

Carol Rees Parrish, M.S., R.D., Series Editor

Bone Health After Major Upper Gastrointestinal Surgery



Sharon Carey

Bone Mineral Disease can be painful, debilitating and result in increased fracture risk. It is highly prevalent in those having had major upper gastrointestinal surgery with multiple contributing factors. Increasing awareness of the risk factors and early screening can help prevent or slow the onset of disease. Once identified, disease progression can be managed with thorough medical and dietetic assessment and intervention. Lifestyle changes, vitamin supplementation, drug therapies and regular bone scans can all play a role in preventing deteriorating bone health.

INTRODUCTION

Bone Mineral Disease (BMD) predominantly affects the aged population and postmenopausal women. It is currently estimated that 44 million US citizens have developed, or are at risk of developing BMD, with 1.5 million people presenting with a fracture each year.¹ Chronic pain and high fracture risk lead to high morbidity and mortality rates and greatly reduce quality of life for people with BMD. The yearly health economic burden is estimated to be 17 to 19 billion US dollars for fracture treatment alone.² The incidence of BMD continues to increase as our population ages. Chronic disease and cancer survivors are also at high risk of BMD, and as survivorship improves, the incidence of BMD in these patient populations is also expected to increase.

Sharon Carey, Department of Nutrition and Dietetics, Royal Prince Alfred Hospital, Missenden Road, Camperdown, NSW, AUS

Bone Mineral Disease Revisited

Bone metabolism is a complex and detailed process. It relies on the availability of calcium, which is stored within the bone, providing density and strength to bone cells.³ Calcium homeostasis in turn relies on the presence of parathyroid hormone (PTH), vitamin D and calcitonin. An imbalance in this system can lead to BMD, altered bone remodelling, and some degree of osteoporosis or osteomalacia.⁴

Osteoporosis vs. Osteomalacia

Osteoporosis is defined as a disorder of reduced bone strength resulting in quantitative loss of bone, bone fragility, and an increased risk of fractures.³ It results from an imbalance in bone turnover and is most commonly found in postmenopausal females and the elderly. Osteomalacia (or rickets in children) is less common than osteoporosis and is a disease in which the newly formed bone is not mineralized properly,³ and is often referred to as a softening of the bone.

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Primary and Secondary Bone Mineral Disease

The most common reasons for primary BMD include post-menopause in females, aging and genetics (for example race and family history). Primary BMD accounts for the majority of people who suffer BMD and it is usually associated with osteoporosis.⁵ Guidelines for treating primary osteoporosis are well documented.⁶

Secondary BMD does not have the same clear guidelines. Secondary BMD affects both males and females, usually resulting from a predisposing medical condition, disease or as a side effect of other treatments or medications such as excessive use of glucocorticoids.⁷ Secondary BMD usually manifests as osteomalacia. It commonly results from inadequate calcium intake and/or vitamin D deficiency.⁸ Low serum vitamin D levels alone lead to poor calcium absorption as well as calcium resorption from the bone. Treatment of secondary BMD must not only address bone health, but also where possible, address the underlying cause. Secondary BMD has been well documented in patients on long term parenteral nutrition also.⁹

Evidence of Bone Mineral Disease after Major Upper Gastrointestinal Surgery

Bone health is often forgotten in people having had major upper gastrointestinal (GI) surgery as health professionals attempt to manage the many other aspects of post-operative care. Yet bone mineral disease is highly prevalent in this population with multiple contributing factors. Upper GI surgeries such as esophagectomy, partial and total gastrectomy and Whipples procedures have all been shown to increase the risk of BMD.^{8, 10, 11} The reasons for this increase in risk are still largely unknown, yet suspected reasons include:

1. Reduced oral intake. People often struggle after gastric surgery to consume adequate amounts of food to maintain their nutritional status, and this reduced intake results in a reduced intake of calcium and vitamin D.^{8, 12}
2. Inadequate oral intake also results in weight loss and subsequent malnutrition. There is also a strong correlation between low body weight and BMD.¹³
3. Higher losses of calcium and vitamin D in the presence of malabsorption. Steatorrhea leads to the formation of insoluble calcium

soaps. Poor mixing of the body's pancreatic enzymes also increases fat (and fat soluble vitamin) malabsorption.^{3, 14}

