VITAMIN D STATUS OF MORBIDLY OBESE BARIATRIC SURGERY PATIENTS
AT A COMMUNITY BARIATRIC CENTER

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ABSTRACT

THESIS: Vitamin D Status of Morbidly Obese Bariatric Surgery Patients at a Community Bariatric Center

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The purpose of this ex-post facto study was to examine the link between serum 25-hydroxyvitamin D, BMI, and percent of excess weight loss after laparoscopic bariatric surgery among morbidly obese men and women at a Midwest bariatric center. Having a normal serum level of 25-hydroxyvitamin D is important for maintaining bone health and preventing osteomalacia in adults. Shown from past research morbid obese patients are often deficient in 25-hydroxyvitamin D. Deficiency in serum 25-hydroxyvitamin D has been documented in 50-80 % of patients after Roux-en-Y gastric bypass, suggesting that 25-hydroxyvitamin D deficiency after bariatric surgery is multifactorial and, in part, is caused by preoperative 25-hydroxyvitamin D deficiency rather than postoperative malabsorption alone. Pearson’s Correlation test, independent samples t-tests, paired-samples t-test and a linear regression was performed to determine what degree BMI, calcium, 25-hydroxyvitamin D and PTH (six and twelve months post-surgery) are affected before surgery, and six and twelve months post-surgery. Statistical significance was set at $p \leq 0.05$. Pre-surgery 25-hydroxyvitamin D mean value was 20.50 ng/mL.
indicating on average that patients involved in this study were deficient prior to surgery. The results of this study show that the patient’s 25-hydroxyvitamin D level did significantly improve when BMI and total body fat decreased post-surgery with the help of the prescribed vitamin D₃ supplementation.
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CHAPTER 1

INTRODUCTION

Bariatric surgery is the most effective therapy offered for the morbidly obese often resulting in substantial and sustained weight loss, significant reduction in co-morbid conditions, and prolonged longevity (Adams et al., 2007; Buchwald et al., 2004; Sjöström et al., 2007). However, bariatric surgical procedures may induce malabsorption and frequently result in nutritional deficiencies (Fujioka, 2005). The low preoperative vitamin concentration and the malabsorption that often follows bariatric surgery may cause these patients to be prone to severe vitamin deficiencies (Aasheim, Hofsø, Hjelmesaeth, Birkeland, & Bøhmer, 2008).

Bariatric surgery decreases calorie ingestion by modifying the anatomy of the gastrointestinal tract. There are two types of operations; they are classified as either restrictive or malabsorptive. Restrictive procedures reduce intake by creating a small gastric reservoir with a narrow outlet to slow down emptying. Malabsorptive procedures bypass varying portions of the small intestine where nutrient absorption occurs (DeMaria, 2007). Adjustable gastric banding includes the insertion of a subcutaneous reservoir so that the gastric resection can be adjusted by means of saline injections. The adjustable gastric band works mainly by decreasing food intake. The balloon can be inflated or deflated depending on the needs of the patient (National Institute of Diabetes and Digestive and Kidney Diseases, 2011). In 2009, the adjustable gastric band was
the most popular treatment of choice for morbid obesity due to the band being less invasive and reversible (Stroh, Hohmann, Schramm, Meyer, & Manger, 2011). Roux-en-Y gastric bypass is regularly referred to as a combination of restriction-malabsorption procedure. The procedure involves stapling of the stomach to create a small (≤ 30.0 ml) upper gastric pouch. The small intestine is then separated at the midjejunum, and the distal portion (called the alimentary, or Roux, limb) is anastomosed to the gastric pouch. The distal portion of the stomach and proximal small intestine are anastomosed together farther down the jejunum (DeMaria, 2007).

According to the National Heart Lung and Blood Institute (National Heart Lung and Blood Institute, 2000), obesity is a complex, multifactorial disease that develops from the interaction between a person’s genotype and the environment. Obesity involves the integration of social, behavioral, cultural, physiological, metabolic, and genetic factors. Obesity substantially increases the risk of morbidity from hypertension, dyslipidemia, type 2 diabetes, coronary artery disease, stroke, gallbladder disease, osteoarthritis, sleep apnea and respiratory problems, as well as cancers of the endometrium, breast, prostate, and colon. Higher body weights are also associated with an increase in mortality from all causes.

Deficiency of 25-hydroxyvitamin D precipitates and exacerbates osteopenia, osteoporosis, and fractures in adults (Holick, 2007). Deficiency of 25-hydroxyvitamin D has been connected with increased risk of common cancers, autoimmune diseases and hypertension (Garland et al., 2006; Mitri, Muraru, & Pittas, 2011; Munger, Levin, Hollis, Howard, & Ascherio, 2006; Piiz, Tomaschitz, Ritz, & Pieber, 2009). A circulating level of 25-hydroxyvitamin D (25(OH)D) of >75 nmol/L, or 30 ng/mL, is essential to maximize vitamin D’s beneficial effects for health (Holick & Chen, 2008). In 1997, a U.S. expert group considered a 25-hydroxyvitamin D concentration of 27.5 nmol/L as an indicator of sufficient 25-
hydroxyvitamin D status from birth through 18 years, and a concentration of >30 nmol/L for adults aged 19–50 years. The group based these values on their relationship with linear growth and bone mass in infants, the lack of signs and symptoms of 25-hydroxyvitamin D deficiency in children, and the relation of 25-hydroxyvitamin D with parathyroid hormone concentrations and calcium balance in adults age 19-50 years (Institute of Medicine, 2013).

Deficiency of 25-hydroxyvitamin D is frequently assessed in obese patients at the time of bariatric surgery, the combination of insufficiency and deficiency (25-hydroxyvitamin D <75 nmol/l) was present in 90% of 41 morbidly obese patients (Goldner et al., 2008). Deficiency of 25-hydroxyvitamin D has also been documented in 50-80% of patients after Roux-en-Y gastric bypass and other malabsorptive procedures (Johnson et al., 2006). These outcomes suggest that deficiency of 25-hydroxyvitamin D after bariatric surgery is multifactorial and, in part, is initiated by preoperative 25-hydroxyvitamin D deficiency rather than postoperative malabsorption alone (Goldner et al., 2008).

**Problem**

In the United States, the prevalence of obesity was 35.7% among adult men and women in 2009-2010. Almost 41 million women and more than 37 million men 20 years and over were obese in 2009-2010 (Ogden, Carroll, Kit, & Flegal, 2012). The most common vitamin deficiency associated with obesity seems to be low concentrations of 25-hydroxyvitamin D (Carlin et.al, 2006; Hyppönen & Power, 2006), which has been associated with an increased risk of diabetes, cardiovascular disease and depression (Kalueff & Tuohimaa, 2007; Martins et al., 2007; Mitri et al., 2011). Since morbidly obese men and women are more prone to 25-hydroxyvitamin D deficiency it is necessary to measure 25-hydroxyvitamin D before and after
bariatric surgery to see the effects the weight loss and prescribed supplementation has on 25-hydroxyvitamin D values. This study investigated 25-hydroxyvitamin D status before bariatric surgery and compared the values to the percent of excess weight loss and BMI at six and twelve months post-surgery. Documenting low serum 25-hydroxyvitamin D values in morbidly obese individuals and determining whether gastric weight loss surgery along with vitamin D₃ supplementation helps normalize serum 25-hydroxyvitamin D values will help practitioners in their treatment of morbidly obese subjects.

**Purpose**

The purpose of this ex-post facto study was to examine the relationship between serum 25-hydroxyvitamin D, BMI, and percent of excess weight loss after laparoscopic gastric weight loss surgery among morbidly obese men and women at a Midwest bariatric center.

**Research Questions**

The following research questions were examined in this study:

RQ#1. What correlation exists between 25-hydroxyvitamin D and BMI before surgery?

RQ#2. Will there be a difference in 25-hydroxyvitamin D level prior to surgery, between six months and twelve months after surgery based on (1) gender (2) race/ethnicity (3) type of surgery?

RQ#3. Will 25-hydroxyvitamin D level increase as body weight percent decreases among men and women who have had bariatric surgery at six months and twelve months?

RQ#4. What correlation exists between 25-hydroxyvitamin D and percent excess weight loss after surgery?
RQ#5. What correlation exists between 25-hydroxyvitamin D status and calcium and PTH six and twelve months after surgery?

**Rationale**

Results of this study were to help define the preoperative and postoperative 25-hydroxyvitamin D status of patients undergoing bariatric surgery. It also highlighted the correlation between a patient’s 25-hydroxyvitamin D level, Vitamin D₃ (cholecalciferol) supplementation intake, BMI and percent of excess weight loss. This study helped to determine if weight loss and the correct amount of supplementation will regulate 25-hydroxyvitamin D in a normal range, >30ng/mL. Keeping 25-hydroxyvitamin D in a normal range will then help to avoid the negative effects of low 25-hydroxyvitamin D.

**Assumptions**

The following assumptions in the implementation of the study and in the interpretation of the data were made:

1. Patients took their vitamin D₃ supplement daily prescribed by the MD, as recorded in their medical chart.
2. Supplements contained the nutrients listed on the label.
3. Patients took their multivitamin and 1500 mg of calcium supplementation as prescribed after surgery.
4. Information entered in the medical chart was accurate.
5. Patient lost weight after laparoscopic bariatric surgery.
Definitions

For the purpose of this study, the following definitions will be used:

1. **Overweight/Obesity/Morbid Obesity.** According to the Center for Disease Control and Prevention, commonly known as the CDC, (Center for Disease Control and Prevention, 2012) overweight, obesity and morbid obesity are labels for ranges of weight that are more than what is commonly measured as healthy for a given height. The terms also classify ranges of weight that have been shown to increase the possibility of certain diseases and other health problems.

2. **Vitamin D.** According to the Institute of Medicine (Institute of Medicine, 2010), vitamin D plays an important role along with calcium, in bone health. Vitamin D functions as a hormone and its key biologic function is to sustain serum calcium and phosphorus concentrations within normal range by enhancing the effectiveness of the small intestine to absorb these minerals from the diet.

3. **Roux-en-Y Gastric Bypass Surgery.** This surgery is the most common bariatric surgery in the United States. This procedure decreases how food is absorbed. Food intake is limited by the small stomach pouch that is created. Food is directly sent from the stomach pouch to the small intestine. This affects how the digestive tract absorbs food. The “old” stomach, duodenum and upper intestine no longer have contact with food (National Institute of Diabetes and Digestive and Kidney Diseases, 2011).

4. **Gastric Banding Surgery.** This surgery is the most common food restrictive procedure. The gastric band works by decreasing food intake. Food intake is limited by placing a small bracelet-like band around the top of the stomach to limit the size of the opening from the throat to the stomach. The surgeon can then control the size of the band
with a circular balloon inside the band. The balloon can be inflated or deflated depending on the patient’s needs (National Institute of Diabetes and Digestive and Kidney Diseases, 2011).

5. **Body Mass Index (BMI).** According to the CDC (Center for Disease Control and Prevention, 2011), body mass index is a number calculated from a person’s weight and height. BMI is a dependable marker of body adiposity for most people and is used to monitor weight categories that may lead to health problems.

**Summary**

Vitamin D plays a vital role in the health and wellbeing of morbidly obese adults. Morbidly obese adults are at higher risk of vitamin deficiencies. If these individuals had bariatric surgery, they are at an even higher risk for vitamin deficiencies due to the restrictive and malabsorptive procedures that were performed. Understanding the relationship between BMI and level of 25-hydroxyvitamin D can help practitioners determine at what level vitamin D₃ supplementation is necessary to maintain 25-hydroxyvitamin D in a normal range.
CHAPTER 2

REVIEW OF LITERATURE

The purpose of this ex-post facto study was to examine the link between serum 25-hydroxyvitamin D, body mass index (BMI), and percent of excess weight loss after laparoscopic bariatric surgery among morbidly obese men and women at a Midwest bariatric center. This chapter will present an overview of the literature on vitamin D functions in the human body, deficiency symptoms, causes of 25-hydroxyvitamin D deficiency in morbidly obese people, calcium metabolism, obesity related diseases, surgical treatment for morbid obesity, and the relationship between 25-hydroxyvitamin D deficiency and bariatric surgery.

