

Bone and Fat: Effects of Diabetes and Antidiabetic Therapies on Bone



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Objectives

- To understand the effects of diabetes on bone
- To understand how agents used to treat diabetes might influence bone



Type 1 Diabetes

- Low BMD and increased fracture risk
 - Meta analysis of 5 studies: hip fracture 6.9 (3.2 to 14.8)
 - Tromso study: 3x risk of nonvertebral fractures compared with nondiabetics
 - Case control study: RR of any fracture 1.9 (1.2 to 3.0)

Vestergaard P, et al. Osteoporosis Int 2007
Ahmed LA, et al. Osteoporosis Int 2006
Vestergaard P, et al. Diabetologia 2005



Why Might Patients with Type 1 DM Fracture?

- Reduced bone density
- Altered bone mineral
 - Low 25(OH)
 - Hypercalciuria, hypomagnesemia
 - Reduced renal function
- Altered turnover
 - Increases in cytokines
- Altered architecture
 - Microvascular disease may reduce blood flow to bone



Type 2 Diabetes and Fracture: A Paradox

- Increase in BMD
 - Increase in weight
 - mechanical loading
 - hormonal factors: insulin, estrogen, leptin
 - Increased circulating insulin
 - promotes bone formation *in vitro* via increased proliferation and differentiation of osteoblasts
- Increase in fractures



Observational Data: Type 2 DM

- An increased risk of hip, proximal humerus, ankle fractures
 - RR of hip fracture: 1.1 to 5.8 in women
 - RR of hip fracture: 1.0 to 7.7 in men
- ? Increased risk of vertebral fracture

De Liefde et al. Osteoporosis International 2005
Bonds et al. JCEM 2006
Schwartz et al. JCEM 2001
Forsen et al. Diabetologia 1999
Nicodemus et al. Diabetes Care 2001
Janghorbani et al. Diabetes Care 2006
Ahmed et al. Osteoporosis International 2006



Why Might Type 2 DM Increase Fractures?

- Increased risk of falls (by 50 to 60%)
- Increased risk for injurious falls
 - Impaired vision
 - Stroke
 - Hypoglycemia
 - Neuropathy



Increase in Falls Not the Entire Explanation

- SOF: Association persisted **after** adjustment history of falls, RF for falls, injurious falls
- Nord-Trondelag Health Survey: RR hip fracture 1.8 partly accounted for by risk factors
- Older Mexican-American adults: 50% increase in hip fracture risk after adjusted for RF

Schwartz et al. JCEM 2001

Forsen et al. Diabetologia 1999

Ottenbacher et al. J Gerontol A Biol Sci Med Sci 2002



Type 1 versus Type 2 DM

- Increased risk in type 1 DM may be partly explained by lower BMD
- Factors common to BOTH type 1 and type 2 may also contribute to fracture risk
 - Hyperglycemia
 - Neuromuscular disability
 - Neuropathy, visual impairment
 - Insulin deficiency?



Insulin

- Associated with an increased risk of fracture and falls
 - Marker for more severe diabetes
 - Hypoglycemia



Thiazolidinediones

- Increase risk of fracture in women
- Increased rate of bone loss
- BUT- most studies on DM and fractures before agents available

Short R, et al. BMJ 2007

Grey A, et al. J Clin Endocrinol Metab 2007