4. Rapid transit and dumping means less time for calcium and vitamin D absorption.^{3, 5} Surgical reconstruction that bypasses the absorptive region of the duodenum and proximal jejunum.⁵
5. Absence of the stomach, which appears to play an important role in calcium absorption. Firstly, the stomach turns insoluble dietary calcium into soluble calcium salts that are easily absorbed. Secondly, the stomach lowers the pH of the proximal duodenum, again favorable for calcium absorption. Finally, there is also some evidence to suggest that the acid producing mucosa of the stomach produces a hormone called gastrocalcin, which stimulates bone uptake of calcium.^{3, 15, 16}
6. The possible role of bacterial overgrowth, which leads to inactivation of lipase resulting in fat and fat soluble vitamin malabsorption,⁵ alterations in bile salts, hence micelle formation.
7. Possible lactose intolerance where anatomy bypasses key absorptive sites. Many people with symptoms of malabsorption may also naturally avoid foods containing lactose.
8. Reduced exposure to sunlight. If patients have significant ongoing weight loss after surgery and are not feeling well, they may be less likely to leave the house. Therefore, outdoor activity may be limited.
9. The patient groups that undergo major upper GI surgeries may already have primary risk factors for BMD, including post-menopausal females, smokers and higher than recommended alcohol intakes.
10. Increased osteoclastic activity in the setting of ongoing inflammatory processes such as malignancy, untreated celiac disease, Crohn's etc.⁹

In partial or total gastrectomy, physiologic changes occur in an attempt to compensate. Urinary calcium losses are much reduced, and raised PTH and 1,25-dihydroxy vitamin D levels increase calcium

Table 1. Key Areas of Nutrition Assessment to Determine Risk of BMD

1. People of a low BMI or with significant weight loss
2. Biochemical review indicating possible BMD (Table 2)
3. Signs of malabsorption - steatorrhea or dumping syndrome
4. Medications - high intake of PPI (common in upper GI surgical patients who may suffer ongoing reflux) antacids, glucocorticoids, and bile acid sequestrants¹
5. Poor intake, especially limited intake of foods high in calcium and vitamin D
6. A medical history that indicates existing risk factors or recent history of fracture
7. A social history that indicates poor exposure to sunlight, for example people who are housebound, or who cover their skin for cultural or religious reasons, or use sunscreen

absorption.^{15, 17} However this compensation does not appear to be sufficient to prevent BMD.

Incidence of Bone Mineral Disease after Major Upper Gastrointestinal Surgery

Much of the research on BMD in upper GI surgeries is dated, and the actual incidence of BMD in this population is still under debate. This is due to the inconsistent use of tools to measure bone density, as new tools have steadily emerged since the 1960's. Early studies used x-ray and bone biopsy, while recent studies have used dual-energy X-ray absorptiometry (DXA) and computed tomography (CT).

Partial and Total Gastrectomy

Of the major upper GI surgeries, the incidence of BMD has been most widely investigated in post-gastrectomy patients. Approximately 20-50% of people having had partial or total gastrectomy surgery will develop BMD.^{8, 18, 19}

Changes in bone health have been well reported, and at greatest risk are those with significant weight loss, rheumatic pains, raised PTH levels, reduced serum 25-hydroxy vitamin D, anemia, people having had chemotherapy, poor nutritional status prior to surgery, and increased length of time since surgery.^{18, 20-22}

Type of reconstructive surgery does not appear to influence the severity of disease,¹⁹ and debate continues

as to whether the BMD is predominantly osteoporosis or osteomalacia.^{16, 21}

Esophagectomy & Pancreoduodenectomy (Whipple) Procedure

Esophagectomy and Whipples procedures are primarily undertaken as a result of cancer and prognosis remains poor. Hence, very little data exists regarding BMD for these groups.^{4, 5} It would not be surprising to find that the prevalence of BMD in these groups would be similar to that of the post-gastrectomy patient population. This is supported by studies that have found hypocalcaemia and vitamin D deficiency in a cohort of esophagectomy patients.¹¹

Monitoring BMD After Major Upper Gastrointestinal Surgery

There are currently no specific guidelines on monitoring bone health in this patient group, however, DXA at time of surgery, would allow initiation of treatment of any pre-existing bone disease, and provide a basis to assess changes in bone health over time. Recommendations in managing secondary BMD include DXA every 2 years;⁶ more frequent screening is not recommended.

Nutritional Assessment after Major Upper Gastrointestinal Surgery

Ideally, patients having had major upper GI surgery

Table 2. Interpreting Serum and Urinary Biochemical Results

	Osteoporosis	Osteomalacia
Serum		
Calcium	Normal	Decreased
Phosphate	Normal	Decreased
Vitamin D	Variable	Decreased
PTH	Unaffected	Elevated
ALP	Variable	Variable
Urinary		
Calcium	Normal	Decreased

should receive nutrition intervention during their acute hospital admission. Outpatient follow-up may only encompass the initial months following discharge and screening for long term complications following surgery are often overlooked.²³ Nutritional review of people following surgery should include assessment of BMD risk (Table 1 and 2).