Vitamin D

Vitamin D (calciferol) is a fat-soluble seco-steroid synthesized in the skin (a hormone) and/or consumed with food (as a vitamin). The two major physiological important forms of vitamin D are D₂ (ergocalciferol) and D₃ (cholecalciferol) (Kalueff & Tuohimaa, 2007). Vitamin D supports calcium absorption in the gut and preserves enough serum calcium and phosphate concentration to support normal mineralization of bone and to inhibit hypocalcemic tetany (Institute of Medicine, 2010). Vitamin D is also required for bone growth and bone remodeling by osteoblasts and osteoclasts. Without adequate vitamin D, bones can turn thin, brittle, or misshapen (Institute of Medicine, 2010). The biological function of vitamin D, exerted through
the active form 1, 25 dihydroxyvitamin D₃ (1, 25(OH)2D), is to maintain physiological appropriate calcium and phosphate levels in the blood. Serum 25-hydroxyvitamin D sufficiency prevents rickets in children and osteomalacia in adults. Together with calcium, vitamin D also helps protect older adults from osteoporosis (Institute of Medicine, 2010).

Vitamin D has other roles in the body, including modulation of cell growth, neuromuscular and immune function, and reduction of inflammation (Dhesi et al., 2004; Icardi et al., 2013; O’Brien & Jackson, 2012). Many genes encoding proteins that control cell proliferation, differentiation, and apoptosis are modulated, in part, by vitamin D. Serum concentration of 25-hydroxyvitamin D is the best gauge for vitamin D status. It reflects vitamin D formed cutaneously and what is gained from food and supplements (Institute of Medicine, 2010). Serum 25-hydroxyvitamin D has a fairly long circulating half-life of 15 days (Jones, 2008).

Vitamin D₃ (cholecalciferol) is made in the skin by photolysis of 7-dehydrocholesterol by ultraviolet radiation from sunlight. Cholecalciferol is transported in blood circulation bound to vitamin D binding protein and is hydroxylated in the liver to 25-hydroxyvitamin D (25(OH)D). Another hydroxylation reaction takes place in the kidney to produce the active hormone 1,25(OH)2D. This response is tightly controlled by induction of the CYP27B1 enzyme which is stimulated by the parathyroid hormone and inhibited by hyperphosphataemia (higher than normal blood level of phosphate) and 1,25(OH)2D (Omdahl, Morris, & May, 2002). Ergocalciferol (vitamin D₂) is created commercially by ultraviolet irradiation of a provitamin D sterol (ergosterol) that takes place in plants (Horst, Reinhardt, Russell, & Napoli, 1984). Vitamin D₂ differs from vitamin D₃ in having an extra methyl group at C24 and a double bond at
C22-23. It undergoes the same hydroxylation responses as cholecalciferol to produce 25OHD$_2$ and 1,25(OH)$_2$D$_2$ (Wootton, 2005).

A 25-hydroxyvitamin D deficiency can arise when an individual’s usual ingestion is lower than the suggested level over time, when their exposure to sunlight is limited, when the kidneys cannot convert 25-hydroxyvitamin D into its active form, or when the absorption of vitamin D from the digestive tract is insufficient (Institute of Medicine, 2010).

In adults, 25-hydroxyvitamin D deficiency can lead to osteomalacia, resulting in weak bones. Signs of bone pain and muscle weakness can indicate insufficient 25-hydroxyvitamin D values, but such symptoms can be subtle and go unnoticed in the preliminary stages (Institute of Medicine, 2010; Jones, 2008; Ryan, Anderson, Turner, & Morris, 2013).

Much debate has taken place over the definition of 25-hydroxyvitamin D deficiency. Most clinicians agree that a 25-hydroxyvitamin D concentration <50 nmol/L, or 20 ng/mL, is indicative of a 25-hydroxyvitamin D deficiency, a 25-hydroxyvitamin D concentration of 51–74 nmol/L, or 21–29 ng/mL, is shown to signify an insufficient intake, and concentrations >30 ng/mL are considered to be sufficient (Dawson-Hughes B. et al., 2005; Holick, 2007; Malabanan, Veronikis, & Holick, 1998; Thomas et al., 1998). These values are based on the observation that intestinal calcium absorption is maximized above 80 nmol/L, or 32 ng/mL, in postmenopausal women and that parathyroid hormone (PTH) concentration in adults continually declines and reaches its lower point at ≈75–100 nmol/L, or 30–40 ng/mL (Thomas et al., 1998).

**Calcium**

Calcium is the fifth most abundant element in the human body (Institute of Medicine, 2010). It plays a vital role in skeletal mineralization, as well as an extensive range of biological...
functions. A person’s calcium requirement is reliant on the state of calcium metabolism, which is controlled by three main mechanisms: intestinal absorption, renal reabsorption, and bone turnover. These in turn are controlled by a set of interacting hormones, including Parathyroid Hormone (PTH), 1,25-dihydroxyvitamin D, ionized calcium, and their corresponding receptors in the gut, kidney, and bone (Peacock, 2010). Calcium plays a key role in a wide range of biological functions, either in the form of its free ion or bound complexes. One of the main purposes as bound calcium is in skeletal mineralization. Most of the total body calcium (>99%) exists in the skeleton as calcium-phosphate complexes, largely as hydroxyapatite, which is responsible for much of the material properties of bone (Wang, 2006). In bone, calcium serves two key purposes: it delivers skeletal strength as well as a dynamic store to sustain the intra- and extracellular calcium pools. Nonbone calcium represents <1% of total body calcium (~10 g in an adult). Nonbone calcium is in constant and rapid exchange within the numerous calcium pools, and regulates a wide range of essential functions, including extra- and intracellular signaling, nerve impulse transmission, and muscle contraction (Bootman et al., 2001).

Calcium balance is the state of the calcium body stores, mostly in bone, which are largely a function of dietary intake, intestinal absorption, renal excretion, and bone remodeling. Calcium homeostasis is the hormonal regulation of serum ionized calcium by PTH, 1,25-dihydroxyvitamin D, and serum ionized calcium itself, together they regulate calcium transport at the gut, kidney, and bone (Peacock, 2010).

**Effects of Vitamin D Deficiency on PTH, Bone Turnover and Bone Density**

An inverse correlation between serum 25-hydroxyvitamin D and serum parathyroid hormone (PTH) is well established. The serum level for 25-hydroxyvitamin D corresponding with the
PTH inflection point has been interpreted as indicative of prime calcium homeostasis, and has been suggested as a marker of 25-hydroxyvitamin D sufficiency (Dawson-Hughes et al., 2005; Holick, 2007; Sai, Walters, Fang, & Gallagher, 2011). This approach to describing the recommended vitamin D intake has been disputed; however, there is substantial variation in the level of 25-hydroxyvitamin D associated with any given serum PTH concentration (e.g., the reported threshold values vary greatly from 8 to 44 ng/dL) (Bates, 2003).

The relative importance of high calcium intake and serum 25-hydroxyvitamin D for calcium homeostasis, as determined by serum intact PTH was investigated (Steingrimsdottir, Gunnarsson, Indridason, Franzson, & Sigurdsson, 2005). The authors divided 2,310 healthy adults of different ages into three equal groups. They were given a food frequency questionnaire, which assessed vitamin D and calcium intake. Participants were then divided into groups according to calcium intake (<800 mg/d, 800-1200 mg/d, and >1200 mg/d) and serum 25-hydroxyvitamin D level (<10 ng/mL, 10-18 ng/mL, and >18 ng/mL). The main analyses were to measure the relationship between serum intact PTH values and both calcium intake and serum 25-hydroxyvitamin D values. A total of 944 healthy participants completed all parts of the study. Serum PTH was lowest in the group with a serum 25-hydroxyvitamin D level ≥18 ng/mL, but highest in the group with a serum 25-hydroxyvitamin D level ≤10 ng/mL. At the low serum 25-hydroxyvitamin D level (<10 ng/mL), calcium intake of less than 800 mg/d versus more than 1200 mg/d was significantly associated with higher serum PTH (p = .04); and, at a calcium intake of more than 1200 mg/d, there was a significant difference between the lowest and highest vitamin D groups (p = .04) (Steingrimsdottir et al., 2005).

This study suggests that 25-hydroxyvitamin D sufficiency may be more important than high calcium intake in maintaining desired values of serum PTH. Vitamin D may have a
calcium sparing effect and as long as 25-hydroxyvitamin D status is ensured, calcium intake levels of more than 800 mg/d may be unnecessary for maintaining calcium metabolism.

Serum 25-hydroxyvitamin D deficiency cause’s secondary hyperparathyroidism, high bone turnover, bone loss, mineralization defects, fractures, myopathy and falls (Dhanwal, Sahoo, Gautam, & Saha, 2013; Snijder, 2006). Serum 25-hydroxyvitamin D deficiency has such significant health consequences that the measurement of serum 25-hydroxyvitamin D was recommended to be part of a routine physical examination for children and adults of all ages (Holick, 2005). The U.S. economic burden caused by 25-hydroxyvitamin D insufficiency from poor exposure to solar UVB irradiance, diet, and supplements was estimated at 40-56 billion USD in 2004 (Grant, 2005).

Poor 25-hydroxyvitamin D status is common in the elderly and is associated with bone loss and fractures (Dhanwal et al., 2013). Vitamin D₃ is synthesized in human skin after the photoisomerization of 7-dehydrocholesterol (7DHC) to previtamin D₃, under the effect of UVB radiation (wavelength, 280–315 nm). The main causes influencing this procedure are either environmental (latitude, season, time of day, ozone and clouds, reflectivity of the surface) or personal (skin type, age, clothing, use of sunscreen) (Webb, 2006). The status of 25-hydroxyvitamin D values in postmenopausal women with osteoporosis in 29 countries across the world according to latitude and economic status, in relation to parathyroid function, bone turnover markers and bone mineral density were measured (Kuchuk, Van Schoor, Pluijm, Chines, & Lips, 2009). The study was performed on 7,441 postmenopausal women from 29 countries participating in a clinical trial on bazedoxifene (selective estrogen receptor modulator), with BMD T-score at the femoral neck or lumbar spine ≤ -2.5, or one to five mild or moderate vertebral fractures. Serum 25-hydroxyvitamin D, PTH, alkaline phosphatase (ALP), bone
turnover markers osteocalcin (OC) and C-terminal cross-linked telopeptides of type I collagen (CTX), and BMD of the lumbar spine, total hip, femoral neck, and trochanter were measured. The average serum 25-hydroxyvitamin D level was 61.2 ± 22.4 nM. The prevalence of 25-hydroxyvitamin D <25, 25–50, 50–75, and >75 nM was 5.9 %, 29.4 %, 43.5 %, and 21.2 %, respectively, in winter and 3.0 %, 22.2 %, 47.2 %, and 27.5 % in summer. Worldwide, a negative relationship between 25-hydroxyvitamin D and latitude was detected. With increasing 25-hydroxyvitamin D categories of <25, 25–50, 50–75, and >75 nM, mean PTH, OC, and CTX were declining (p < 0.001), whereas BMD of all sites was increasing (p < 0.001). A threshold in the positive relationship between 25-hydroxyvitamin D and different BMD parameters was visible at a 25-hydroxyvitamin D level of 50 nM. The authors concluded there is a high prevalence of low 25-hydroxyvitamin D in postmenopausal women with osteoporosis worldwide. These results confirm that hypovitaminosis D is a worldwide problem that needs to be addressed (Kuchuk et al., 2009).

