# 50 F with history of duodenal switch presenting for low BMD Rajesh Jain MD

Endorama

#### HPI

- 50 F presenting with low BMD referred by PCP
- She has a history of malnutrition following duodenal switch procedure five years earlier
- Peak weight: 411 LB, current weight: 158 LB
- Previous fractures: Toe fracture (years ago)
- ROS: +Generalized muscle and joint pains

### MEDICINE

#### **Extended History**

**PMH**: Learning disability, morbid obesity

Past surgical history: Staged duodenal switch procedure

- 1. 6 years prior: Sleeve gastrectomy at BMI 70
- 2. 1.5 years after initial surgery: had weight loss of about 100 LB but plateaued, BMI at that time 51.7. Underwent duodenal switch procedure

"common channel"

#### **Extended History**

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- Multiple vitamin deficiencies post-operatively, thought to be at least partially adherence related (learning disability & financial)

Family history: Negative for osteoporosis, breast cancer in mother, lung cancer in father

**Social history**: Quit smoking many years ago. Does not drink. She did graduate high school – special education. She lives with her parents. On disability due to cognitive impairment

**Medications**: Vitamin D 50,000 IU BID gel cap, iron, multivitamin, zinc, vitamin A, vitamin K, Allegra, Prilosec, selenium

#### **Physical Exam**

Vitals: Height 61 inches, Weight 158 LB (BMI 29.9), BP 114/62, HR 96

General: No distress

HEENT: Poor dentition, missing teeth. Thyroid exam, nodule on the left about 2 cm. Normal consistency of thyroid gland Lungs: CTAB

CV: tachycardic, regular rhythm

Abd: Soft, non-tender.

Extremities: No edema

Skin: Pigmentations on the abdomen

Neuropsych: Decreased cognitive function

MSK: Unstable, antalgic gait

#### **Initial BMD**

L1-L4: BMD 0.632 g/cm2, T-score -4.6, Z-score -5.1 Total hip: BMD 0.284 g/cm2, T-score -5.7, Z-score -6.4

# CHICAG( MEDICINE

# Bone loss after bariatric surgery

- Multiple etiologies: weight loss itself, vitamin D deficiency, calcium malabsorption, secondary hyperparathyroidism
- Vitamin D deficiency is common both before and after bariatric surgery
- Even with optimal vitamin D intake (>30 ng/mL), calcium absorption is significantly affected after surgery
  - One study of 33 patients after Roux-En-Y showed intestinal calcium absorption decreased from 32.7% pre-operatively to 6.9% post-operatively despite adequate 25-OH vitamin D. There were simultaneous increases in bone turnover markers

Schafer et al. Intestinal calcium absorption decreases dramatically after gastric bypass surgery despite optimization of Vitamin D status. J Bone Min Res 2015; 30.8: 1377-85.

