Fracture Risk Following Bariatric Surgery: A Growing Problem in a Shrinking Patient

Matt Biller
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Abstract

Background Obesity is reaching epidemic proportions in the US. In response, many are turning to gastric bypass surgeries to correct their weight and to decrease risk for cardiovascular disease. The most common procedure for surgical correction of obesity is the Roux-en-Y gastric bypass (RYGB). Like many other gastric bypass procedures, RYGB alters the absorption of essential vitamins and minerals in the gut. Multiple studies explored various causes of osteopenia, osteoporosis and fractures in post-operative gastric bypass patients. Is an operation used to reduce cardiovascular disease and diabetes, increasing the patient’s risk for developing fractures?

Methods An extensive literature search of CINAHL, EBM Reviews, and MEDLINE, using search terms: bariatric surgery, bypass surgery, bone mineral density, fracture risk and fractures. Relevant articles were assessed for quality using the GRADE criteria.

Results Three studies met inclusion criteria for this systematic review. One retrospective survey examined 167 patients, all of whom underwent the RYGB surgery, and were followed for 12-60 months post-operatively. Five percent of patients reported suffering a fracture and 7.2% were diagnosed with osteoporosis. A cross-sectional study consisted of 36 patients who had gastric bypass surgery between 1971 and 1992 in a single surgical center. Of the five subgroups, men and post-menopausal women not being treated with hormone replacement therapy, had significantly decreased bone mineral density and clinical osteopenia and osteoporosis. A prospective study of 59 women, who all underwent the RYGB procedure, found that at 3 years post-operatively, the bone mineral density showed a total decrease of 12.9±5.9% at the femoral neck and a 6.3±4.2% loss in the lumbar spine. This study mentioned estrogen as a major factor influencing bone mineral density post-operatively.

Conclusion Gastric bypass surgery decreases bone mineral density. Dramatic weight losses, estrogen, nutrient deficiency, as well as others, have been suggested to influence fracture risk. The harm of increasing risk of fracture in gastric bypass patients, does not outweigh the benefits of reducing their risk for cardiovascular disease and of developing diabetes. As the link is still unclear, further research should be completed focusing on the link between gastric bypass surgery and the risk for fractures.

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Fracture Risk Following Bariatric Surgery: A Growing Problem in a Shrinking Patient
Biography

[Redacted for privacy]
Abstract

Background

Obesity is reaching epidemic proportions in the US. In response, many are turning to gastric bypass surgeries to correct their weight and to decrease risk for cardiovascular disease. The most common procedure for surgical correction of obesity is the Roux-en-Y gastric bypass (RYGB). Like many other gastric bypass procedures, RYGB alters the absorption of essential vitamins and minerals in the gut. Multiple studies explored various causes of osteopenia, osteoporosis and fractures in post-operative gastric bypass patients. Is an operation used to reduce cardiovascular disease and diabetes, increasing the patient’s risk for developing fractures?

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An extensive literature search of CINAHL, EBM Reviews, and MEDLINE, using search terms: bariatric surgery, bypass surgery, bone mineral density, fracture risk and fractures. Relevant articles were assessed for quality using the GRADE criteria.

Results

Three studies met inclusion criteria for this systematic review. One retrospective survey examined 167 patients, all of whom underwent the RYGB surgery, and were followed for 12-60 months post-operatively. Five percent of patients reported suffering a fracture and 7.2% were diagnosed with osteoporosis. A cross-sectional study consisted of 36 patients who had gastric bypass surgery between 1971 and 1992 in a single surgical
center. Of the five subgroups, men and post-menopausal women not being treated with hormone replacement therapy, had significantly decreased bone mineral density and clinical osteopenia and osteoporosis. A prospective study of 59 women, who all underwent the RYGB procedure, found that at 3 years post-operatively, the bone mineral density showed a total decrease of 12.9±5.9% at the femoral neck and a 6.3±4.2% loss in the lumbar spine. This study mentioned estrogen as a major factor influencing bone mineral density post-operatively.