Moderate weight loss has been reported to reduce bone mineral density and ultimately lead to a greater risk of fracture (Ensrud et al., 2003; Hinton et al., 2012). When there is more dramatic weight loss, such as when undergoing Roux-en-Y gastric bypass (RYGB) and other surgical procedures for the treatment of morbid obesity, there is an increased risk of low bone mass and bone mineral density (Bano, Rodin, Pazianas, & Nussey, 1999; J. M. Johnson et al., 2005; Williams, 2011). Forty-four women (23 pre- and 21 postmenopausal) who had undergone RYGB for morbid obesity; at least three years after surgery with a BMI of 34 or above were enrolled in a study wherein the subjects underwent bone density screening using dual energy x-ray absorptiometry (DXA). These RYGB patients were compared with a historical control group of 65 women (23 pre and 42 postmenopausal) of the same body weight and age. Of the 44
women selected, 29 were found to have low bone mass. 21 of the patients with low bone mass agreed to follow six months of dietary supplementation, 8 dropped out within the first 2 months because of personal reasons and 13 completed the next study. These 13 RYGB (7 pre and six postmenopausal) women who presented with low bone mass were supplemented to a total of 1.2 g calcium a day and 8 ug vitamin D₃ a day over six months. The 13 RYGB women were compared with an unsupplemented 13 women from the historical control group who were age and weight matched. Bone mass, turnover, PTH and 25-hydroxyvitamin D were measured. As a result, bone mass did not differ between premenopausal RYGB and the historical control group of women, whereas postmenopausal RYGB women had higher bone mineral density and bone mineral content in the spine and neck. Before and after dietary supplementation, bone mass was similar. RYGB subjects showed considerably higher values of serum PTH at baseline (p < 0.001) and after supplementation (p < 0.001) compared to the 13 women in the historical control group (Goode, Brolin, Chowdhury, & Shapses, 2004).

Weight loss has shown to decrease bone mass (Ensrud et al., 2003). In this study it was determined that bone mass does not differ between premenopausal women with and without RYGB, but is altered in postmenopausal RYGB women (Goode et al., 2004). Also, RYGB women presented with evidence of secondary hyperparathyroidism and elevated bone resorption that cannot be inhibited by elevating their dietary intake of calcium and vitamin D to suggested levels. This study raises the question that greater supplementation of calcium and vitamin D₃ may be necessary to subdue PTH and bone resorption in this RYGB population (Goode et al., 2004).
Morbid Obesity

According to the National Heart, Lung and Blood Institute (National Heart, 2000), morbid obesity is measured as a body mass index (BMI; kg/m$^2$) greater than 40, or greater than 35 with weight related co-morbidity. Morbid obesity impairs quality of life, increases the risk of coronary heart disease and shortens life expectancy (Berrington de Gonzalez et al., 2010; McTigue et al., 2006). The most recent national data on obesity among U.S. adults shows that more than one-third of adults were obese in 2009–2010. Differences in prevalence between men and women diminished between 1999–2000 and 2009–2010, with the prevalence of obesity among men reaching the same level as that among women (Ogden et al., 2012).

In the late 1990s estimates suggested that 1 in 2 adults in the United States was overweight or obese, an increase of more than 25% in the past three decades (Flegal, Carroll, Kuczmarski, & Johnson, 1998). Excess weight is associated with an increased incidence of cardiovascular disease, type 2 diabetes mellitus (DM), hypertension, stroke, dyslipidemia, osteoarthritis, and some cancers (Burton & Foster, 1985).

Conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention, NHANES III was designed to offer nationwide representative data to estimate the prevalence of major diseases, nutritional disorders, and potential risk factors. Data is now collected every two years. Current data will be discussed but historical data is important to discuss first. Data was collected from 1988 to 1994, the complete sample included 33,199 people and 16,884 were at least 25 years of age. Normal reference categories were used for BMI as normal 18.5 to 24.9 kg/m$^2$; overweight 25-29.9, obesity class 1, 30-34.9, obesity class 2, 35-39.9 and obesity class 3, ≥40. The NHANES III sample displayed approximately 63% of men and 55% of women aged 25 years or older in the US population were overweight or obese.
Specifically, 42% of men and 28% of women were overweight, and 21% of men and 27% of women were obese. For both men and women, high blood pressure was the most common overweight and obesity associated health condition and its prevalence presented a strong increase with increasing weight status category. The prevalence of type 2 Diabetes, gallbladder disease, and osteoarthritis increased severely among both overweight and obese men and women associated to the increasing weight classes. Ethnicities were compared in this study as well; an increase in comorbidities was more apparent even for the overweight class in every ethnic group as weight class increased (Must et al., 1999).

NHANES data from 1988-1994 presented that the prevalence of obesity in adults had increased by roughly 8% in the United States since 1976-1980, after being relatively constant over the period from 1960-1980 (Flegal et al., 1998; Kuczmański & Flegal, 1994). Analyses of data from 1999-2000 showed further increases in obesity for both men and women and in all age groups (Flegal, Carroll, Ogden, & Johnson, 2002). The increases in obesity from 1976-1980 to 1988-1994 were statistically significant in all sex and age groups. The increases in obesity from 1988-1994 to 1999-2000 were statistically significant in all sex and age groups except men age 40 to 59. Analyses of data from 2001-2002 and 2003-2004 suggested increasing trends since 1999-2000 among men, but not among women (Hedley et al., 2004; Ogden et al., 2006). Comparisons between 2003-2004 and 2005-2006 showed no significant changes (Flegal, Carroll, Ogden, & Curtain, 2010).

Beginning in 1999, NHANES became a continuous survey (without a break between cycles) and data is released in 2-year cycles. In 2007-2008, data for 2,750 adult men and 2,805 non-pregnant adult women with measured weights and heights from the most recent two years of
the continuous NHANES 2007-2008, in addition to data from NHANES 1999-2006 were looked at. The same BMI categories were used as previous NHANES studies.

Each participant was grouped by age at the interview: 20-39 years, 40-59 years, and 60 years or older. Results determined that the prevalence of obesity in the United States is high, above 30% in most age and sex groups except for men age 20 to 39. Among men, age adjusted obesity prevalence was 32.2% overall and within racial groups extended from 31.9% among non-Hispanic white men and 37.3% among non-Hispanic black men. For women, the age adjusted prevalence was 35.5%, extending from 33.0% among non-Hispanic white women to 49.6% among non-Hispanic black women (Flegal et al., 2010).

For women, the prevalence of obesity showed no statistically significant changes over the 10-year period from 1999 through 2008. For men, there was a significant linear trend over the same period. Estimates for the period 2003-2004, 2005-2006, and 2007-2008 were not significantly different from each other for men. This data suggests that the rise in the prevalence of obesity previously observed between 1976-1980 and 1988-1994 and between 1988-1994 and 1999-2000 may not be continuing at a comparable level over the period 1999-2008, particularly for women and most likely for men. In conclusion, although obesity is still high it does not appear to be continuing at the same rate from 1999-2008 as it did in previous years (Flegal et al., 2010).

In a Women’s Health Initiative Observational Study 90,185 women between the age of 50-79 were recruited from 40 U.S. clinical centers to determine how cardiovascular and mortality risks differ across weight categories in women with a focus on extreme obesity. These women were followed for an average of seven years. BMI based criteria was assigned for women in five different categories: normal (18.5-24.9 kg/m2), overweight (25-29.9), obesity 1
(30-34.9), obesity 2 (35-39.9), and extreme obesity (>40). Mortality rates by race/ethnicity (black vs. non-Hispanic white), age, baseline smoking status, and presence of diabetes or hypertension were examined. To see how much these risk factors contributed to obesity related mortality risk, all-cause mortality in women without smoking, hypertension, or diabetes were examined as well. For each BMI category race/ethnicity-specific cardiac heart disease (CHD) mortality was examined also. At baseline the prevalence of extreme obesity was highest among black (9.6%) and lowest among Asian (0.9%) women. Significant trends for increasing baseline prevalence of hypertension, diabetes, and hyperlipidemia across increasing weight class were found. All-cause mortality increased with increasing weight category and ranged from 68.4% in women with a normal BMI to 116.9% in women with extreme obesity. CHD related mortality at baseline was also highest in women with extreme obesity. Mortality rates were higher among those with CHD risk factors (smoking, diabetes or hypertension) at baseline than those without such risk factors, regardless of race/ethnicity. The interaction models showed that the relationship between BMI and all-cause mortality, CHD mortality, and incidence did not differ by race/ethnicity (P>.05). However, among white women, a significant interaction was found between BMI and age (P<.001), and among black women, a significant interaction was noted between BMI and smoking (P=.03). All obesity classes (but not overweight) were significantly associated with increased all-cause mortality in age adjusted models for white women.

Compared with BMI in the normal range, risk for mortality was 18% higher for obesity 1, 49% higher for obesity 2, and more than doubled for extreme obesity. In this study of varied older women, obesity was linked with substantial health risk. Accounting for degree of excess weight is imperative in understanding weight-related health risk. Overall, extremely obese women were more likely to die in the seven year average follow-up (McTigue et al., 2006).
The escalating prevalence of extreme obesity may exasperate the health effects and health-related expenditures resulting from the U.S. obesity epidemic. Although prevalence of different weight categories differs by race/ethnicity, similar weight-related health risks appear in white and black women. Results from this study show weight-related health risk clearly varies with degree of excess weight and we cannot consider obesity as a homogenous condition but have to look at degree of obesity (McTigue et al., 2006).

Metabolic syndrome is a constellation of hypertension, dyslipidemia, and diabetes risk factors that cluster within individuals. It is generally observed that the probability of having metabolic abnormalities increases with the level of obesity. By comparison with normal weight men, the odds of having metabolic syndrome ranged from 5.2 to 25.2 to 67.7 times across overweight, moderately obese respectively, and severely obese men in the National Health and Nutrition Examination Survey III (NHANES III) (Park et al., 2003).

Between 1979 and 1995 data was collected on 19,173 men ages 20-83 (Katzmarkzyk, Church, Janssen, Ross, & Blair, 2005). The sample of men was controlled to a BMI of ≥ 18.5 with no history of heart disease, stroke, or cancer at the baseline examination. The clinical assessment included a medical history questionnaire, physical examination, electrocardiogram, phlebotomy, anthropometric, blood pressure measurements and a maximal exercise test. Metabolic syndrome was diagnosed by a blood pressure (≥130/80 mmHg), central obesity (waist circumference >102 cm), high triglycerides (≥1.69 mmol/l), low HDL cholesterol (<1.04 mmol/l), and high fasting plasma glucose level (≥6.1 mmol/l). Standard BMI categories were used as normal BMI (18.5-24.9 kg/m²), overweight (25-29.9), or obese (≥30). At baseline 3,745 (19.5%) men were classified as having metabolic syndrome. The prevalence of metabolic syndrome was increasingly higher across normal weight (4.7%), overweight (19.8%), and obese
(61.1%) categories. As expected, men with metabolic syndrome were older in life. Within each BMI category, men with metabolic syndrome had a higher mortality rate than healthy men. Independent of metabolic syndrome status, obese men had higher mortality rates than overweight and normal weight men. The results also determine that there is a higher risk of cardiovascular disease (CVD) mortality attributable to obesity, even without metabolic syndrome (Katzmarkzyk et al., 2005).

These research studies suggest that clinicians are likely to encounter morbidity more frequently among their patients with elevated BMI. Without focused initiatives to prevent and treat obesity in adults, the health care system will progressively be overwhelmed with individuals who need management for obesity-related health conditions (Must et al., 1999).

**Vitamin D Deficiency in the Morbidly Obese**

The most common vitamin deficiency associated with obesity appears to be low concentration of 25-hydroxyvitamin D (Carlin et. al, 2006). Low values of 25-hydroxyvitamin D are found in individuals with larger amounts of belly fat or visceral obesity as vitamin D appears to be absorbed by the fat-tissue and is not easily released in the blood stream (Wortsman, Matsuoka, Chen, Lu, & Holick, 2000). An alternate explanation for the low 25-hydroxyvitamin D observed in morbidly obese individuals is that the increased blood volume tends to dilute the quantity of 25-hydroxyvitamin D when tested (Moyad, 2008).

Another potential explanation for the low values of 25-hydroxyvitamin D observed in morbidly obese individuals is that obese individuals may avoid exposure to solar ultraviolet (UV) radiation, which is indispensable for the cutaneous synthesis of vitamin D₃ (Compston et al., 1981). Alternatively, it has been proposed that the production of the active vitamin D
metabolite 1,25-dihydroxyvitamin D is enhanced in the morbidly obese. It has been hypothesized that the higher concentration leads to a negative feedback control on the hepatic synthesis of 25-hydroxyvitamin D (Bell et al., 1985). It has also been suggested that the metabolic clearance of 25-hydroxyvitamin D may increase in obese individuals, possibly with enhanced uptake by adipose tissue (Earthman, Beckman, Masodkar, & Sibley, 2012).