#### Systematic Review

	Before	e surgery		After	surgery			Mea	in Difference		Mean Difference
Study or Subgroup	Mean [g/cm2]	SD [g/cm2]	Total	Mean [g/cm2]	SD [g/cm2]	Total	Weight	IV, Rand	om, 95% CI [g/cm2]	IV, I	Random, 95% CI [g/cm2]
8.1.1 Hip BMD						1.1					
Carrasco 2009	1.28	0.09	42	1.14	0.09	42	14.1%	11%	0.14 [0.10, 0.18]		
Casagrande 2012	1.03	0.15	22	0.94	0.16	22	7.2%	8.7%	0.09 [-0.00, 0.18]		
Nogues 2010	1.054	0.07	7	0.929	0.05	7	10.4%	9.7%	0.13 [0.06, 0.19]		
Pereira 2007	0.961	0.04	8	0.849	0.03	8	14.7%	11.6%	0.11 [0.08, 0.15]		
Subtotal (95% CI)			79			79	46.3%		0.12 [0.10, 0.15]		•
Heterogeneity: Tau <sup>2</sup> =	= 0.00; Chi <sup>a</sup> = 1.6	4, df = 3 (P = 0	).65); P	= 0%							1 N 1
Test for overall effect:	Z = 10.38 (P < 0	.00001)									
8.1.2 Spine BMD											
Carrasco 2009	1.49	0.11	42	1.38	0.14	42	11.8%	7.4%	0.11 (0.06, 0.16)		
Casagrande 2012	1.13	0.11	22	1.04	0.09	22	11.0%	7.9%	0.09 [0.03, 0.15]		
Nogues 2010	1.1	0.1	7	1.026	0.07	7	7.3%	7.6%	0.07 [-0.02, 0.16]		
Pereira 2007	1.135	0.04	8	1.108	0.02	8	15.2%	6.7%	0.03 [-0.00, 0.06]		-
Tsifsis 2009	1.193	0.139	26	1.113	0.152	26	8.4%		0.08 [0.00, 0.16]		
Subtotal (95% CI)			105			105	53.7%		0.07 [0.03, 0.11]		•
Heterogeneity: Tau <sup>a</sup> =	= 0.00; Chi <sup>a</sup> = 8.9	6, df = 4 (P = 0	0.06); P	= 55%							
Test for overall effect:	Z = 3.63 (P = 0.0	0003)									
Total (95% CI)			184			184	100.0%		0.09 [0.06, 0.13]		•
Heterogeneity: Tau <sup>2</sup> =	= 0.00; Chi <sup>2</sup> = 25.	77, df = 8 (P =	0.001)	; l <sup>a</sup> = 69%					_	0.0	
Test for overall effect:	Z = 5.86 (P < 0.0	00001)								-0.2	-0.1 0 0.1 0.2
Test for subaroup diff	ferences: Chi <sup>z</sup> =	4.90. df = 1 (P	= 0.03	0, I⁼ = 79.6%							yanı ioss

Fig. 2. Forest plot of hip and column BMD one year post bariatric mixed-procedure surgery.

Rodriguez-Carmona et al. Bone mineral density after bariatric surgery. A systematic review. Int J Surg 2014;12:976-82.

#### Extent of weight loss and bone



Fleischer et al. Decline in hip bone density after gastric bypass surgery is associated with extent of weight loss. JCEM 2008; 93:3735-3740.

#### Longer follow up



Johnson JM et al. Effects of gastric bypass procedure on bone mineral density, calcium, parathyroid hormone, and vitamin D. J Gastro Surg 2005;9:1106-11.

#### What about fractures?

- One U.K. study looked at 2,079 patients and matched them to controls & followed them for mean 2.2 years
- Overall no significantly increased risk of fracture compared to controls (8.8 vs 8.2 per 1000 person years)
- However, in patients who were followed for 3-5 years, there was a trend towards increased fracture risk

### MEDICINE

Lalmohamed A et al. Risk of fracture after bariatric surgery in the United Kingdom: population based, retrospective cohort study. BMJ 2012;345:e5085-95.



Fig 2 Spline regression plot of time since bariatric surgery and risk of any fracture in bariatric surgery patients versus matched controls. Risk adjusted for confounders as shown in table 2

Lalmohamed A et al. Risk of fracture after bariatric surgery in the United Kingdom: population based, retrospective cohort study. BMJ 2012;345:e5085-95.

#### With longer term follow up

- Study of 258 patients from Minnesota with mean BMI of 49 followed for median 7.7 years after surgery
- Most patients had undergone Roux-en-Y
- RR fracture was 2.3-fold compared to expected



Nakamura et al. Fracture risk following bariatric surgery: a population-based study. Osteoporos Int 2014;25:151-58.