Conclusion

Gastric bypass surgery decreases bone mineral density. Dramatic weight losses, estrogen, nutrient deficiency, as well as others, have been suggested to influence fracture risk. The harm of increasing risk of fracture in gastric bypass patients, does not outweigh the benefits of reducing their risk for cardiovascular disease and of developing diabetes. As the link is still unclear, further research should be completed focusing on the link between gastric bypass surgery and the risk for fractures.

Keywords:

bariatric surgery, bypass surgery, bone mineral density, fracture risk, fractures
Acknowledgements

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List of Abbreviations

RYGB............................................................................................................Roux-en-Y Gastric Bypass
BMD............................................................................................................Bone Mineral Density
PTH.............................................................................................................Parathyroid Hormone
BMI.............................................................................................................Body Mass Index
HRT.............................................................................................................Hormone Replacement Therapy
FN.............................................................................................................Femoral Neck
LS.............................................................................................................Lumbar Spine
IGF-I...........................................................................................................Insulin-like-growth-Factor I
Fracture Risk Following Bariatric Surgery: A Growing Problem in a Shrinking Patient

BACKGROUND

As of 2009, 37.5% of adult Americans were obese, and that number is expected to continue to rise.¹ A growing trend with this population is surgical intervention to correct weight. In a period of 6 years, from 1998-2004, the prevalence of gastric bypass surgeries increased by nearly 950%.² There are numerous options in weight reduction surgery, including the Roux-en-Y gastric bypass (RYGB), gastric banding (GB), vertical banded gastroplasty (VGB) and biliopancreatic diversion.² At nearly two-thirds of all gastric bypass surgeries, RYGB is the most common procedure for morbid obesity.² The RYGB procedure bypasses the duodenum, which is the main absorptive area for the essential vitamins and minerals needed for skeletal strength. This procedure is termed as both restrictive and malabsorptive.

While these patients are reducing their risk for type II diabetes, for hyperlipidemia and for cardiovascular diseases, they may be increasing their risk for fractures after gastric bypass procedures. There are many theories regarding the relationship between gastric bypass surgery and decreased bone mineral density (BMD). One theory is that there is a lack of essential vitamins and minerals due to malabsorption in the gut. Decreasing the absorption of calcium, vitamin D and iron causes an increase of parathyroid hormone (PTH), which increases osteoclast activity and leads to resorption of calcium from the bones. Anemia from iron depletion poses the threat of dizziness, fatigue, somnolence, cardiac irregularities, cognitive impairment
and syncope.² Post-operative patients have a combination of weak bones and a risk of falling or of loss balance, which predisposes them to a fracture.

Also, a large decrease in weight can lead to major modifications in the patients’ skeletal system.² Patients are considered overweight when their BMI is between 25.0-29.9, and obese when their BMI is greater than 30.0.³ In one retrospective study, patients dropped from an average pre-operative BMI of 43.9 kg/m² to 29.1 kg/m². Drastically decreased weights, like those described in these studies, cause a major change in osteoclast activity, which leads to increased bone turn over and alteration in skeletal architecture.⁴ With increased bone resorption and decreased absorption of vitamins and minerals, the patients’ skeletal system is prone to becoming weak.

An alternate hypothesis is a possible connection in sex steroid hormones and their relationship with osteoclast and osteoblast activity.⁵ Bano et al⁵ describe a study of 5 subgroups that are divided due to their relative estrogen levels, and examine their BMD focusing specifically on the lumbar spine and femoral neck.

Regardless of the cause, the current concern is development of osteomalacia, osteoporosis, or even fractures. Osteoporosis is defined as 2.5 standard deviations or more below the average peak bone mass. Both osteomalacia and osteoporosis quickly lead to fractures. When combined with comorbidities and pharmaceutical influence, these conditions propose a substantial risk for fractures in gastric bypass patients.
METHODS

An extensive literature search was conducted using CINAHL, EBM Reviews, and MEDLINE, and search terms; bariatric surgery, bypass surgery, bone mineral density, fracture risk and fractures. Eligibility criteria included studies with these qualities, English language, a length of follow up of at least 1 year, adult patients, mention of osteoporosis, fracture, or BMD in post-operative care. Each article was assessed using the GRADE evaluation criteria for validity.6

RESULTS

The search resulted in 15 articles, of which 12 studies were excluded, resulting in 3 articles. All three studies were retrospective observational studies.2,4,5 Finally, the National Institute of Health (NIH), clinical trials site, reported one trial7 regarding the effects of gastric bypass surgery on calcium and the skeleton. The study was currently in a participant recruiting phase. The study included a primary outcome of intestinal calcium absorption up to 6 months post-operatively, and secondary outcomes of bone mineral density and bone structure between 6 and 12 months post-operatively.