The impact of obesity on the cutaneous production of vitamin D₃ (cholecalciferol) and the intestinal absorption of vitamin D₂ (ergocalciferol) has been observed (Wortsman et al., 2000). Subjects included 19 healthy white adults of normal body weight (BMI; in kg/m²) ≤ 25) and 19 healthy, obese subjects (BMI > 30). All of the subjects either received whole-body ultraviolet radiation or a pharmacologic dose of 50,000 IU of vitamin D₂ orally. Obese subjects had significantly lower basal 25-hydroxyvitamin D concentrations and higher PTH concentrations than did the age-matched control subjects. The assessment of blood vitamin D₃ concentrations 24 hours after whole-body irradiation indicated that the incremental rise in vitamin D₃ was 57% lower in obese than in nonobese participants. The content of the vitamin D₃ precursor 7-dehydrocholesterol in the skin of obese and nonobese subjects did not compare considerably between groups nor did its conversion to previtamin D₃ after irradiation in vitro. BMI was inversely correlated with serum vitamin D₃ concentrations after irradiation (r = -0.55, P = 0.003) and with peak serum vitamin D₂ concentrations after vitamin D₂ intake (r = -0.56, P = 0.007). Obesity did not change the capacity of the skin to produce vitamin D₃, but may have changed the release of vitamin D₃ from the skin into rotation. Obesity-associated 25-hydroxyvitamin D insufficiency is likely due to the reduced bioavailability of vitamin D₃ from cutaneous and dietary sources because of its deposition in body fat compartments (Wortsman et al., 2000).
Less than 20 ng/ml of 25-hydroxyvitamin D is prevalent in as many as one half of middle-aged to older adults in developed countries (Holick, 2009). Notably, one of the clinical characteristics most constantly related with 25-hydroxyvitamin D deficiency is obesity (Hyppönen & Power, 2006; Liu et al., 2005; Martins et al., 2007; Parikh et al., 2003).

Obese individuals are at risk for a number of metabolic and endocrine abnormalities (Proietto, 2010). Among the endocrine imbalances of obesity is hyperparathyroidism, believed to be secondary to hypovitaminosis D (Yanoff et al., 2006). In 2002 to 2003, 302 healthy adults that were required to be free of significant medical diseases and to be taking no medications on a consistent basis known to influence body weight or calcium homeostasis were studied. The correlation between calcitropic hormones and body adiposity were examined. Serum intact PTH (iPTH), 25-hydroxyvitamin D, and 1,25-hydroxyvitamin D were measured in the post absorptive state in the 302 healthy adults who were Caucasian, African-American, and of other race/ethnicity. Each participant underwent a full history and physical examination, anthropometric measurements and a whole-body DXA for body composition analysis. Of the 302 enrolled subjects, 152 obese subjects were comparable in age, gender, and race/ethnicity related to the 148 nonobese subjects. Mean serum 25-hydroxyvitamin D in the obese group was 23.5 ng/ml, significantly lower (P<0.0001) than that of the nonobese group, 31 ng/ml. Serum iPTH concentrations were significantly higher (P<0.0001) in obese subjects (53.8 ± 19 vs. 43.4 ± 14.3 pg/ml). Serum 1,25-hydroxyvitamin D was significantly lower (P < 0.0001) in obese (44 ± 15.3 pg/ml;114.4 ± 39.8 pmol/liter) compared with nonobese subjects (52 ± 15.3 pg/ml; 135.2 ± 39.8 pmol/liter). Results of this study demonstrate a lower 25-hydroxyvitamin D and 1,25-hydroxyvitamin D and higher iPTH concentrations in obese adults, independent of age, sex, or
race/ethnicity. Showing there is a negative relationship between serum 1,25-hydroxyvitamin D and adiposity (Parikh et al., 2003).

Established factors of vitamin D status, as measured by serum 25-hydroxyvitamin D are exposure to sunlight and intake of vitamin D, either from foods or vitamin supplements (Fraser, 1995; Holick, 2007; Lips, 2006). Decreased physical activity, obesity and low social status have also been related to low 25-hydroxyvitamin D values in Europe and the USA (Hintzpeter, Mensink, Thierfelder, Müller, & Scheidt-Nave, 2008; Hirani, Mosdøl, & Mishra, 2009).

A study was performed to identify predictors of 25-hydroxyvitamin D status. The 25-hydroxyvitamin D status was measured along with age and season at blood collection, demographics, anthropometry, physical activity, diet and other lifestyle factors on 1,357 male and 1,264 females. This was done with a questionnaire and a food frequency survey over a twelve month period. Subjects in this study were healthy controls, age-matched to case distributions. As the aim of this study was to identify predictors of 25-hydroxyvitamin D values, initial data screening was performed in order to identify statistically significant and biologically meaningful variables associated with continuous and categorical 25-hydroxyvitamin D status.

Very little 25-hydroxyvitamin D deficiency was found in the studied population. Only 3% of the population had 25-hydroxyvitamin D <25 nmol/L; 12%, 29%, 79% and 95% had values of serum 25-hydroxyvitamin D <37 nmol/L, <50 nmol/L, <80 nmol/L, <100 nmol/L. The average age was 63 ± 5 years, 6% were non-Caucasian origin, 8% were current smokers and 36% had an education above college level. Forty percent had engaged in vigorous activity > 3 h/week during the last year and average BMI was 27 ± 5 kg/m². Serum 25-hydroxyvitamin D values varied by season of blood collection. The highest values were during the summer and fall and lowest values during winter and spring. Mean 25-hydroxyvitamin D values were significantly higher in
females than in males (p<0.001). However, when mean 25-hydroxyvitamin D values of females not taking a menopausal hormone therapy (measured by questionnaire) were compared to those of males, there were no significant differences between males and females (p=0.05). There were significant differences between females and males over the year (p<0.001). However, when mean 25-hydroxyvitamin D values of females not taking vitamin D supplementation were compared to the mean of males, there was no significant differences (Brock et al., 2010).

In a univariate analysis, many factors were found to be significantly (p<0.01) associated with 25-hydroxyvitamin D status. The factors were donating blood in the winter, being of non-Caucasian background, female, obese (BMI ≥30 kg/m²), inactive, low dietary vitamin D intake and taking vitamin D and calcium supplements. Vigorous physical activity was a strong and modifiable contributor to 25-hydroxyvitamin D status. The findings of high BMI being associated with low 25-hydroxyvitamin D values is consistent with many other studies that have been performed (Brock et al., 2010).

Globally from 1994-2004, obesity was more prevalent among women than men, with up to 70% of extremely obese persons being women (Ogden et al., 2006). As of 2009-2010 there was no significant difference in prevalence between men and women at any age. Overall, adults aged 60 and over were more likely to be obese than younger adults (Ogden et al., 2012). Women have fairly more body fat than men and collect more fat in the gluteal–femoral region, while men normally store more fat in the visceral (abdominal) depot (Blaak, 2001). Some studies have found a greater occurrence of 25-hydroxyvitamin D deficiency among men than women (Aasheim et al., 2008; Lagunova, Porojnicu, Lindberg, Hexeberg, & Moan, 2009). As vitamin D is a fat soluble vitamin that may possibly be sequestrated in adipose tissue one could assume that
a gender difference in the prevalence of 25-hydroxyvitamin D deficiency is related to differences in the amount of body fat and/or its distribution.

Between 2005 and 2010, 2,026 morbidly obese patients were examined consecutively at a tertiary care center. In addition, subgroups of 154 patients were examined between December 2005 and May 2006 in order to assess total vitamin D intake and macronutrient composition. The main outcome variables were the prevalence of 25-hydroxyvitamin D deficiency (serum concentration of 25-hydroxyvitamin D <50 nmol/l) and serum 25-hydroxyvitamin D concentration. Explanatory variables were gender, age, season of blood sampling (winter (1 November through till 28 February) or summer (1 March through till 31 October)), intake of vitamin D supplements, total vitamin D intake, current smoker, central obesity and overall obesity (BMI). Vitamin D intake was comparable between men and women in this study and could not explain the difference in prevalence of 25-hydroxyvitamin D deficiency between genders. It was found that men had significantly lower 25-hydroxyvitamin D concentrations than women during the winter season, mean 45.3 (17.8) nmol/l versus 51.6 (22.4) nmol/l (P<0.001), whereas there was no difference in the summer season, mean 53.0 (23.9) nmol/l versus 54.8 (22.3) nmol/l, respectively (P=0.21). Both men (P<0.001) and women (P=0.009) had higher 25-hydroxyvitamin D concentrations during the summer season than the winter season. Overall, about half of the patients had 25-hydroxyvitamin D deficiency. In addition, 25-hydroxyvitamin D deficiency was more prevalent in men than in women, 56% versus 47% (P<0.001). The main finding in this study of 2,026 morbidly obese patients is that obese men had approximately 40% higher adjusted odds of 25-hydroxyvitamin D deficiency than obese women (L. K. Johnson et al., 2012).
Numerous studies have linked obesity with poorer vitamin D status, as reflected by lower serum 25-hydroxyvitamin D values (Bell et al., 1985; Compston et al., 1981; Parikh et al., 2003; Wortsman et al., 2000). Both obesity and low serum 25-hydroxyvitamin D values are more common in African-American women than in Caucasian women (Coney et al., 2012; Hedley et al., 2004; Looker, Dawson-Hughes, Calvo, Gunter, & Sahyoun, 2002). The following study uses data from 6,402 adolescent and adult females, aged twelve years and older, from the third National Health and Nutrition Examination Survey (NHANES III, 1988–1994) to examine the extent to which body fat differences between the race/ethnicity contributes to serum 25-hydroxyvitamin D differences. In addition, it assesses whether the relationship between body fat and serum 25-hydroxyvitamin D varies by race/ethnicity in women, and if so, whether this difference is constant across age (Looker, 2005).

Of the 6,402 females, 3,567 were non-Hispanic whites and 2,475 were non-Hispanic blacks. Serum 25-hydroxyvitamin D values were measured by a Radioimmunoassay (RIA) kit and percent body fat was calculated from bioelectrical impedance analysis. It was determined that Non-Hispanic black women were younger and had more body fat than white women. The negative relationship between serum 25-hydroxyvitamin D and percent body fat was noticeably stronger in whites than in blacks of the same age. Values of 25-hydroxyvitamin D by race/ethnicity before and after adjusting for percent body fat were 1.4-1.9 times higher in white women than in black women before adjusting for percent body fat. After adjusting for percent body fat, it reduced, but did not remove the white/black difference; serum 25-hydroxyvitamin D values remained 1.3-1.9 times higher in whites. Percent body fat was significantly related to serum 25-hydroxyvitamin D in white women regardless of age, but among black women, the relationship was significant only among women less than 50 years of age. In conclusion, the
relationship between body fat and serum 25-hydroxyvitamin D in women is complex; it is weaker in blacks than in whites, and within race/ethnicity, it is weaker in older than in younger subjects. Thus, it appears to depend on both race/ethnicity and age (Looker, 2005).

**Surgical Treatment for Morbid Obesity**

The increasing prevalence of obesity, joined with the absence of effective conservative treatment and with the development of laparoscopic surgery, has led to a significant increase in the number of bariatric surgical procedures performed in most Western countries (Buchwald & Oien, 2009). Bariatric surgery has been shown to create effective and sustainable weight loss, which in turn results in improvement of obesity connected comorbidities, quality of life, and prevention of mortality (Sjöström et al., 2004).

Bariatric surgical procedures reduce calorie intake by modifying the anatomy of the gastrointestinal tract (DeMaria, 2007). These operations are categorized as either restrictive or malabsorptive. Restrictive procedures reduce intake by creating a small gastric reservoir with a narrow outlet to prolong emptying. Restrictive operations assist with weight loss by decreasing the amount of oral intake mainly by the small volume of the pouch and the small diameter of the opening obstructing the path of food (Poirier et al., 2011). Malabsorptive procedures bypass varying sections of the small intestine where nutrient absorption takes place (DeMaria, 2007).