#### Labs (1 month later)



#### Around the same time...

 Patient complaining of back pain x 2 weeks (no clear trauma) to PCP and underwent X-rays



#### Around the same time...

 Patient complaining of back pain x 2 weeks (no clear trauma) to PCP and underwent X-rays

> Acute appearing non-displaced fractures of the right third and seventh ribs Healing/healed nondisplaced fractures of multiple lower ribs Demineralized bones, which may indicate osteoporosis/osteopenia

LOWER RIBS # 11788731

12/1/2011 10:54:53

A

JPPER



#### Labs (1 month later)



#### Osteomalacia

- Patients can present with diffuse bone and joint pain, muscle weakness, and difficulty walking
- Fractures may occur with little or no trauma, typically involving the ribs, vertebrae, and long bones
- Alkaline phosphatase usually elevated, PTH elevated
  - In one study of histologically confirmed osteomalacia and controls, elevated alkaline phosphatase had a 14% false negative and 8% false positive rate.
  - Our patient had consistently normal alkaline phosphatase likely related to other nutritional deficiencies (particularly zinc, which is known to lower alkaline phosphatase and of which our patient had a chronic deficiency)
- Can occur from Vitamin D deficiency or resistance, as well as phosphate wasting syndromes

Peach et al. Value of plasma calcium, phosphate, and alkaline phosphatase measurements in the diagnosis of histological osteomalacia. J Clin Pathol 1982;35:625-30.

#### Absorption



**FIG. 1.** Serum 25OHD levels are unchanged despite a marked increase in vitamin D intake after RYGB. \*, Change from preoperative baseline at P < 0.05.

Fleischer et al. Decline in hip bone density after gastric bypass surgery is associated with extent of weight loss. JCEM 2008; 93:3735-3740.

#### Common!



Slater et al. Serum fat-soluble vitamin deficiency and abnormal calcium metabolism after malabsorptive bariatric surgery. Soc Surg Aliment Tract 2004;8: 48-55.

#### Vitamin D formulations



# Vitamin D after malabsorptive bariatric surgery

- Gel caps with oil or coated pills may be poorly absorbed in patients after malabsorptive bariatric surgery
- Dry powders, liquid, or chewables may be better absorbed, but no trials looking at this issue
  - U.S. guidelines recommend 3000 units daily initially in the early post-operative periods
- Patches may be options to bypass the GI tract but can be expensive over time. E.g. \$20 or more per month with no insurance coverage

Mechanick et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient---2013 Update: cosponsored by the American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery. Obesity 2013;21:S1-S27.

#### Patient course continued...

- Patient's course complicated by financial difficulties (various forms of vitamin D are not covered by insurance) and difficulty with adherence (related to learning disability)
  - Mixing up different formulations of Vitamin D/Calcium so taking the wrong dose
  - Being unable to afford the Vitamin D (pills, patch)
  - Running out of her medications
  - Being told to mix dry vitamin D with apple sauce, running out of apple sauce, and then not realizing she can mix the dry vitamin D with other things



#### Patient course

- Follows up routinely, last visit in October 2015
- No further clinical fractures
- Current meds: Vitamin D 50,000 IU dry powder daily, Citracal chewables [calcium 250 mg each] TID (less than recommended), Centrum Silver daily [Calcium 500 mg]

## MEDICINE



	т	rend: L1-L4	Char	ide vs
Measured Date	Age (years)	BMD (g/cm <sup>2</sup> )	Baseline (%/yr)	Previous (%)
07/30/2015	54.3	0.574	-2.2 *	-8.5 *
06/20/2013	52.2	0.627	-0.4	-0.8
05/26/2011	50.2	0.632	baseline	-

COMMENTS:

#### BMD - 2015

Height / Weight: 6 Sex / Ethnic: 6	50.7 in. 167.6 lbs. Female Black	Measured: Analyzed:		07/30/2015 9:17:09 07/30/2015 9:25:53	AM (13.50) AM (13.50)
	Dua	Femur Bone Density Tren	nd		
	N		$\langle \rangle$	1	
				SIT	
			11		
Densitometry Ref: Total (BMD) BMD (g/cm <sup>2</sup> ) YA T-sco	) Trend: Total Mean (BMD "Change vs Baseline	Image not for diagnosis	BMD	2,7 Young-Adult	Age-Matched
Densitometry Ref: Total (BMD BMD (g/cm <sup>2</sup> ) YA T-sco 1.386	) Trend: Total Mean (BMD re %Change vs Baseline	Image not for diagnosis () Region	BMD (g/cm <sup>2</sup> )	2,7 Young-Adult T-score	Age-Matched Z-score
Densitometry Ref: Total (BMD BMD (g/cm²) YA T-sco 1.386 1.260 1.134	) Trend: Total Mean (BMD re %Change vs Baseline 3 12 2 10	Image not for diagnosis () Region Neck Left	BMD (g/cm <sup>2</sup> )	Young-Adult T-score	Age-Matched Z-score
Densitometry Ref: Total (BMD) BMD (g/cm <sup>2</sup> ) YA T-sco 1.386 1.260 1.134 1.008	) Trend: Total Mean (BMD) re %Change vs Baseline 3 12 2 10 1 8	Image not for diagnosis () Region Neck Left Right	BMD (g/cm <sup>3</sup> ) 0.331 0.337	2,7 Young-Adult T-score	Age-Matched Z-score
Densitometry Ref: Total (BMD BMD (g/cm <sup>2</sup> ) YA T-sco 1.386 1.260 1.134 1.008 0.882	) Trend: Total Mean (BMD) re %Change vs Baseline 3 12 2 10 1 8 0 6	Image not for diagnosis () Region Neck Left Right Mean	(g/cm <sup>2</sup> ) 0.331 0.337 0.334	2,7 Young-Adult T-score -5.1 -5.0 -5.1	Age-Matched Z-score
Densitometry Ref: Total (BMD BMD (g/cm <sup>2</sup> ) YA T-sco 1.386 1.260 1.134 1.008 0.882 0.756	) Trend: Total Mean (BMD %Change vs Baseline 3 12 2 10 1 8 0 6 -1	Image not for diagnosis () Region Neck Left Right Mean Difference	1 BMD (g/cm <sup>2</sup> ) 0.331 0.337 0.334 0.006	2,7 Young-Adult T-score -5.1 -5.0 -5.1 0.0	Age-Matched Z-score -5.3 -5.2 -5.2 0.0
Densitometry Ref: Total (BMD BMD (g/cm <sup>2</sup> ) YA T-sco 1.386 1.260 1.134 1.008 0.882 0.756 0.630	) Trend: Total Mean (BMD %Change vs Baseline 3 12 2 10 1 8 0 6 -1 -2 4 2 2	Image not for diagnosis () Region Neck Left Right Mean Difference Total	1 BMD (g/cm <sup>3</sup> ) 0.331 0.337 0.334 0.006	2,7 Young-Adult T-score -5.1 -5.0 -5.1 0.0	Age-Matched z-score -5.3 -5.2 -5.2 0.0
Densitometry Ref: Total (BMD BMD (g/cm <sup>2</sup> ) YA T-sco 1.386 1.260 1.134 1.008 0.882 0.756 0.630	) Trend: Total Mean (BMD %Change vs Baseline 3 12 2 10 1 8 0 6 -1 4 -2 4 -3 2 4 0	Image not for diagnosis () Region Neck Left Right Mean Difference Total Left	1 (g/cm <sup>3</sup> ) 0.331 0.337 0.334 0.006 0.315	2,7 Young-Adult T-score -5.1 -5.0 -5.1 0.0 -5.5	3 Age-Matched Z-score -5.3 -5.2 -5.2 0.0 -6.1
Densitometry Ref: Total (BMD BMD (g/cm <sup>2</sup> ) YA T-sco 1.386 1.260 1.134 1.008 0.882 0.756 0.630 0.504 Right	) Trend: Total Mean (BMD %Change vs Baseline 3 12 2 10 1 8 0 6 -1 -2 4 -3 2 -4 0	Image not for diagnosis () Region Neck Left Right Mean Difference Total Left Right Right	1 BMD (g/cm <sup>3</sup> ) 0.331 0.337 0.334 0.006 0.315 0.321	2,7 Young-Adult T-score -5.1 -5.0 -5.1 0.0 -5.5 -5.4	3 Age-Matched Z-score -5.3 -5.2 -5.2 -5.2 0.0 -6.1 -6.1 -6.1
Densitometry Ref: Total (BMD BMD (g/cm <sup>2</sup> ) YA T-sco 1.386 1.260 1.134 1.008 0.882 0.756 0.630 0.504 Right	) Trend: Total Mean (BMD %Change vs Baseline 3 12 2 10 1 8 0 6 -1 -1 -2 4 -3 2 -4 0 -5 -2	Image not for diagnosis () Region Neck Left Right Mean Difference Total Left Right Mean	I BMD (g/cm <sup>3</sup> ) 0.331 0.337 0.334 0.006 0.315 0.321 0.318	2,7 Young-Adult T-score -5.1 -5.0 -5.1 0.0 -5.5 -5.4 -5.5	3 Age-Matched Z-score -5.3 -5.2 -5.2 0.0 -6.1 -6.1 -6.1 -6.1
Densitometry Ref: Total (BMD BMD (g/cm <sup>2</sup> ) YA T-sco 1.386 1.260 1.134 1.008 0.882 0.756 0.630 0.504 Right 0.378 0.252 20 40 Lert 80 10	) Trend: Total Mean (BMD %Change vs Baseline 3 12 2 10 1 8 0 6 -1 -2 4 -3 2 -4 0 -5 -2 -6 -4 5 10 520 530	Image not for diagnosis () Region Neck Left Right Mean Difference Total Left Right Mean Difference 54.0	I (g/cm <sup>3</sup> ) 0.331 0.337 0.334 0.006 0.315 0.321 0.318 0.006	2,7 Young-Adult T-score -5.1 -5.0 -5.1 0.0 -5.5 -5.4 -5.5 -5.4 -5.5 0.0	Age-Matched Z-score -5.3 -5.2 -5.2 0.0 -6.1 -6.1 -6.1 -6.1 0.0
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#### **Reversal of surgery?**

