Bone Loss After Bariatric Surgery

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Disclosures

Research support:
– Investigator-initiated research grant from Amgen
– Research support from Radius
– Dietary supplements for research studies donated by Bariatric Advantage and Tate & Lyle
Case presentation

61 y.o. man with obesity, type 2 diabetes

- 423 → 375 lbs (BMI 54 → 48 kg/m²)
- Roux-en-Y gastric bypass surgery
  - 240 lbs (BMI 31)
  - Insulin discontinued
- New low back pain

Why did he fracture?
Overview

• Obesity, weight loss, and bone health
• Skeletal effects of bariatric surgery
  – What happens?
  – Who is at risk?
  – Potential mechanisms
• Implications for clinical practice
Obesity and fracture risk

• High BMI is associated with high bone mineral density (BMD)\(^1\) and protection against fracture\(^2\)

• However, the protective effect of higher BMI may disappear in frank obesity\(^3\)

• Meta-analysis: After adjustment for their higher BMD, obese women fractured more\(^4\)

Potential skeletal effects of obesity

<table>
<thead>
<tr>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>➤ Mechanical loading</td>
<td>➤ Impact with falling</td>
</tr>
<tr>
<td>Soft tissue padding</td>
<td>Vitamin D deficiency</td>
</tr>
<tr>
<td>➤ Aromatase → Estradiol</td>
<td>Hypogonadism</td>
</tr>
<tr>
<td>➤ Leptin (peripheral)(^1)</td>
<td>Hyperglycemia</td>
</tr>
<tr>
<td>➪ Adiponectin(^2)</td>
<td>➤ Inflammation</td>
</tr>
</tbody>
</table>

\(^1\) Cornish, J Endocrinol 2002; \(^2\) Biver, J Clin Endocrinol Metab 2011
Weight loss, BMD, and fracture risk

• Weight loss (even voluntary) is associated with *loss* of bone mass and *increased* fracture risk
  
  — Older women: 2-fold higher risk of hip fracture compared to stable weight

*Ensrud, Arch Int Med 1997; Ensrud, J Clin Endocrinol Metab 2003*
Bone loss during weight loss: Potential mechanisms

- Decreased mechanical loading
- Nutritional factors
  - ↓ vitamin D and Ca intake
  - ↓ Ca absorption\(^1,2\)
- Change in adipokines
  - ↓ estradiol
  - ↑ adiponectin
- Loss of muscle mass
- Marrow fat changes

\(^1\)Cifuentes, Am J Clin Nutr 2004; \(^2\)Shapses, Am J Clin Nutr 2013
Growing demand for bariatric surgery

- US: 42% obese, 9% with BMI ≥40 kg/m²
- Marked and durable weight loss
- Comorbidities improve, mortality rates decline

1 NCHS 2020; 2 Sjostrom, NEJM 2007; 3 Arterburn, JAMA 2015
Bone loss during weight loss: Potential mechanisms

DRAMATIC! RAPID!

- Decreased mechanical loading
- Nutritional factors + MALABSORPTION
  - ↓ vitamin D and Ca intake
  - ↓ Ca absorption$^{1,2}$
- Change in adipokines
  - ↓ estradiol
  - ↑ adiponectin + SURGERY-INDUCED NEUROHORMONAL EFFECTS
- Loss of muscle mass
- Marrow fat changes ∆ GUT MICROBES

$^{1}$Cifuentes, Am J Clin Nutr 2004; $^{2}$Shapses, Am J Clin Nutr 2013
Early studies: bariatric surgery negatively affects the skeleton

- Increases in bone turnover
- Decreases in BMD$^{1-3}$

$^1$Coates, J Clin Endocrinol Metab 2004; $^2$Fleischer, J Clin Endocrinol Metab 2008; $^3$Carrasco, Obes Surg 2009
Concern for early fracture-related morbidity and mortality among bariatric surgery patients

What skeletal changes occur?
Who is at risk?
Why?
Gastric bypass cohort design

- Prospective, pre-post cohort (N=54)
- Obese men and women scheduled for gastric bypass
- University and VA hospitals
Study schema