Roux-en-Y gastric bypass is the most frequently performed bariatric surgery in the United States (Bruno et al., 2010; Hampson, Sinclair, & Smith, 2011). This operation involves reducing the size of the stomach to 15 mL by cutting off the topmost upper portion of the stomach and connecting it to the small intestine further down in the digestive system. The stomach remains viable, but is bypassed of all food intake, and the new stomach has a
dramatically smaller capacity. The duodenum is bypassed of all food intake, resulting in decreased macronutrient absorption, which may modulate postprandial hormonal responses (Laferrière et al., 2007). The reduction of appetite may be partially explained by modulations in serum peptide YY and glucagon-like peptide (Borg et al., 2006). Bypassing the duodenum also contributes to decreased micronutrient absorption such as iron and calcium, making lifelong supplementation a necessity (Aills, Blankenship, Buffington, Furtado, & Parrott, 2008).

The adjustable gastric band is a restrictive procedure that involves an implanted silicone device that includes an inflatable band attached to a reservoir port. The topmost part of the upper stomach is encircled by the band, which inhibits expansion circumferentially just beneath the esophagogastric junction when filled with saline injected through the reservoir port (Poirier et al., 2011).

The duodenal switch procedure (DS) is a complex weight-loss procedure that combines moderate restriction with moderate malabsorption to attain a high degree of weight loss. The essential components of the operation include gastric restriction via a pylorus-preserving sleeve, or vertical gastrectomy, and malabsorption via a duodenal switch with functional shortening of the small intestine. The duodenum is divided 4cm distal to the pylorus and anastomosed to the distal 250cm of ileum to create a 100cm common channel and a 150cm enteric limb (Buchwald, Cowan, & Pories, 2007).

The laparoscopic gastric sleeve (LGS) is a relatively new bariatric procedure. It was originally presented as either the restrictive component of biliopancreatic diversion with duodenal switch (BPD-DS) or the first step of a staged approach for weight loss. In the latter, super obese patients with increased operative risks undergo LGS to initiate enough weight loss to allow for a second stage gastric bypass (Silecchia et al., 2006). It has been recently used as a
definitive bariatric surgery following reports of significant reduction in BMI and comorbidities (Baltasar et al., 2005). LGS is considered a restrictive bariatric procedure, in which the fundus and the greater curvature of the stomach are removed, leaving a narrow gastric tube or “sleeve.” The small intestine is neither bypassed nor removed during this procedure, minimizing the micro nutritional deficiencies typically observed after malabsorptive procedures (Baltasar et al., 2005; Iannelli, Dainese, Piche, Facchiano, & Gugenheim, 2008).

Studies have shown that in the past two decades bariatric procedures have continued to increase over the years (Pope, Birkmeyer, & Finlayson, 2002). Bariatric surgical procedures in the United States increased from 4,925 in 1990 to 12,541 in 1997, and a reported increase to approximately 41,000 procedures in 2000. The American Society for Bariatric Surgery estimates that its members performed 63,000 bariatric procedures nationwide in 2002 (Pope et al., 2002). As of 2008, 344,221 bariatric surgery operations were performed by 4,680 bariatric surgeons (Buchwald & Oien, 2009). More than 220,000 of these surgeries were performed in the United States (John & Hoegerl, 2009). This data suggests that growth in bariatric surgery has continued to increase substantially over the last two decades.

**Relationship between Vitamin D Deficiency and Bariatric Surgery**

Deficiency in 25-hydroxyvitamin D is gradually becoming recognized as common in many groups especially after bariatric surgery. Serum 25-hydroxyvitamin D insufficiency and deficiency (25-hydroxyvitamin D <75 nmol/l) are exceedingly common in the obese population, and the combination is present in 90% of morbidly obese patients at the time of bariatric surgery, unexplained by the factors that influence 25-hydroxyvitamin D (Goldner et al., 2008).
Laparoscopic gastric banding is now one of the most commonly performed bariatric procedures. It causes a substantial reduction of food intake, and thereby a significant weight reduction, especially during the first postoperative year. Because of the major nutritional restriction, there are potential risks of mineral and vitamin deficiencies (Pugnale et al., 2003). Nutrient deficits are possible to show because of low nutrient consumption and avoidance of nutrient-rich foods in the early months post-surgery and later perhaps as a result of excessive band restriction. Food with high nutritional value such as meat and fibrous, fresh fruits and vegetables may be hard to tolerate (Aills et al., 2008). Unfortunately, the literature lacks data related to bone metabolism and 25-hydroxyvitamin D deficiency after gastric banding.

Calcium is absorbed preferentially in the duodenum and proximal jejunum, and its absorption is enabled by vitamin D in an acid environment (Aills et al., 2008). Vitamin D is absorbed preferentially in the jejunum and ileum. As the malabsorptive effects of surgical procedures increase, so does the likelihood of fat-soluble vitamin malabsorption associated to the bypassing of the stomach, absorption locations of the intestine, and reduced mixing of bile salts. Reduced dietary intake of calcium and vitamin D-rich foods, associated to intolerance from surgery, can also grow the risk of deficiency after all surgical procedures (Aills et al., 2008).

Lactose intolerance can happen after bariatric surgery, especially after Roux-en-Y gastric bypass. Cramping, bloating and diarrhea are common from dairy products after surgery; this could be part of the reason why there are deficiencies of calcium and vitamin D. Low 25-hydroxyvitamin D values are connected in view of the increased risks of poor bone health in patients with morbid obesity, all surgical candidates should be screened for 25-hydroxyvitamin D deficiency and bone density abnormalities preoperatively (Aills et al., 2008).
Recommendations from the American Society of Metabolic and Bariatric Surgery suggests that if a patient is 25-hydroxyvitamin D deficient, a suggested dose for correction is 50,000 IU ergocalciferol taken orally, once weekly, for 8 weeks (Aills et al., 2008).

The preoperative and postoperative 25-hydroxyvitamin D status of patients undergoing bariatric surgery has not been well-defined (Fish et al., 2010). Although, the reported prevalence of 25-hydroxyvitamin D deficiency prior to surgery ranges between 54 and 80% (Carlin et al., 2006; Stein et al., 2009). A more recent study conducted a retrospective analysis performed on patients that underwent bariatric surgery. Serum 25-hydroxyvitamin D, parathyroid hormone, and calcium were analyzed. The mean patient age was 45y; 82% of patients were women. Of 127 total patients, 84% were 25-hydroxyvitamin D deficient preoperatively. This program measured 25-hydroxyvitamin D values less than 30 ng/mL (75 nmol/L) to be deficient. Those patients found to be deficient in 25-hydroxyvitamin D received 50,000 IU three times weekly of vitamin D₃ for one month prior to surgery. Post operatively, all patients were started on 1200-1500 mg of calcium citrate plus 1200 IU of vitamin D₃ daily. Patients previously deficient received an additional 800 IU of vitamin D₃ daily or 50,000 IU once monthly. These patients had a higher preoperative BMI than those with normal 25-hydroxyvitamin D values on initial assessment (BMI 44 versus 50 kg/m², P < 0.01). A correlation was found between preoperative BMI and low 25-hydroxyvitamin D (r² = 0.12, P < 0.01) and PTH values (r² = 0.07, P < 0.01). One year following gastric bypass surgery, 20% of patients with elevated PTH values had normal 25-hydroxyvitamin D values. The incidence of observed deficiencies for adjustable gastric band versus gastric bypass did not differ statistically at any interval. Morbidly obese patients seeking bariatric surgery are often deficient in 25-hydroxyvitamin D, a fact that should be accounted for when evaluating the impact of bariatric surgery on 25-hydroxyvitamin D.
values. Elevated BMI and increasing degrees of obesity may be risk factors for both 25-hydroxyvitamin D deficiency and secondary hyperparathyroidism (Fish et al., 2010).

Another study evaluated the effectiveness of a standard multivitamin in the prevention and treatment of nutritional deficiencies in obese patients after bariatric surgery (Gasteyger, Suter, Gaillard, & Giusti, 2008). This study aimed to assess the type, frequency, and pattern of development of nutritional deficiencies over the first 24 months after Roux-en-Y gastric bypass. A total of 137 morbidly obese patients were involved, 110 women and 27 men. For vitamin D, nutritional supplements were prescribed orally at 1000 mg/d; vitamin D₃. Ninety patients had a BMI ≤ 48.0 (group 1) and the other 47 patients had a BMI >48.0 (group 2). Patients received specific supplements at three, six, twelve, 18, and 24 months after Roux-en-Y gastric bypass. Patients (59.8%) received at least three supplements a day and 37.2% received 4 or more types of supplements a day at the end of follow-up. In group 2, the amount of patients who needed calcium and vitamin D₃ supplementation at year two after surgery was significantly higher than that in group 1 (74% compared with 52%, respectively; P= 0.02). This could have been due to BMI or the length of the Roux-en-Y-limb being 100 cm in the patients with a BMI ≤ 48 and with a BMI >48, a Roux-en-Y limb of 150 cm. Hypovitaminosis D with secondary hyperparathyroidism was found in up to 80% of patients both pre and postoperatively (Gasteyger et al., 2008).

In 2006, a total of 243 patients underwent routine laboratory testing after having gastric bypass surgery. The testing included measurements of 25-hydroxyvitamin D, PTH, calcium, and albumin values. Of these 243 patients, 41 had long limb bypasses (LL-GBP), Roux >100 cm and 202 patients had a short limb bypass (SL-GBP), Roux <100 cm. BMI was higher in those who underwent LL-GBP. Mean corrected calcium values were 9.3 mg/dL (8.5–10.8 mg/dL), and no
difference existed between the LL-GBP and SL-GBP groups. The average 25-hydroxyvitamin D level for the entire group was 21.7 ± 11.3 ng/mL (laboratory normal >8.9 ng/mL). Individuals who underwent LL-GBP had lower 25-hydroxyvitamin D values and higher PTH values (laboratory normal range, 12.0–65 pg/mL) than those who had a SL-GBP. Of the individuals with low 25-hydroxyvitamin D values (n=36), 88.9% had elevated PTH (P <0.0001), and 42.1% of those with laboratory normal 25-hydroxyvitamin D values (n =207) had an elevation in PTH (P< 0.0001). When making 30 ng/mL the cut off for normal 25-hydroxyvitamin D values, the majority (78.9%) of patients who underwent a LL-GBP and whose 25-hydroxyvitamin D values were <30 ng/mL also had elevated PTH values. Only three of 41 LL-GBP patients had 25-hydroxyvitamin D values ≥30 ng/mL. Almost half (49.0%) of SL-GBP patients with a 25-hydroxyvitamin D <30 ng/mL had an elevated PTH level. Fully, 28.5% of SL-GBP patients with 25-hydroxyvitamin D values ≥30 ng/mL had elevated PTH values (J. M. Johnson et al., 2006).