- Reversal of malabsorptive part of her surgery was recommended but she declined
- "I have had numerous and extensive prior discussions with her regarding her nutrition and specifically my recommendation that she undergo revision of her malabsorptive component of her duodenal switch and did so again today. Unfortunately, she continues to adamantly refuse to do so, as she is terrified of weight regain. I spent 20 minutes explaining the rationale for revision and the fact that her sleeve would remain undisturbed and would still provide her with a weight loss tool." – Surgery attending

#### Reversal of Malabsorptive Surgery

- Malabsorption is related to the length of the common channel (shorter channel is associated with greater deficiencies)
- Our patient had a 100 cm common channel, which is a common length, with shorter length (e.g. 75 cm) showing higher rates of secondary hyperparathyroidism in 165 patients (38.9% versus 14.9%) compared to 100 cm
- In one large Portuguese series of 1,423 patients who had undergone duodenal switch, rate of revision due to malnutrition was 0.7% and total reversal was 0.2%

Hamoui et al. The significance of elevated levels of parathyroid hormone in patients with morbid obesity before and after bariatric surgery. Arch Surg 2003;138:891-7.

Marceau et al. Duodenal switch: long-term results. Obesity Surg 2007;17:1421-30.

#### **Clinical course**

- Over the past 6 months or so, patient now is getting the dry vitamin D automatically sent to her home
- Last 25-OH Vitamin D level in November was 16
- Change in management?

#### An aside: what about GLP-1s?

GLP-1s appear to reduce bone loss in the setting of weight loss



 Total body BMD and bone turnover markers (CTX-1, P1NP, osteocalcin, BSAP) assessed at screening, randomization, and after 52 weeks

lepsen et al. GLP-1 receptor agonist treatment increases bone formation and prevent bone loss in weight-reduced obese women. JCEM 2015;100:2909-17.



No significant difference in total body BMD, though BMC decrease was lower Higher P1NP (bone formation marker) in liraglutide group Exact mechanisms of GLP-1 agonists on bone are unclear



#### References

- Rodriguez-Carmona et al. Bone mineral density after bariatric surgery. A systematic review. Int J Surg 2014;12:976-82.
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