Berarducci et al

A retrospective survey2 was conducted to examine the need for further research to evaluate the effects of bariatric surgery on bone metabolism. Patients who underwent the RYGB surgery at a university-based bariatric surgical center in Florida, who were 12-60 months post-operative, were invited to participate in the study. Of the
444 eligible patients, 167 agreed to participate. There was no further description of inclusion or exclusion criteria for participants in the study, nor further description of the participants given. The survey was generated by a principal investigator and a panel of five expert consultants in the field of bariatric surgery. Patients participated in telephone interviews with a scripted survey, which was conducted by the principal investigator. The survey questions focused on each patient’s risk for falls and fractures. The study did not attempt to contact any medical providers or obtain medical files on any of the participants, so all data was provided by the patients.²

According to the answers provided by the patients, 8 (5%) participants reported having a fracture. Types of fractures included wrists, arms, ankles, thumbs and toes. Besides the fracture information, the study also examined the risk for fractures, which included data on actually falling and fall risk. Nearly 14% of patients reported falling once after surgery, and just over 20% said they had fallen at least twice. Researchers noted, while falling does not represent actual fracture, falls in general pose a great risk to the patients for fractures, and falls occurring in over a third of the patient population is major issue. Osteoporosis was diagnosed in 7.2% of the patients post-operatively. While it was not a goal of their study, the authors report that menopausal women are at increased risk for developing osteoporosis and fractures prior to bariatric surgery, and these patients needed to be closely monitored post-operatively. Patients reported not receiving follow-up BMD scans post-operatively, which could have provided useful information for providers to examine development of osteomalacia and osteoporosis.
Even when providers recommend prophylaxis, only 77% and 15% of patients take their calcium and vitamin D supplements, respectively.²

**Bano et al**

This cross-sectional study⁵ consisted of patients who had gastric bypass surgery for morbid obesity between 1971 and 1992 in St. George Hospital. Patients were invited by letter to participate in a study examining risk factors of decreasing bone mineral density (BMD). Forty patients agreed to participate and 36 patients completed the entire study. Patients were divided into 5 subgroups (premenopausal women, postmenopausal women without hormone replacement therapy (HRT), postmenopausal women with HRT, men and post-menopausal women who had reversed gastric bypass). Patients who had their bypass reversed, did so because of significant complications and medical problems associated with the initial bypass. The study used multiple pieces of data to analyze the BMD of the patients in the study. Each patient was given a questionnaire that analyzed his or her risk factors for a fracture postoperatively. Researchers collected plasma from each of the participants for analysis of calcium, phosphate, alkaline phosphatase, albumin, bilirubin and alanine transaminases. They examined bone mineral density at the lumbar spine and the femoral neck using a DEXA scan. Using the information provided by patients, as well as the diagnostic data, the researchers calculated an absolute BMD and fracture risk for each patient.⁵

Of the 5 subgroups, only men and post-menopausal women without HRT had absolute BMD scores that were significantly low. Men had significantly lower BMD at
both the lumbar spine (LS) and femoral neck (FN) than their female counterparts. Male BMD: [LS-BMD - .99 g/cm² = -2.08 T score and FN-BMD .89 g/cm² = -1.48 T score]. Post-menopausal women had significantly lower BMD at the lumbar spine (LS): [LS – BMD 1.053 g/cm² = -1.21 T score]. Both men and post-menopausal women without HRT, had Z scores that were negative, which is diagnostic for osteopenia and osteoporosis. On average, patients who had their bypasses reversed, had them for 7 years prior to reversal, and had normal BMD levels. 