Preoperative normalization of calcium and vitamin D metabolism, personalized postoperative supplementation regimens, and prompt treatment of calcium and 25-hydroxyvitamin D deficits identified after surgery should become the corner-stones for the avoidance of bone loss after Roux-en-Y gastric bypass. To date, rational guidelines for preoperative correction of 25-hydroxyvitamin D deficiencies in morbid obese patients are not offered (Fendrikova, Verka, Thomsen, Merugu, & Salomone, 2009; Goldner et al., 2009). Correction of postoperative 25-hydroxyvitamin D deficiencies is even more difficult to achieve because the dose corrections that are needed to overcome malabsorption are currently not known (Aarts et al., 2011).
A study done in 2011 focused on intestinal cholecalciferol (Vitamin D₃) absorption and attempts to quantify the changes induced by Roux-en-Y gastric bypass (Aarts et al., 2011). Absorption of vitamin D₃ was studied in 14 morbidly obese, premenopausal women with a BMI of 35-50 kg/m² before and 4 weeks after laparoscopic Roux-en-Y gastric bypass. All patients received vitamin D₃ treatment preoperatively to correct the pre-existent 25-hydroxyvitamin D deficiencies. Levels were corrected if it was <75 nmol/l. Serum vitamin D₃ values were measured at baseline and 1, 2, 3, and 14 days after a single oral dose of 50,000 IU solubilized vitamin D₃. Serum total calcium, phosphate and PTH values were within normal range. Baseline serum vitamin D₃ was significantly higher preoperatively than postoperatively (18.8±3.0 vs. 5.8 ± 1.3, P<0.001), while all other parameters were not different on the two occasions. In all patients, peak values were observed on the first day after the oral dose, before and after surgery. Substantial inter-individual variability was observed, and a methodical underestimation of the true decrease in vitamin D₃ absorption is suspected. In conclusion, Roux-en-Y gastric bypass reduced the peak cholecalciferol levels by about 25%. Further analysis did suggest that the timing of sampling in the current study was not optimal. The interval of 2 weeks between the loading dose of vitamin D₃ and the basal serum sample of the test might have been too short. This might have caused an underestimation of the true decrease in vitamin D₃ absorption induced by Roux-en-Y gastric bypass. A repeat study is necessary to obtain a more reliable estimate of the change in 25-hydroxyvitamin D availability after Roux-en-Y gastric bypass. Although, this study did show that vitamin D₃ is decreased after Roux-en-Y gastric bypass (Aarts et al., 2011).

As stated earlier there are no consensus guidelines regarding vitamin D supplementation sufficient to prevent and treat 25-hydroxyvitamin D deficiency after surgery. Current
recommendation for vitamin D supplementation following surgery is 400-800 IU of vitamin D per day, usually in the form of a multivitamin. This dose is typically inadequate (Aills et al., 2008).

Forty one patients planning to undergo Roux-en-Y gastric bypass were given one of three doses of vitamin D₃ supplementation after surgery: 800, 2,000, and 5,000 IU/day. All patients were also instructed to take 2,000 mg of calcium daily (Goldner et al., 2009). All patients were above the age of 19 years. Participants were not eligible if they planned to undergo another bariatric surgery, had evidence of hypercalcemia (calcium >2.63 mmol/L), hypocalcaemia (calcium <1.75 mmol/L), renal insufficiency (GFR <50 ml/min) a history of primary hyperparathyroidism, renal tubular acidosis, sarcoidosis, granulomatous disease, or malignancy. Baseline labs were drawn at the time of surgery and follow up visit labs were drawn at six weeks, three, six, nine, twelve, 18, and 24 months post-surgery. Baseline information obtained included age, height, weight, BMI, sex, race/ethnicity, and season of vitamin D measurements.

Vitamin D deficiency was defined as 25-hydroxyvitamin D<50 nmol/L and insufficiency was defined as 25-hydroxyvitamin D 50-75 nmol/L. Ninety percent of the patients at the time of surgery were insufficient in 25-hydroxyvitamin D. Results showed that the 25-hydroxyvitamin D was significantly higher and the iPTH was significantly lower in the 5,000 IU group compared with the 2,000 IU group. Dropout rates were high so data focused primarily on six and twelve months after surgery. At six months, the 25-hydroxyvitamin D in the 800-IU group had increased by a mean of 13.5±31.2 nmol/L, and the 5,000-IU group increased by 45.0±41.2 (p=0.04). The maximum increase in each group was 52.4, 100, and 100 nmol/L. At twelve months, the mean increase in the 800, 2,000 and 5,000 IU group was 27.5±1.0, 60.2±37.4, and 66.1±42.2 nmol/L. The maximum increase in 25-hydroxyvitamin D for each group was 87.4,
114.8, and 129.8 nmol/L. At twelve months, 44% of the 800 IU group, 78% of the 2,000 IU group and 70% of the 5,000 U group attained a 25-hydroxyvitamin D≥75 nmol/L (p=0.38). Of the patients still participating at 24 months 67%, 50% and 78% of the 800, 2,000, and 5,000 IU group attained a 25-hydroxyvitamin D≥75 nmol/L (p=0.48). When evaluating twelve month 25-hydroxyvitamin D values compared to baseline values, 100% of patients who started with a 25-hydroxyvitamin D≥62.5 nmol/L achieved the goal of a 25-hydroxyvitamin D of ≥75 nmol/L (Goldner et al., 2009).

In conclusion, higher doses of vitamin D₃ supplementation trend towards higher values of 25-hydroxyvitamin D. Vitamin D₃ supplementation as high as 5,000 IU/day or more is safe and necessary in many patients to treat 25-hydroxyvitamin D deficiency following Roux-en-Y gastric bypass (Goldner et al., 2009).

Summary

Normal serum 25-hydroxyvitamin D is important for maintaining bone health and preventing osteomalacia (weak bones) in adults. As shown from past research morbid obese patients are often deficient in 25-hydroxyvitamin D (Fish et al., 2010). All patients having bariatric surgery are morbidly obese. It is crucial for health care providers to check patient’s 25-hydroxyvitamin D before bariatric surgery. If patients are deficient before surgery it is necessary to start supplementation and continue this supplementation after surgery. Bariatric surgery is either restrictive or malabsorptive for food intake and can make 25-hydroxyvitamin D status worse, affecting bone health. It is important to research the correlation between BMI, 25-hydroxyvitamin D and percent of weight loss after surgery to continue to understand the amount
of vitamin D₃ supplementation that is necessary for obese and non-obese patients to maintain a normal 25-hydroxyvitamin D level (Goldner et al., 2008).
CHAPTER 3

METHODOLOGY

The purpose of this ex post facto study was to examine the link between serum 25-hydroxyvitamin D, body mass index (BMI), and percent of excess weight loss after laparoscopic bariatric surgery among morbidly obese men and women at a Midwest bariatric center. In this chapter, the methodology adopted in this study will be explained, which includes the Institutional Review Board information, the research questions, data collection process and statistical tests used for data analyses, including Pearson’s Correlation, independent-samples t-tests, paired-samples t-tests and linear regression.

Institutional Review Board

Permission was granted from both the Ball State University Institutional Review Board (BSU IRB Number: 301195-1) and a Community Hospital Institutional Review Board prior to implementing this study (Appendix A & B). The PI conducting these analyses completed the Collaborative Institutional Training Initiative (CITI) training (Appendix C) prior to the study. In addition, this study also received permission from the Director of the Midwestern Bariatric Center used in this study to access and analyze the data previously collected (Appendix D). Prior to surgery, all patients were informed that lab values entered into charts might be used for research purposes. Each patient that agreed to participate in potential future research studies
signed a consent form that included authorization for the release of their health information (Appendix E).

**Subjects**

Subjects in the study included patients who received gastric bypass or gastric banding at a Midwestern bariatric center between January 2008 and December 2011. Subjects included both males and females between the ages of 18 to 71 years. To be considered eligible to receive the surgery, patients had to meet the following criteria: be at least 18 years or older, with a body mass index (BMI) between 35 and 39 with one co-morbid condition, or a BMI at 40 or above with no co-morbid condition. The last two criteria is necessary since a normal BMI is between 18.5 to 24.9; anyone whose BMI is at least 30 or above is considered obese (Center for Disease Control and Prevention, 2012). In addition, patients must have shown a five year history of being obese, engaged in diet programs in the past (i.e. Weight Watchers, Atkins, reduced calorie diets) and cannot have had an addiction to drugs or alcohol. All patients must have seen a dietitian at least three times, and psychologist at least once preoperatively. This was not standardized; it could have taken a patient three to nine months to meet all criteria to have bariatric surgery.

**Data Collection**

Previous collected data from a Midwestern community bariatric center was used in this study. The data was collected at three different time frames: prior to the surgery, six months and twelve months after the surgery. Demographic information was collected for each patient, such as their height, gender and race/ethnicity at their first appointment. Additionally, weight, blood work, including calcium and 25-hydroxyvitamin D was collected prior to surgery, at six months
and twelve months post-surgery. Parathyroid hormone was only collected at six months and twelve months post-surgery. Vitamin D₃ supplementation that each patient was prescribed prior to surgery, six months post-surgery and twelve months post-surgery was also collected. The percentage of excess weight loss and 25-hydroxyvitamin D level change were also calculated.

Collected data were first entered into an Excel spreadsheet then converted into an SPSS file. The PI assigned each patient a personal unique identification number to maintain confidentiality, which was used for data entry into both the Excel and SPSS data processing systems. Data stored on a laptop computer were password protected. A backup file of the data was saved to a flash drive and kept locked in a file draw. Only the PI had access or knowledge of which patient corresponded to which assigned number.

**Pre-surgery**

Prior to the surgery, all patients had blood drawn to measure their serum 25-hydroxyvitamin D and calcium. All patients were also weighed and their BMI were calculated. If a patient’s serum 25-hydroxyvitamin D was below 30 ng/mL, the clinic protocol dictated that their physician should prescribe a vitamin D₃ (cholecalciferol) supplement, with the dosage depending on their 25-hydroxyvitamin D serum level. Specifically, if a patient’s 25-hydroxyvitamin D level was equal or lower than 8 ng/mL, they were given a prescription of 50,000 International Unit (IU) weekly of vitamin D₂ for six weeks, then retested and put on a maintenance dose depending on their level. If a patient’s 25-hydroxyvitamin D was 9-10 ng/mL, they were prescribed a supplement of 5,000 IU of D₃ daily; if a patient’s level was 11-15 ng/mL, they were prescribed a supplement of 4,000 IU D₃ daily; if their level was 21-25 ng/mL, they were prescribed a supplement of 2,000 IU D₃ daily; if their level was 26-29 ng/mL, they were prescribed 1,000 IU D₃ daily.
Post-surgery

All patients were weighed and BMI was calculated at their six and twelve month post-surgery visits. The patients were instructed to take vitamin D₃ daily until their six-month post-surgical labs were drawn, which included 25-hydroxyvitamin D, calcium and PTH. If at that time the patient’s 25-hydroxyvitamin D was still low, he/she was told to take a vitamin D₃ supplement prescribed based on his/her 25-hydroxyvitamin D status. The patients’ blood were drawn again at twelve months after the surgery to re-check their overall vitamin status, including 25-hydroxyvitamin D. Again, patients continued supplementation depending on their 25-hydroxyvitamin D level status.

Gastric bypass patients were recommended to take two multivitamins daily and 1500 mg of calcium citrate daily, while gastric banding patients were recommended to take one multivitamin daily and 1500 mg of any kind of calcium daily. These supplements typically add an additional 250-400 IU D₃ per capsule depending on the brand.

Data Analyses

Each patient’s 25-hydroxyvitamin D value, BMI, percent of weight loss and serum calcium were compared to the patient’s pre-surgical and post-surgical levels at six and twelve month time points. (PTH was not collected pre-surgery but was compared between the data collected at six and twelve months after the surgery.) Descriptive statistics on gender, race/ethnicity, age and frequency counts were executed and followed up by additional analyses measuring the relationship between these variables at the different time points. In addition to descriptive statistics, four different statistical techniques were used to assess the data collected in this study, including Pearson Product–Moment Correlation Coefficient (Pearson’s Correlation),
independent-samples t-tests, paired-samples t-tests, and linear regression. Pearson’s Correlation test was performed to measure the relationship between 25-hydroxyvitamin D and BMI before surgery and was performed again to see the correlation between 25-hydroxyvitamin D and percent excess weight loss after surgery. Pearson’s Correlation test was also used to assess the correlation between 25-hydroxyvitamin D status, calcium and PTH at six and twelve months after surgery.

Independent samples t-test was used to assess the difference in 25-hydroxyvitamin D level prior to surgery, between six and twelve months after surgery based on gender, ethnicity/race and type of surgery.

Paired samples t-test was used to assess the difference in the 25-hydroxyvitamin D level prior to surgery and between six and twelve months after surgery. The paired samples t-test was also used to assess the difference in the 25-hydroxyvitamin D level prior to surgery and between six and twelve months based on gender, race/ethnicity and type of surgery.

Linear regression was used to assess the relationship between the 25-hydroxyvitamin D level and the body weight decrease percentage at six months and twelve months post-surgery. Statistical significance was set at $p \leq 0.05$ for all of the tests performed (Pallant, 2005).

