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Opinion Article

Crosstalk Between Adipose Tissue and Bone in Metabolic Disorders

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ABOVE THE STUDY

The traditional view of adipose tissue as a passive energy reservoir has been fundamentally revised, with growing recognition of its role as an active endocrine organ. In parallel, bone is no longer regarded solely as a structural framework but as a metabolically dynamic tissue involved in systemic homeostasis. The emerging concept of crosstalk between adipose tissue and bone has opened new avenues for understanding the pathophysiology of metabolic disorders such as obesity, type 2 diabetes, and metabolic syndrome. This bidirectional communication involves a complex network of hormones, cytokines, and cellular interactions that influence both skeletal integrity and metabolic regulation.

Adipose tissue secretes a wide array of bioactive molecules known as adipokines, including leptin, adiponectin, resistin, and pro-inflammatory cytokines such as Tumor Necrosis Factor-alpha (TNF-α) and Interleukin-6 (IL-6). These factors have significant effects on bone metabolism. Leptin, for instance, exerts both central and peripheral actions: centrally, it influences bone mass through hypothalamic pathways, while peripherally, it can promote osteoblast differentiation. However, in obesity, leptin resistance may blunt these beneficial effects, contributing to impaired bone formation. Adiponectin, generally considered protective, enhances insulin sensitivity and has been associated with increased bone formation, though its exact role remains complex and context-dependent.

Bone, in turn, functions as an endocrine organ through the secretion of osteokines such as osteocalcin and Fibroblast Growth Factor 23 (FGF23). Osteocalcin, particularly in its undercarboxylated form, has been shown to regulate glucose metabolism by enhancing insulin secretion and sensitivity. This highlights a feedback loop in which bone influences energy metabolism, while adipose tissue modulates bone remodeling. Disruption of this loop in metabolic disorders can lead to both skeletal fragility and metabolic dysregulation.

A key cellular link between adipose tissue and bone is the Mesenchymal Stem Cell (MSC), which serves as a common progenitor for both osteoblasts and adipocytes. In conditions such as obesity and aging, there is a shift in MSC differentiation toward adipogenesis at the expense of osteogenesis. This results in increased marrow adiposity and reduced bone formation, contributing to decreased bone mineral density and increased fracture risk. The molecular mechanisms underlying this shift involve transcription factors such as PPARγ, which promotes adipocyte differentiation while inhibiting osteoblast development.

Chronic low-grade inflammation, a hallmark of metabolic disorders, further exacerbates the imbalance between adipose tissue and bone. Pro-inflammatory cytokines derived from adipose tissue stimulate osteoclastogenesis through the RANK/RANKL/OPG pathway, leading to increased bone resorption. At the same time, inflammation impairs osteoblast function and survival, thereby reducing bone formation. This dual effect accelerates bone loss and compromises skeletal integrity.

Insulin resistance, another central feature of metabolic disorders, also plays a role in bone health. Insulin has anabolic effects on bone, promoting osteoblast proliferation and activity. In insulin-resistant states, these effects are diminished, further contributing to impaired bone formation. Additionally, hyperglycemia can lead to the accumulation of Advanced Glycation End products (AGEs) in bone collagen, reducing bone quality and increasing fragility.

From a clinical perspective, the relationship between obesity and bone health is complex. While increased body weight has traditionally been thought to protect against osteoporosis due to greater mechanical loading, recent evidence suggests that excess adiposity, particularly visceral fat, may have detrimental effects on bone quality. This paradox underscores the importance of considering both quantity and distribution of adipose tissue when assessing fracture risk.

Looking forward, targeting the adipose–bone axis presents a promising strategy for managing metabolic disorders and their skeletal complications. Therapeutic approaches aimed at modulating adipokine signaling, reducing inflammation, and promoting osteogenic differentiation of MSCs are under investigation. Lifestyle interventions, including diet and exercise, remain foundational, as they can simultaneously improve metabolic health and support bone integrity.

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In conclusion, the crosstalk between adipose tissue and bone represents a critical intersection of metabolism and skeletal biology. Disruptions in this interplay contribute to the pathogenesis of metabolic disorders and associated bone complications. A deeper understanding of these mechanisms will be essential for developing integrated therapeutic strategies that address both metabolic and skeletal health in affected individuals.