Vilarassa et al

This prospective study examined the main determinants of the development of bone disease post-operatively. Multiple variables were examined for each patient. The study used a DEXA scan for their bone mineral density (BMD) at their lumbar spine (LS) and femoral neck (FN), serum concentrations of calcium, parathyroid hormone and 25-hydroxyvitamin D and insulin-like growth factor-I (IGF-I) were made prior to surgery, at 12 months and 3 years post-operatively. The study’s primary exclusion criteria was an acute major cardiovascular event in the previous 6 months, recent or ongoing infection, history of cancer disease, or treatment with anti-inflammatory drugs, women with known osteoporosis, taking hormone replacement therapy (HRT), or who had any disease processes known to influence calcium or bone metabolism. Sixty-two morbidly obese, white women were initially included in the study, and all had the RYGB procedure. At three years, three women were unable to be contacted and were no longer included in the data. A total of 59 women were followed post-operatively for
three years. Each patient was prescribed a daily dose of 800 UI of vitamin D and 1200 mg of calcium. The study used the WHO classifications to determine obesity after calculating the BMI of each patient.\textsuperscript{4}

Initial findings 1 year after bariatric surgery showed significant decrease in BMI, from an average of 43.9 kg/m\textsuperscript{2} down to 29.1 kg/m\textsuperscript{2}. At three years post-operatively, the average BMI had increased to 30.7 kg/m\textsuperscript{2}, which was supposed to be mainly due to fat mass. Values for serum PTH, IGF-I, and 25-hydroxyvitamin D were nearly the same when comparing the preoperative values to 12 months post-operative values. Though, at 3 years, there was a major shift in all three variables. PTH increased dramatically from 5.4±2.6 to 8.05±3.8. IGF-I decreased from 20.1±15 to 12.8±4.7 and 25-hydroxyvitamin D decreased from 58.6±19.6 to 37.9±14.1. These values signify a deficiency in essential vitamins and minerals.

At 12 months post-operative, the BMD showed a decrease of 10.2±5.7% at the femoral neck and a decrease of 3.2±4.4% in the lumbar spine (LS). At 3 years, the BMD showed a total decrease of 12.9±5.9% FN and a 6.3±4.2% total loss in the LS. The study went into further analysis and compared BMD loss between premenopausal and post-menopausal women. When comparing premenopausal and post-menopausal women, researchers found no differences in BMI, weight loss, fat mass, calcium, PTH, 25-hydroxyvitamin D, or IGF-I values. Nevertheless, the BMD of post-menopausal women was significantly lower in both the femoral neck and lumbar spine at 3 years post-
operatively. While the data showed evidence of decreased BMD and metabolic changes, there were no documented fractures in this study.\(^4\)

Limitations mentioned by the authors include exploring the relationship between sex steroid levels and changes in BMD, the number of post-menopausal patients was small, direct markers of bone turnover and the limit of time to only three years. They explain that their data emphasizes that the RYGB procedure is not harmful for bone health, but that menopausal women are at a higher risk for developing osteomalacia and further progression to osteoporosis.\(^4\)

**DISCUSSION**

It is apparent that skeletal changes occur in patients receiving gastric bypass surgery. The studies in this systematic review, describe, decreasing bone mineral density, elevated levels of PTH and the occurrence of fractures. What these studies are unable to describe, is a direct correlation between gastric bypass and increasing fracture risk. Once that connection is clear, providers will be able to focus and provide proper prophylaxis to their patients. Each study was examined using the GRADE guidelines.\(^6\) The studies began at low because they were observational studies. Each study was further downgraded for having small sample sizes, no control groups and recall bias. Over all, the quality of evidence is very low (see table 1).
Berarducci et al

The authors list the most notable limitation of this study as being patient reporting all vital information: medical conditions, medication use, weight measurement and height. With self-reporting, patients may give false information to present them in a better way, or they may forget some information. The fact that patients all came from the same surgical center could be both detrimental and beneficial. It could be detrimental, because it is drawing from a specific area and population, which may not represent all patients requiring bariatric bypass. A benefit of only one surgical center involved in a study is a uniform pre-operative and post-operative patient management plan. The authors of this study recommend further research on this issue to get a more precise cause of decrease in BMD, as well as, to generate guidelines for management of these patients in the future.