**Summary**

This study examined the link between morbid obesity and 25-hydroxyvitamin D values in patients having gastric surgery. A patients’ 25-hydroxyvitamin D, PTH and calcium values impact their overall bone health. This study will help researchers better understand the amount of vitamin D$_3$ supplementation that is needed to keep the 25-hydroxyvitamin D status of the
morbidly obese population in the normal (>30 ng/mL) range in an attempt to improve their overall bone health.
CHAPTER 4

RESULTS

The purpose of this ex post facto study was to examine the link between serum 25-hydroxyvitamin D, body mass index (BMI), and percent of excess weight loss after laparoscopic bariatric surgery among morbidly obese men and women at a Midwest bariatric center. This chapter presents the results of data analyses and testing. In addition to descriptive statistics, four statistical techniques were employed to analyze the data collected in this study. SPSS 21.0 for Windows was used for descriptive statistics, Pearson’s Correlation, paired-samples t-test, independent-samples t-test and linear regression. Statistical significance was set at $p \leq 0.05$ (Pallant, 2005).

Demographics

A total of 96 patients participated in this study. The majority of patients received gastric bypass surgery ($n=75$) while the remaining received gastric banding surgery ($n=21$). These patients underwent surgery between January 2008 and December 2010. The entire data set was collected between January 2008 and December 2011, including patients’ pre-surgical and post-surgical lab values at six and twelve months. Of the 96 patients, 78.1% were females (75 patients) and 21.9% were males (21 patients). Race/ethnic variance were 80.2% Caucasian (77 patients), 18.8% African-American (18 patients) and 1% Chinese-American (1 Patient). The age
groups included 21-37 (6.25%) (6 patients), 38-54 (50.00%) (48 patients) and 55-71 (43.75%) (42 patients) and the mean age of the participants was 51.5 years. The results are listed in Table 1.

Table 1 Demographic Information of Participants (N=96)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Race/Ethnicity</th>
<th>Age Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (78.10%) (75)</td>
<td>Caucasian (80.20%) (77)</td>
<td>21-37 (6.25%) (6)</td>
</tr>
<tr>
<td>Male (21.90%) (21)</td>
<td>African American (18.80%) (18)</td>
<td>38-54 (50.00%) (48)</td>
</tr>
<tr>
<td></td>
<td>Asian American (1.00%) (1)</td>
<td>55-71 (43.75%) (42)</td>
</tr>
</tbody>
</table>

Research Findings

A power test was performed that indicated the sample size was too small with the independent samples. The composite score from the total sample was used to assess the difference at the three different time frames (prior to surgery, six and twelve months post-surgery). The remaining analyses included pooled data.

Prior to the data analysis, patients’ blood lab results were measured and recorded to establish a benchmark, with the exception of PTH. Post-surgically these same biomarkers were measured and averaged at six and twelve months (Table 2).

Table 2 Participants’ Biomarkers (N=96)

<table>
<thead>
<tr>
<th></th>
<th>Pre-Surgery</th>
<th>6 Months Post-Surgery</th>
<th>12 Months Post-Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D</td>
<td>20.50 ng/mL</td>
<td>34.80 ng/mL</td>
<td>34.10 ng/mL</td>
</tr>
<tr>
<td>PTH</td>
<td>No Data</td>
<td>41.50 pg/mL</td>
<td>40.80 pg/mL</td>
</tr>
<tr>
<td>Calcium</td>
<td>9.40 mg/dL</td>
<td>9.40 mg/dL</td>
<td>9.10 mg/dL</td>
</tr>
</tbody>
</table>
RQ #1: What correlation exists between 25-hydroxyvitamin D and BMI before surgery?

The first research question raised in this study was to assess the relationship between 25-hydroxyvitamin D and BMI before surgery. A Pearson’s Correlation test was performed. Based on the results, BMI and the 25-hydroxyvitamin D level was significantly inversely correlated ($r = -.262$, $p = .01$), which means when BMI increased, the 25-hydroxyvitamin D level decreased.

RQ #2: Will there be a difference in 25-hydroxyvitamin D level prior to surgery, between six months and twelve months after surgery based on (1) gender (2) race/ethnicity or, (3) type of surgery?

A paired-samples t-test was performed to determine if there was a difference in 25-hydroxyvitamin D level before and after the surgery among patients. Specifically, the PI investigated whether there was any difference in 25-hydroxyvitamin D level between the time frames of pre-surgery and six months and between six months and twelve months post-surgery to assess whether progress was sustained. The results show there was a statistically significant difference between the initial 25-hydroxyvitamin D level (20.51 ng/mL ± 7.46) and six months after the surgery (34.80 ng/mL ± 11.20) ($t(95) = -12.18, p = .00$) The results suggest that after patients underwent surgery, their 25-hydroxyvitamin D level increased. However, no significant difference was identified in the 25-hydroxyvitamin D level between six months (34.80 ng/mL ± 11.20) and the twelve months post-surgery (34.08 ng/mL ± 10.60) ($t(95) = .79, p = .43$). The results suggest patients’ 25-hydroxyvitamin D levels did not change significantly between six-months and twelve-months after the surgery. The results are shown in Table 3.

The PI separated the collected data to investigate if 25-hydroxyvitamin D levels were different between the time frames of pre-surgery and six months post-surgery and between six
and twelve months post-surgery based on gender, race/ethnicity and the type of surgery the patient received (gastric band or Roux-en-Y gastric bypass).

Independent-samples t-tests were executed to see if there were differences on these variables pre-surgery, six months and twelve months after surgery. The correlation shows there were no significant difference in gender related to 25-hydroxyvitamin D levels, before or after the surgery. The results are listed in Table 4.

The PI also investigated if race/ethnicity was a factor in 25-hydroxyvitamin D pre and post-surgery. Since there was only one patient that was Asian-American, that patient was excluded, and the comparison was conducted with Caucasian and African-American patients. The results are listed in Table 5. The results indicated there was a difference in 25-hydroxyvitamin D levels between Caucasian (22.20 ng/mL ± 6.60) and African-American patients (13.78 ng/mL ± 7.12) before the surgery ($t_{93} = 4.80, p =.00$), but no difference was identified post surgery at six and twelve months.

The PI also investigated if there was any difference between type of surgery and 25-hydroxyvitamin D levels post-surgery (gastric band and Roux-en-Y gastric bypass). No difference was identified at six months and twelve months when assessing the difference in 25-hydroxyvitamin D level based on the type of surgery received by patients. The results are listed in Table 6 and no significant difference was identified.

Table 3 Vitamin D Level Difference Based on Time Frames (N=96)

<table>
<thead>
<tr>
<th></th>
<th>Mean Diff.</th>
<th>Std. Deviation</th>
<th>Sig. (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Vitamin D Level &amp;</td>
<td>-14.29</td>
<td>11.50</td>
<td>.00</td>
</tr>
<tr>
<td>Vitamin D Level at 6 Months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D at 6 &amp; 12 Months</td>
<td>0.72</td>
<td>8.99</td>
<td>.43</td>
</tr>
</tbody>
</table>
Table 4 Vitamin D Level by Gender and Post Follow-up Assessment (N=96)

<table>
<thead>
<tr>
<th></th>
<th>Male (n=21)</th>
<th>Female (n=75)</th>
<th>Mean Diff.</th>
<th>t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Vitamin D</td>
<td>18.29 ng/mL ±7.06</td>
<td>21.13 ng/mL ±7.49</td>
<td>-2.85</td>
<td>-1.56</td>
</tr>
<tr>
<td>Vitamin D at 6 Months</td>
<td>34.10 ng/mL ±10.45</td>
<td>35.00 ng/mL ±11.47</td>
<td>-.90</td>
<td>-.33</td>
</tr>
<tr>
<td>Vitamin D at 12 Months</td>
<td>33.24 ng/mL ±10.00</td>
<td>34.32 ng/mL ±10.14</td>
<td>-1.08</td>
<td>-.43</td>
</tr>
</tbody>
</table>

Table 5 Vitamin D Level Difference Assessment Based on Race/Ethnicity (N=95)

<table>
<thead>
<tr>
<th></th>
<th>Caucasian (n=77)</th>
<th>African American (n=18)</th>
<th>Mean Diff.</th>
<th>t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Vitamin D</td>
<td>22.20 ±6.60</td>
<td>13.79 ±7.12</td>
<td>8.42</td>
<td>4.80***</td>
</tr>
<tr>
<td>Vitamin D at 6 Months</td>
<td>34.95 ±11.77</td>
<td>34.61 ±8.85</td>
<td>.34</td>
<td>.114</td>
</tr>
<tr>
<td>Vitamin D at 12 Months</td>
<td>33.71 ±9.89</td>
<td>35.94 ±11.07</td>
<td>-2.23</td>
<td>-.843</td>
</tr>
</tbody>
</table>

***p<.001

Table 6 Vitamin D Level Difference Assessment Based on Type of Surgery

<table>
<thead>
<tr>
<th></th>
<th>Bypass (n=75)</th>
<th>Band (n=21)</th>
<th>Mean Diff.</th>
<th>t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Vitamin D</td>
<td>20.80 ±7.21</td>
<td>19.48 ±8.37</td>
<td>1.32</td>
<td>.48</td>
</tr>
<tr>
<td>Vitamin D at 6 Months</td>
<td>35.65 ±10.55</td>
<td>31.76 ±13.12</td>
<td>3.89</td>
<td>.16</td>
</tr>
<tr>
<td>Vitamin D at 12 Months</td>
<td>34.80 ±9.70</td>
<td>31.52 ±11.14</td>
<td>3.27</td>
<td>.19</td>
</tr>
</tbody>
</table>

**RQ #3: What correlation exists between 25-hydroxyvitamin D and percent excess weight loss after surgery?**

Previous studies suggest that bariatric surgery is a tool to help with a significant amount of weight loss and improve quality of life (Sjöström et al., 2004). After losing a significant amount of weight, patients are typically healthier overall with controlled type 2 diabetes and improved blood pressure and cholesterol. The most common vitamin deficiency associated with obesity appears to be low concentration of 25-hydroxyvitamin D (Carlin et al., 2006). In this
study it was important to see if 25-hydroxyvitamin D increased after weight decreased. A Pearson Correlation test was performed to determine if a correlation existed between 25-hydroxyvitamin D and percentage of excess weight loss after surgery. The results indicate that the 25-hydroxyvitamin D level had a significant and positive relationship with the percentage of excess weight loss after surgery ($r=.344, p=.001$). This suggested that when the percentage of excess weight loss increased after surgery, 25-hydroxyvitamin D level increases.

**RQ #4: Will 25-hydroxyvitamin D level increase as body weight percent decreases among men and women who have had bariatric surgery at six months and twelve months?**

A linear regression model was used to assess the relationship between the 25-hydroxyvitamin D level and the body weight decrease percentage at six months and twelve months post-surgery. The PI wanted to determine if body weight decrease percentage can predict 25-hydroxyvitamin D level. The linear regression equation can contain one dependent variable and one or more independent variables, the dependent variable was represented by the 25-hydroxyvitamin D level while the independent variable was set with the body weight decrease percentage. The regression equation is depicted as follows:

$$25\text{-hydroxyvitamin D Level}_{x \text{ months}} = \beta_0 + \beta_1 \text{Body Weight Decrease Percentage}_{x \text{ months}}$$

The results below indicate that, at six months, 25-hydroxyvitamin D level is positively and significantly related to the excess weight loss percentage ($R=.34, R^2=.12, \Delta R^2=.11, p=.00$). At twelve months, 25-hydroxyvitamin D level is positively and significantly related to the excess weight loss percentage ($R=.26, R^2=.07, \Delta R^2=.06, p=.01$). All correlations were significant at the $p=.05$ level, which suggests that all variables were highly correlated to each other, both at six months and twelve months. R-square is the percentage of variance in the response and can be explained by the regression model containing the independent variable (body weight decrease...
percentage). When assessing the proposed model, in which the 25-hydroxyvitamin D level is the dependent variable, the results suggest that body weight loss percentage can explain nearly 12% of the variance at six months. However, when assessing the model with the twelve months data, the results indicate that the independent variable can only explain about 7% of the variance.

