

Additive Effect of Type 2 Diabetes Mellitus on Estrogen Depletion-Induced Bone Changes in Female ZSD Rats

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Post-menopausal women with type 2 diabetes mellitus (T2DM) have reduced bone mass due to estrogen loss and it is known that hyperglycemic conditions negatively impact bone matrix properties. Epidemiologic studies demonstrate that post-menopausal women are at greater risk of developing T2DM than pre-menopausal women, suggesting a preventive role for estrogen.

This study was designed to investigate the bone changes caused by diet-induced T2DM in estrogen-depleted rats. ZSD female rats were ovariectomized or sham operated (n=8 each) at 20 wks/old, allowed to recover for 6 wks, and then fed a high-fat diet for 12 wks before sacrifice. Bone phenotype was investigated using DEXA, micro-CT and mechanical testing.

During this study, none of the Sham animals became diabetic, while half of the OVX group became diabetic, based on blood glucose levels. Therefore, the OVX group was further divided into diabetic (OVX-D) and non-diabetic (OVX-ND) subgroups. The OVX-D animals had lower BMD and BMC than the OVX-ND and sham groups. The diabetic condition within the OVX animals also altered bone architecture, shown by lower %BV/TV, Tb.Th, Tb.N, anterior Cr.Th and higher SMI compared to non-diabetic OVX animals. Mechanical testing showed reduced material properties such as decreased ultimate load, stiffness, yield, stress and modulus in the OVX-D group compared to OVX-ND animals. The Sham group had stronger bones than both OVX groups.

Our data indicate that T2DM has an additive effect in altering the architectural and material properties of bone during estrogen depletion, further increasing bone fragility.