Management of Bone Mineral Disease

Diagnosis

Diagnosis of BMD is based on bone density and clinical assessment. The World Health Organization definitions of bone health,²⁴ ranging from normal to severe osteoporosis are based on hip or spine DXA readings (Table 3). Plain x-ray can be helpful in flagging bone health as a concern, where it may otherwise have gone undiagnosed and untreated; and in differentiating between osteoporosis and osteomalacia. Specialist interpretation of DXA and x-rays are needed to determine the degree and type of bone disease. Risk equations also exist to help refine future fracture risk utilising BMD and other clinical risk factors (FRAX).²⁵ CT and magnetic resonance imaging (MRI) are also highly sensitive tools that can be used in diagnosing BMD, but both are expensive in comparison to DXA, and so are not usually used specifically for this purpose, nor are they validated in predicting future risk of fractures. Clinical assessment should involve assessing presence of risk factors and biochemistry. Biochemical

Table 3. WHO Working Group Definition of Osteoporosis¹⁸

Definition	DXA Values
Normal Bone Health	T score between +1.0 and -1.0 SD
Osteopenia	T-score between -1.0 and -2.5 SD
Osteoporosis	T-score \leq -2.5 SD
Severe Osteoporosis	T-score \leq -2.5 SD with 1 or more osteoporotic fractures

testing should include serum calcium, phosphate, creatinine, liver function, blood count, testosterone in males, 25-hydroxy vitamin D, and thyroid-stimulating hormone (TSH), as recommended by the American Association of Clinical Endocrinologists.²⁶ Additional tests may also include, but are not confined to, serum PTH, 24-hour urinary calcium and celiac serology.

Treatment

There is no evidence to suggest that supplementation of calcium and vitamin D should be uniformly recommended in all people who have had major upper GI surgery.²⁷ Nutrient supplementation and medications are still only recommended for those with diagnosed BMD. However, lifestyle recommendations should be encouraged not only for people with diagnosed BMD, but for all people who have had major upper GI surgery, with the aim to prevent or slow the onset of disease. Treatment recommendations are summarized in Table 4.

Dietary Recommendations

Dietary intervention should include counselling to ensure adequate calcium and vitamin D intakes, and supplementing where needed. The current US RDA for calcium and Vitamin D are 1500mg and 600-800IU respectively for the older population.²⁸ Choosing foods naturally high or fortified in calcium and vitamin D should be recommended. People should also be encouraged to enhance calcium uptake at the brush

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border by avoiding iron-rich foods, oxalates and caffeine when consuming calcium rich foods or supplements.

As BMD is strongly linked to low body weight and weight loss, counselling also needs to be tailored to prevent or correct weight loss through a high energy and protein diet, and oral nutrition supplements if required. Meeting a persons' protein requirements appear particularly important in improving lower extremity muscle mass and strength, and reducing the risk of fracture.²⁵

Identifying symptoms of malabsorption as an impediment to weight gain should be a priority. Pancreatic enzyme replacement therapy should be considered in people who have had pancreatic resection, but also in those with other upper GI surgeries where there is a mismatch of foodstuffs and pancreato-biliary secretions, resulting in symptoms of malabsorption.²⁹

Lifestyle Recommendations

Smoking and heavy alcohol consumption are both independent risk factors for the development of BMD.⁸ All people should be encouraged to cease smoking and limit their intake of alcohol to within recommended guidelines. People must be encouraged to spend small amounts of time exposed to sunlight, which is needed for the activation of vitamin D₃. For this patient group, sun exposure may be limited due to weakness secondary to weight and muscle loss, or debilitating symptoms such as steatorrhea. Time of day and year, cloud cover, degree of pollution, skin type, and sunscreen all effect vitamin D synthesis rates. Although people living in high latitudes will not get enough sun exposure in the winter months to meet their vitamin D requirements, geographical latitude does not appear to be a strong contributor to vitamin D deficiency.²⁸ As the liver and fat cells store vitamin D, there is opportunity for people to have adequate sunlight exposure in the spring, summer and fall months to allow vitamin D synthesis for the full year.²⁸ In direct sunlight, it may only take approximately 8-10 minutes of sunlight per day on the face, arms and hands to produce a third of a persons' daily vitamin D requirements. Exercise is well known to promote bone growth and strength, especially high impact weight bearing activity. Most people having had major surgery usually do not return to such intense exercise regimens, so less intense weight bearing exercise such as walking and resistance training should be encouraged. Exercise that is not weight bearing such as swimming and cycling

do not promote bone health. When people have already presented with a fracture, gentle strengthening exercise under the supervision of a physical therapist is advised.

