Obesity and Bone Health

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No conflicts of interest

Addressing the skeletal health of an increasingly obese population

• Low body weight is an established risk factor for fracture
• However, a large proportion of the elderly is overweight or obese
  ▫ 34% of women and 37% of men ≥60 y.o. have BMI ≥30 kg/m²

How do we approach the skeletal health of obese patients?

Case

65 y.o. woman presents for routine follow-up and healthcare maintenance
• PMH: Obesity, type 2 DM, HTN
• 5’5”, 240 lbs. (BMI 40 kg/m²)
• No family hx osteoporosis
• Hx ankle fracture 10 years ago

Needs mammogram, colonoscopy . . .

Refer for DXA for routine BMD screening?
Objectives

- Describe the epidemiology of obesity and fracture
- Identify mechanisms that may link adiposity to bone health and fracture risk
  - Regional deposition of fat tissue
- Recognize challenges in BMD assessment in the setting of obesity
- Discuss the skeletal implications of weight loss

BMI and fracture risk

- Low BMI is associated with low BMD\(^1\)
- Low BMI increases fracture risk\(^2\)
- However, relationship is non-linear:
  - Obesity is less protective than low body weight is risky\(^3, 4\)

\(^1\)Felson 1993, \(^2\)Cummings 1995, \(^3\)De Laet 2005, \(^4\)Armstrong 2011

BMI and fracture risk

- The weak protective effect of higher BMI may even disappear in frank obesity
  - GLOW: Obese women fractured at same overall rates as normal weight women, and had more ankle and leg fractures\(^1\)
- WHO cohorts: After adjustment for their higher BMD, obese women fractured more\(^2\)

\(^1\)Compston 2011, \(^2\)Johansson 2011
An increasing burden of fractures are in the overweight and obese

Small decrease in fracture risk with high BMI

+ Majority of elderly are overweight or obese

= High proportion of fractures occur in those with BMI ≥25 kg/m²

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Supporting a positive association between fat and bone

- Greater mechanical loading on skeleton
- Fat tissue provides padding with falls
- Increased aromatase activity → higher estradiol levels
- Leptin may act peripherally to stimulate bone formation

1Cornish 2002
Supporting a **negative** association between fat and bone

- Inflammatory cytokines impair bone formation
- Hyperglycemia and insulinopenia impair bone formation
- Leptin inhibits bone formation via sympathetic nervous system\(^1,2\)
- Fatty acids stimulate resorption
- Vitamin D deficiency common in obesity
- Hypogonadism common in obesity

\(^1\text{Ducy 2000, }^2\text{Takeda 2002}\)

Regional fat mass

- Body weight and total fat mass: imperfect measures of adiposity
- Visceral and subcutaneous adipose tissue (VAT and SAT), fat infiltration of muscle, bone marrow fat
- Central obesity, or VAT, linked to diabetes, cardiovascular disease\(^1,2\)

\(^1\text{Goodpaster 2003, }^2\text{Miyawaki 2004}\)

Regional fat mass and bone

- Studies using DXA-derived total fat mass: varying associations between fat and BMD
- Greater VAT is associated with lower BMD and impaired bone structure\(^1,2\)

\(^1\text{Russell 2010, }^2\text{Gilsanz 2009}\)

Fat infiltration of muscle

- Obesity is associated with fat accumulation in and around muscle
  - “Sarcopenic obesity”
- Greater fat infiltration of muscle is associated with increased fracture risk\(^1,2\)

\(^1\text{Lang 2010, }^2\text{Schafer 2010}\)

Vitamin D deficiency common in obesity

\(^1\text{Schafer 2010}\)
Bone marrow fat

- Bone and fat are intimately related within the marrow microenvironment
- Bone and fat cells share a common mesenchymal stem cell precursor

Bone marrow fat

- Greater bone marrow fat is associated with lower BMD and with compromised bone health
- Do bone marrow adipocytes induce low bone formation? Or just fill space?
- Does bone marrow fat provide information complementary to BMD?
- Does bone marrow fat predict fracture?

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DXA in the setting of obesity

- Max weight of scanners: 275-350 lbs.
- DXA artifacts in obesity
  - Large amounts of soft tissue may ↑ or ↓ apparent spine BMD
  - Fat increases variability of measurements
  - Bone marrow fat may ↓ apparent BMD
- Potential bias in setting of weight loss

1Blake 2009, 2Totill 1997, 3Van Loan 1998
Options for BMD assessment

• Perform DXA (if weight allows) and interpret thoughtfully
• DXA of distal radius
• CT BMD (g/cm³) spine
• FRAX calculation without BMD

Osteoporosis treatment in obesity

• Bisphosphonates effective in obesity
  ▫ Women with BMI ≥25 kg/m² had greater fracture risk reduction w/ zoledronic acid¹
• Obese women may receive therapy for osteoporosis less often
  ▫ GLOW: 27% of obese women w/ incident fracture were treated, vs. 41% of overweight women and 57% of normal weight women²

¹Eastell 2009, ²Compston 2011

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Weight loss, BMD, & fracture risk

- Weight loss (involuntary or voluntary) is associated with bone loss and increased fracture risk\textsuperscript{1}
  - In older women, 2-fold higher risk of hip fracture compared to stable weight

\textsuperscript{1}Ensrud 1997, 2003

Bone loss: Potential mechanisms

- Signals about decreased loading
- Nutritional factors
  - Lower vitamin D and calcium intake
  - Decreased calcium absorption\textsuperscript{1,2}
- Changes in fat-secreted hormones
  - Decreased estradiol
  - Adipokines
- Loss of muscle mass

\textsuperscript{1}Cifuentes 2004, \textsuperscript{2}Shapses 2013

Bariatric surgery and bone loss

- Roux-en-Y gastric bypass induces abnormalities in bone metabolism\textsuperscript{1-3}
  - Increases in bone turnover
  - Decreases in BMD (up to ~10% at 1 year)

- Check and replete 25(OH)D pre-op
- Daily Ca + vitamin D supplement
- Check 25(OH)D, Ca, alb, phos, PTH, alk phos q 6 mo after malabsorptive surgery\textsuperscript{4}
- DXA pre-op and annually?\textsuperscript{4}

\textsuperscript{1}Coates 2004, \textsuperscript{2}Fleischer 2008, \textsuperscript{3}Carrasco 2009, \textsuperscript{4}Heber (Endocrine Society) 2010

Maintaining adequate bone health during weight loss

- RCT of diet, exercise, diet+exercise, or control in 107 obese older adults\textsuperscript{1,2}
  - Diet alone or diet+exercise → weight loss
  - Diet alone or diet+exercise → BMD loss
    - Diet+exercise: less BMD loss than diet alone
  - Diet alone → increase in CTX; diet+exercise → no increase

\textsuperscript{1}Villareal 2011, \textsuperscript{2}Shah 2011
Maintaining adequate bone health during weight loss
- Addition of exercise to weight loss therapy
  - Attenuates weight loss-induced bone loss
  - Improves physical performance
- Attention to nutrition: Ca, vit D, protein
- Pharmacologic approaches (e.g., bisphosphonates) for high-risk patients?

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