Pre-op study visit

Enroll when surgery is scheduled

6-month study visit

Surgery

D$_2$ repletion

Post-op month

12-month study visit

Vitamin D$_3$ to maintain 25(OH)D level $\geq$ 30 ng/dL

Total daily Ca intake 1200mg (Ca citrate)
Weight loss is dramatic

Mean ± 1 SD

39 ± 8 kg = 32% of pre-op weight

Schafer, JBMR 2018
Bone turnover increases early

![Graphs showing changes in CTX and P1NP levels over time.](Schafer, JBMR 2018)
BMD decreases substantially by both DXA and QCT

Femoral neck aBMD (DXA)  Spine vBMD (QCT)

* p<0.05
Mean ±1 SD

Schafer, JBMR 2018
BMD declines at non-weight-bearing radius and weight-bearing tibia

Radius total vBMD (HR-pQCT)

Tibia total vBMD (HR-pQCT)

*S p<0.05
Mean ±1 SD

Schafer, JBMR 2018
Postmenopausal women experience worst BMD declines.

**Total hip aBMD (DXA)**

- **Post-w**
- **Pre-w**
- **Men**

12-month % change (mean ± SE)

*p<0.05 pre- vs. post-menopausal*

*Schafer, JBMR 2018*
Detrimental effects on bone microstructure and estimated strength

- Trabecular deterioration tibia
- Decreased strength radius and tibia (FEA)
Cortical porosity increases most in postmenopausal women

Tibial cortical porosity

Post-w

Pre-w

Men

p<0.05 for post- vs. pre-menopausal and post- vs. men

12-month % change (mean ± SE)

Schafer, JBMR 2018
Do detrimental skeletal changes persist after weight stabilizes?
Bone loss persists 5 years after gastric bypass

**BTMs still above pre-op baseline:**
- CTX by 150%
- P1NP by 34%

Lindeman, JCEM 2018; Crawford, Endocr Pract 2018
Is bone loss simply the expected physiologic adaptation to the new lower weight?
Gastric bypass → lower bone mass than controls with same post-op BMI

- Adults 10+ yrs s/p gastric bypass and band
- Nonsurgical controls matched for age, sex, current BMI

![Femoral Neck aBMD and Plate Bone Volume Fraction: Tibia graphs]

*Lindeman, JBMR 2020*
aBMD decline appears greater after gastric bypass than sleeve

Hofsø, J Clin Endocrinol Metab 2021; Guerrero-Pérez, Obes Surg 2020
Fracture risk increases after bariatric surgery

Rousseau, BMJ 2016
Fracture risk increases after bariatric surgery

Fracture risk increases after bariatric surgery

Paccou, JBMR 2020
Fracture risk increases after bariatric surgery

- Increased risk after gastric bypass
  - Compared to gastric band
  - Regardless of diabetes status
- Possibly not after sleeve gastrectomy
- Studies vary substantially in control group, follow-up time
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- Marrow fat changes \(\Delta \) GUT MICROBES

\(^1\)Cifuentes, Am J Clin Nutr 2004; \(^2\)Shapses, Am J Clin Nutr 2013
What are RYGB’s effects on fractional calcium absorption?

- $25(OH)D \geq 30 \text{ ng/mL}$
- Ca intake $1200 \text{ mg/day}$

*DeMaria, N Engl J Med 2007; Christakos, Bonekey Rep 2014*
Pre-op FCA was normal

25(OH)D: 42 ± 11 ng/mL

Schafer, JBMR 2018
FCA decreased precipitously

\[ 33 \pm 14\% \]

\[ 7 \pm 4\% \]

24h UCa ↓
PTH ↑
1,25(OH)2D ↑

Lower post-op
FCA: greater increase in CTX

Schafer, JBMR 2018
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\(^1\)Cifuentes, Am J Clin Nutr 2004; \(^2\)Shapses, Am J Clin Nutr 2013
Post-op increases in PYY are associated with greater declines in spinal vBMD

\[ r = -0.36, \ p=0.02 \]
Also after bariatric surgery . . .

