complex: remarkably, both a lowered body weight (and even a recent weight loss of only 5%) and excessive weight can be risk factors for increased bone loss and increased risk of fractures. Further, obese patients who are followed longitudinally after gastric bypass surgery and who have subsequently lost considerable weight, can lose significant bone mineral density, according to Rosen and Bouxsein, but a patient's age, sex, ethnicity, and lean body mass are contributing factors for the development of osteoporosis.

As we age, there tends to be a fatty infiltration of bone marrow, confirmed by MRIs, and this is associated with a greater tendency for bones to be fragile. According to studies reported by Lecka-Czernik and

Stechschulte (2014) in the *Archives of Biochemistry and Biophysics*, adipose tissue accumulates in our long bones and vertebrae. Postmenopausal women can have twice the fat in their bone marrow as premenopausal women.

Kawai et al, writing in the *Journal of Internal Medicine* (2012) describe how there has been a “paradigm shift” in thinking of adipose tissue as an inert energy storage substance to a focus on it as a major “endocrine modulator of satiety, energy balance, and pubertal development.” These adipocytes in the marrow, just like adipocytes elsewhere in the body, can secrete inflammatory substances (cytokines) that may lead to bone resorption. Furthermore, there is another connection between fat and bone because the fat hormone leptin, which regulates energy balance among its many other functions, can also influence bone mass. Rosen and Bouxsein note, though, that the function of fat in bone marrow is not completely known and may be either protective or harmful. Lecka-Czernik and Stechschulte raise the question whether adipocytes in bone marrow actually have a negative effect on bone mass or whether it is the low bone mass that stimulates the accumulation of adipocytes. Furthermore, both brown and beige adipocytes have been found in bone marrow and may also be involved in regulating bone mass. For example, Kawai et al speculate that these may even create a “favorable microenvironment” for bone formation by functioning as its energy source or even as a regulator of temperature.

Bottom line: The relationship between fat and bone is an extraordinarily complex and poorly understood one. If there are any beneficial effects of fat accumulation in bone marrow, according to Lecka-Czernik and Stechschulte, they may ultimately lead to new therapeutic possibilities for treatment of both osteoporosis and obesity.

About the Author



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In Print: *The Gravity of Weight: A Clinical Guide to Weight Loss and Maintenance*

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