Bano et al

There is no data showing direct correlation between surgery and fractures. The researchers provided evidence of a protective quality of estrogen on the bones for post-operative management. Women who were premenopausal or were post-menopausal and being treated with HRT had high post-operative T-scores. Post-menopausal women who had their bypass reversed had the highest scores of all participants. While all patients were being instructed on the importance of calcium supplements and vitamin D supplements, it appears that estrogen therapy is imperative for preventing fractures after bariatric surgeries.
The authors suggest that their data demonstrates a sex-steroid regulation of BMD. They hypothesize that osteoclast and osteoblast activity may be related to serum estrogen levels. It is also proposed that the decreased BMD could be a result of a small bowel pathology created after the bypass, for example dumping syndrome or chronic diarrhea. While the authors of this study do not address the limitations of this data, it is fairly old information. Bariatric surgery has progressed substantially from the 1970’s when this data was first being collected. Advancements in tools, techniques and overall patient management potentially place patients in a better position in regards to BMD and skeletal health. Also, the subgroups were very small and it would be difficult to extrapolate their information to represent a greater population. This study suggests that further investigations be performed to determine a direct link between gastric bypass and decreasing BMD.5

**Vilarassa et al**

There was no blinding involved in this study, as each patient voluntarily participated in surgery. In addition, evaluations of BMD and blood samples were completed by their physicians. All patients had the same gastric surgery [RYGB] performed. Perhaps alternate procedures could lead to alternate BMD changes post-operatively. A lack of diversity in the patients does not allow for extrapolation of data into other patient cohorts.

The significant drop in BMI after the first 12 months would coincide with major bone remodeling leading to decreased trabecular bone. With the minimal increase in BMI
from months 12-36, the bones potentially increased in strength and trabecular mass, therefore decreasing their risk for fracture. In total, the loss of BMI would have a physiologic influence on bone mass and would lead to an overall increase in fracture risk. An increase in plasma PTH represents a calcium deficiency in the consumption or absorption of calcium, causing the body to attempt to collect calcium from the bones. It is suggested by Vilarrasa et al\textsuperscript{4} that weight loss is much less determinant of BMD than are serum levels of estrogen.

The study was greatly limited by a very small patient population. While this study did well with follow up, the patients could have been followed for a longer period of time. A lengthier study would provide more time for osteoporosis to develop and more evidence to either support or refute the fracture claims.

\textbf{CONCLUSION}

Patients who undergo gastric bypass surgery have significant changes to their bone biochemistry. Each study suggested possible causes for decreases in BMD, though none was suggested as the sole cause. The possible causes of decreased BMD include significant decrease in weight, change in gut absorption of calcium and vitamin D, age, polypharmacy and influence of estrogen. Of the three studies, only Berarducci et al\textsuperscript{2} measured an actual fracture rate (5\% of the participants). No direct correlation between gastric bypass surgery and fractures was clearly indicated. Evidence provided in these studies supports the potential development of osteopenia and osteoporosis after
surgery, but does not support the development of fractures. Determining the cause of the decrease in bone mineral density will allow providers to find a resolution and practice fracture prophylaxis in post-operative gastric bypass patients. Further studies should be conducted following patients for longer time periods post-operatively and examining the development of fractures.
References


3. Available at: http://en.wikipedia.org/wiki/obesity


6. Available at: http://gradeworkinggroup.org/.

7. Available at: http://www.clinicaltrials.gov/ct2/show/NCT01330914?term=gastric+bypass+and+fractures&rank=1
### Quality Assessment

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### Summary of Findings

**Lumbar Spine T-Score (Standard deviation from normal BMD)**

- Bano et al<sup>1</sup> 13/36 38.11% NNT Very low Important
- Vilarassa et al<sup>2</sup> 13/59 22.09% NNT

**Femoral Neck T-score (standard deviation from normal BMD)**

- Bano et al<sup>1</sup> 5/36 13.88% NNT Very low Important
- Vilarassa et al<sup>2</sup> 0 NNT

**Fracture**

- Berarducci et al<sup>2</sup> 8/167 5% NNT Very Low Critical

### TABLE 1

Characteristics of Gastric Bypass surgery and risk for developing Fractures, GRADE profile

Abbreviations: GRADE: Grading of Recommendations, Assessments, Development and Evaluation.

A – Both studies were not RCT, small sample sizes, no control groups were used.

B – High risk for recall bias based on data gathered via survey of patients.