- Those with post-op increases in bone marrow adiposity have more BMD loss\(^1\)
- "Uncoupling" of bone turnover correlates with BMD loss\(^2\)
- Post-op increases in gut microbial diversity might be protective against BMD decline

\(^1\)Kim, JBMR 2017; \(^2\)Kim, Bone 2020
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Why did he fracture?
- Not taking Ca or vitamin D supplements
- DXA: Total hip T-score -1.8

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<th>Alb (3.3-5.2)</th>
<th>Phos (2.5-4.5)</th>
<th>Cr (0.6-1.3)</th>
<th>25OH D (30-50)</th>
<th>PTH (12-65)</th>
<th>24h Uca (100-250)</th>
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<tr>
<td>8.4</td>
<td>3.6</td>
<td>2.5</td>
<td>1.1</td>
<td>17</td>
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- Vitamin D repletion course, daily Ca carbonate and vitamin D maintenance

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<td>80</td>
<td>58</td>
</tr>
<tr>
<td>8.4</td>
<td>3.7</td>
<td>2.8</td>
<td>1.3</td>
<td>34</td>
<td>144</td>
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- Increased Ca intake and switched to citrate
Implications for patient care

✓ Check and replete 25(OH)D pre-op
✓ Universal post-op supplementation
  • Multivitamin
  • Calcium (as citrate) \((1200mg-1500mg\ daily)\)
  • Vitamin D \((3000\ IU\ daily – \text{often in MVI})\)
✓ Labs q 6 mo x 2 yrs then annually
  • Ca, albumin, Cr, 25(OH)D, PTH
  • 24h urinary Ca if additional data needed

Kim, SOARD 2015; Mechanick (AACE/TOS/ASMBS), SOARD 2013
Implications for patient care

- Protein intake 60-75 g/day
- Post-op exercise/resistance training\(^1\)

**RYGB or SG**

\[ \text{Ca + D + protein + exercise} \]

- no supplements, no obligatory exercise

**Attenuated increases in BTMs and decreases in aBMD, lean mass\(^2\)**

- DXA or QCT when indicated; higher-risk pts

\(^1\)Diniz-Sousa, J Bone Miner Res 2016; \(^2\)Muschitz, J Bone Miner Res 2021
Pharmacologic therapy?

? High-risk pts as they undergo surgery

✓ Dramatic high bone turnover state → antiresorptive agent
  ✓ Parenteral (ZOL, DMAB)
  ✓ Only when Ca, vit D status adequate
Conclusions

• Gastric bypass negatively impacts axial and appendicular BMD and bone microstructure
  – Weight-bearing and non-weight-bearing sites
  – Bone loss continues after weight loss complete
  – Postmenopausal women particularly affected

• Sleeve gastrectomy may be less detrimental, but more data needed

• Mechanical unloading and Ca malabsorption contribute, but other mechanisms also at play
Acknowledgments

Schafer Lab
Karin Wu, MD
Nicole King
Eileen Koh, MD
Kate Condra
Heather Freasier, RD
Sheena Patel, MPH
Aldric Chau

Other key collaborators:
Deborah Sellmeyer, MD
Connie Weaver, PhD

UCSF/SFVA collaborators

Endocrinology
Dolores Shoback, MD
Carl Grunfeld, MD, PhD
Tiffany Kim, MD

Epidemiology
Dennis Black, PhD
Eric Vittinghoff, PhD

Radiology
Galateia Kazakia, PhD
Thomas Lang, PhD

Surgery
Lygia Stewart, MD
Stanley Rogers, MD
Jonathan Carter, MD
Andrew Posselt, MD, PhD

VA | U.S. Department of Veterans Affairs
Nutrition & Obesity Research Center
UCSF Academic Senate
NIDDK
National Institute of Diabetes and Digestive and Kidney Diseases
ASBMR
The American Society for Bone and Mineral Research
CTSI at UCSF