Calcium Supplementation

Calcium supplementation of 1500mg/day is recommended for the elderly and those with existing BMD.³⁰ The most easily accessible and cheapest form of calcium supplementation is calcium carbonate. This specific supplement requires an acidic environment to optimise absorption, and so does not work well in people who are taking Proton Pump Inhibitor's (PPI) or H₂-antagonists, which work to reduce gastric acid secretions, or in those with low acid states as a result of gastric resection or truncal vagotomy. Many people who have had major upper GI surgery require these medications to aid in reducing side effects of reflux.⁴ Other forms of calcium supplementation, such as calcium citrate do not require gastric acidity for absorption, and may be better absorbed and tolerated in this patient group. Calcium citrate should be taken on an empty stomach.

Calcium absorption is inhibited in the presence of caffeine and iron-rich foods or supplements; and absorption peaks at 500mg, therefore doses >500mg are not beneficial.⁴ Total supplementation therefore should be split into morning, midday and evening doses. As oral absorption can be inefficient, careful monitoring of a range of biochemical markers is needed, including 24-hour urinary calcium levels, to ensure therapeutic levels are reached resulting in normocalcemia.³¹

Calcium supplementation in high doses can result in gas, bloating or constipation. Doses meeting RDA do not appear to contribute to the formation of kidney stones in those adequately hydrated.^{32, 33}

Vitamin D Supplementation

Supplementation of vitamin D (usually referred to as Calciferol) should be guided by serum 25-hydroxy vitamin D levels. For people with chronic disease and reduced serum 25-hydroxy vitamin D levels, oral vitamin D₃ supplementation of 800-1000 IU/day is recommended.²⁷

For those individuals with severe vitamin D deficiency (25-hydroxy vitamin D levels below 20nmol/ml or 8ng/ml), higher vitamin D supplementation doses may be needed to treat and then sustain serum levels.

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Medications and Bone Health

Absorption of calcium or vitamin D can be altered or inhibited by many medications and have been discussed in detail elsewhere.^{1, 31, 34} Medications of particular relevance for people who have had major upper GI surgery include antacids and PPI's. Medications that affect vitamin D and/or calcium metabolism include anti-seizure medications.³⁵ (phenobarbital, phenytoin, primidone and valproic acid), glucocorticoids, bile acid sequestrants (cholestyramine otherwise known as questran™ or prevalite™) and anti-tuberculosis medications (rifampin). If it is suspected that medications are impacting on BMD, then consultation with a pharmacist is needed to consider alternate options. In these cases higher doses of calcium or vitamin D may also be required.

Drug Therapy

There is a lack of research assessing the use of drug therapies in managing post-surgical BMD; however, bisphosphonates are often used in clinical practice. Prior to commencing drug therapy vitamin D levels need to be replenished to prevent hypocalcaemia. Bisphosphonate medications should be taken first thing

in the morning with water, and the person should remain upright for 30 minutes afterwards. As they interact with calcium they should be taken separately to any calcium supplementation. Hormone replacement therapy and calcitonin are well researched, but largely outdated treatment options in postmenopausal BMD.²⁷, and have not been trialled in people who have undergone major upper GI surgery. The enormity of the burden of BMD on health costs means that new drug therapies will continue to emerge in upcoming years.

CONCLUSION

It is evident that people who have had major upper GI surgeries have an increased incidence of BMD. The exact reasons for this appear to be multifaceted. In addition, many people who have had major upper GI surgery already have underlying risk factors for BMD, such as cigarette smoking, high alcohol intakes and increased age. Health professionals need to be vigilant in screening for and managing BMD. BMD can be managed through calcium and vitamin D supplementation, lifestyle changes and, where necessary, medications. While there is still a lack of research and consensus in this area, all patients should have baseline screening and ongoing monitoring for BMD. ■

Table 4. Key Recommendations for Managing BMD Following Major Upper GI Surgery

1. Addressing significant weight loss with dietary modification and nutrition support.
2. Assess and treat malabsorption with dietary counselling where needed, and pancreatic enzyme replacement therapy if required.
3. Educate on meeting recommended oral intakes for calcium and vitamin D. Do not mix foods high in iron, oxalates and caffeine with calcium-rich foods.
4. Encourage lifestyle changes:
 - a. Cease smoking
 - b. Limit alcohol to within recommended guidelines
 - c. Weight bearing exercise
 - d. Sunlight exposure
5. Calcium and vitamin D supplementation in consultation with medical advice.
6. Drug therapies where medically recommended.
7. Ongoing regular monitoring, including DXA every 2 years.

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