Table 7 Regression Model Summary

<table>
<thead>
<tr>
<th>Model</th>
<th>R</th>
<th>R Square</th>
<th>Adjusted R Square</th>
<th>F Change</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months</td>
<td>.34^a</td>
<td>.12</td>
<td>.11</td>
<td>12.65</td>
<td>.00</td>
</tr>
<tr>
<td>12 months</td>
<td>.26^a</td>
<td>.07</td>
<td>.06</td>
<td>6.75</td>
<td>.01</td>
</tr>
</tbody>
</table>

a. Predictors: (Constant), body weight loss percentage

In addition to the above assessment of the regression model, the ANOVA table below also presents the examination results of the overall significance of the model. The results are depicted in Table 8; the significance of the $F$ value was below 0.05 ($p=.001$ at six months and $p=.011$ at twelve months), which indicates the model was statistically significant, both at the six months and the twelve months. The 25-hydroxyvitamin D level can be explained by the body weight loss percentage.

Table 8 ANOVA Results N=96

<table>
<thead>
<tr>
<th></th>
<th>Model</th>
<th>Mean Square</th>
<th>F</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months</td>
<td>Regression</td>
<td>1414.75</td>
<td>12.65</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>Residual</td>
<td>111.84</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>Regression</td>
<td>644.34</td>
<td>6.75</td>
<td>.011</td>
</tr>
<tr>
<td></td>
<td>Residual</td>
<td>95.51</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. Predictors: (Constant), body weight loss percentage; Dependent Variable: Vitamin D

Since the overall model appeared to be statistically significant, an examination of the regression model with the decreased body weight percentage was conducted, which had a
statistically significant impact on the 25-hydroxyvitamin D level as depicted in Table 9.

Additionally, the model did not appear to have a significant multicollinearity issue, with the independent variable having a close-to-one tolerance and variance inflation factor (VIF) value.

As the result, the regression equation model can be demonstrated as:

25-hydroxyvitamin D Level_{6 \text{ months}} = 24.401 + .188 \text{ Body Weight Decrease Percentage}_{6 \text{ months}}

25-hydroxyvitamin D Level_{12 \text{ months}} = 26.653 + .104 \text{ Body Weight Decrease Percentage}_{12 \text{ months}}

The results from the linear regression analysis determined that an individual’s body weight loss percentage can predict his or her 25-hydroxyvitamin D level.

Table 9 Beta Coefficients and Other Coefficients for the Model

<table>
<thead>
<tr>
<th>Model</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>Std. Error</td>
</tr>
<tr>
<td>1 (Constant)</td>
<td>24.40</td>
<td>3.12</td>
</tr>
<tr>
<td>% Weight Loss 6 Month</td>
<td>.18</td>
<td>.05</td>
</tr>
<tr>
<td>2 (Constant)</td>
<td>26.65</td>
<td>3.03</td>
</tr>
<tr>
<td>% Weight Loss 12 Month</td>
<td>.10</td>
<td>.04</td>
</tr>
</tbody>
</table>

a. Model 1: 6 months; Model 2: 12 months

RQ #5: What correlation exists between 25-hydroxyvitamin D status and calcium and PTH six and twelve months after surgery?

Serum 25-hydroxyvitamin D, calcium and PTH can be affected by each other; this study assessed what correlation exists among 25-hydroxyvitamin D, calcium and PTH at six and twelve months after surgery. Pearson’s Correlation tests were used to assess the relationship among 25-hydroxyvitamin D, calcium and PTH at the six and twelve month time frames. Based on the results, there is no relationship among the three variables at six months (Table 10). At
twelve months, both 25-hydroxyvitamin D and calcium are significantly related to PTH. In addition, the results suggest that 25-hydroxyvitamin D was negatively related to PTH and calcium was positively related to PTH. However, calcium was not related to 25-hydroxyvitamin D (Table 10).

Table 10 Relationship of Vitamin D, Calcium and PTH at Six and Twelve Months (N=96)

<table>
<thead>
<tr>
<th></th>
<th>6 and 12 Month Vitamin D Level</th>
<th>6 and 12 Month Calcium</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Month Calcium</td>
<td>.12</td>
<td></td>
</tr>
<tr>
<td>6 Month PTH</td>
<td>- .10</td>
<td>-.17</td>
</tr>
<tr>
<td>12 Month Calcium</td>
<td>.06</td>
<td></td>
</tr>
<tr>
<td>12 Month PTH</td>
<td>-.24**</td>
<td>.25**</td>
</tr>
</tbody>
</table>

**p<0.05

Summary

Morbidly obese patients seeking bariatric surgery are often 25-hydroxyvitamin D deficient. Based on the results of this study it is clear that the patient’s 25-hydroxyvitamin D level did improve when BMI decreased post-surgery with the help of vitamin D₃ supplementation. Baseline until six months after surgery the most significant change in 25-hydroxyvitamin D values were presented. Pre-surgery 25-hydroxyvitamin D mean value was 20.50 ng/mL and six month post-surgery mean value was 34.80 ng/mL. Between six and twelve months post-surgery there was not a significant change in 25-hydroxyvitamin D values. Six month 25-hydroxyvitamin D mean value was 34.8 ng/mL and twelve month mean value was 34.1 ng/mL. When assessing the relationship on gender, race/ethnicity and type of surgery the only significant difference was the initial 25-hydroxyvitamin D level, based on race/ethnicity.

As the patients lost excess weight their 25-hydroxyvitamin D increased at six months. It was also determined that a patient’s body weight loss can predict his or her 25-hydroxyvitamin D...
level. When assessing the correlation between 25-hydroxyvitamin D, calcium and PTH the correlation was not significant until twelve months after surgery. Overall, the results of this study indicate that after bariatric surgery, as body weight percent decreases, 25-hydroxyvitamin D values increase.
CHAPTER FIVE

DISCUSSION

The purpose of this ex post facto study was to examine the link between serum 25-hydroxyvitamin D, body mass index (BMI), and percent of excess weight loss after laparoscopic bariatric surgery among morbidly obese men and women at a Midwest bariatric center. This chapter will discuss the findings in this study.

It was demonstrated with the morbidly obese population in this study that the average 25-hydroxyvitamin D level prior to bariatric surgery was below the recommended >30 ng/mL. The patient’s mean 25-hydroxyvitamin D level prior to surgery was 20.5 ng/mL. As the patients started the recommended vitamin D₃ supplementation, completed bariatric surgery and decreased in body weight, their 25-hydroxyvitamin D values improved, at six months to an average of 34.8 ng/mL and at twelve months to 34.1 ng/mL. It is clear that as the patient’s percent excess weight loss improved their 25-hydroxyvitamin D status improved as well.

Relationship between 25-Hydroxyvitamin D and BMI before Surgery

The present study found an inverse relationship between 25-hydroxyvitamin D and BMI before bariatric surgery. As BMI would increase, 25-hydroxyvitamin D level would decrease. In a related study patients who were 25-hydroxyvitamin D deficient pre bariatric surgery had a
significantly higher preoperative BMI than those who had 25-hydroxyvitamin D values that were normal (>30 ng/mL) upon initial assessment (Fish et al., 2010). Other studies have also reported preoperative 25-hydroxyvitamin D deficiencies among bariatric surgery patients ranging from 54% to 90% (Gemmel, Santry, Prachand, & Alverdy, 2009; Goldner et al., 2008). Researchers have demonstrated that the inverse 25-hydroxyvitamin D and obesity relationship can be explained by “trapping” of the vitamin D parent compound, cholecalciferol, in adipose tissue (Wortsman et al., 2000). Therefore, this suggests that when a patient’s BMI is higher their 25-hydroxyvitamin D is lower.

This study did not compare morbidly obese patients that were 25-hydroxyvitamin D deficient and those patients who were 25-hydroxyvitamin D sufficient. In future studies it may be important to compare these patients to know more specifically the level of supplementation to provide a patient dependent on their BMI.

**The Difference in 25-Hydroxyvitamin D level Based on (1) Gender (2) Race/Ethnicity (3) Type of Surgery**

Results of the present study indicated that there was an increase in 25-hydroxyvitamin D values between, pre-surgery values and six months after surgery values. The results of this study did not find a significant increase in 25-hydroxyvitamin D values between six and twelve months after surgery. In addition, there was no significant difference with 25-hydroxyvitamin D value between pre-surgery and six months post-surgery and between six and twelve month’s post-surgery with gender, race/ethnicity and type of surgery. The only exception was the significant relationship is the 25-hydroxyvitamin D level prior to surgery in relation to race/ethnicity.

Many reasons could explain why the patient’s 25-hydroxyvitamin D value increased between the initial 25-hydroxyvitamin D value and six month 25-hydroxyvitamin D value and
not between six and twelve months. The sample mean BMI decreased the most between initial BMI (47.8) and six months post-surgery BMI (35.3), decreasing an average of 12.5 points. Between the six month BMI (35.3) and the twelve month BMI (32.1), the BMI only decreased an average of 3.2 points. This suggests that the patients in this study lost the most significant amount of weight between baseline and the first six months after surgery. Factors could also include that the patients were taking their vitamin D₃ supplementation more faithfully during the first six months; dietary intake that included vitamin D could have been higher during this period of time, increased physical activity and blood could have been drawn in the spring/summer months meaning the patients could have absorbed more vitamin D from the sun. All of these factors could affect the 25-hydroxyvitamin D values (Brock et al., 2010).

Low concentrations of 25-hydroxyvitamin D are common with obesity. The relationship between weight loss and effects on 25-hydroxyvitamin D has been studied. (Mason et al., 2011) investigated the effects of twelve months of weight loss through calorie restriction, exercise intervention or both together on serum 25-hydroxyvitamin D concentrations. Overweight and obese postmenopausal women (n=439) were randomly dispensed to four groups. The four groups included: 1) diet modification, 2) exercise, 3) diet and exercise, and 4) control. Women who lost <5%, 5-9.9%, 10-14.9%, or ≥15% of baseline weight had a mean increase in 25-hydroxyvitamin D of 2.1, 2.7, 3.3, and 7.7 ng/mL. A greater degree of weight loss is associated with increased 25-hydroxyvitamin D concentrations (Mason et al., 2011).

In a related study on weight loss association with increased 25-hydroxyvitamin D, 383 overweight or obese women who participated in a 2 year clinical trial of a weight loss program that included a diet pill, 1,200 -2,000 calorie a day, increased physical activity and behavior counseling were assessed. At 24 months the participants who lost 5-10% of their baseline weight
had an increased 25-hydroxyvitamin D level by 2.7 (9.1) ng/mL, those who lost >10% saw an increase of 25-hydroxyvitamin D by 5.0 (9.2) ng/mL. At baseline, 51% of the participants met or exceeded the recommended serum 25-hydroxyvitamin D concentration of 20 ng/mL. By the end of the study, 64% of overweight or obese women met the goal of 20 ng/mL and 83% of those whose weight loss achieved a normal BMI met the goal of at least 20 ng/mL of 25-hydroxyvitamin D levels (Rock et al., 2012). These research studies relate to the data found in the present study that weight loss does affect 25-hydroxyvitamin D levels.

Past research also explains that vitamin D is absorbed preferentially in the jejunum and ileum. As the malabsorptive effects of the bariatric surgical procedures increase so does the likelihood of fat-soluble vitamin malabsorption related to the bypassing of part of the small intestine, absorption sites of the intestine, and poor mixing of bile salts. Decreased dietary intake of calcium and vitamin D-rich foods, related to intolerance from surgery, can also increase the risk of deficiency after all surgical procedures (Aills et al., 2008). This could also explain why as the patients had increased malabsorption from bariatric surgery; their 25-hydroxyvitamin D values did not change significantly after the first six months.

In this population, when separating the data according to gender, race/ethnicity and type of surgery the patient received 25-hydroxyvitamin D did not differ significantly between the patients pre-surgery, six months or twelve months post-surgery. The results did confirm significance between race/ethnicity and the initial 25-hydroxyvitamin D value. African American patients had a significantly lower 25-hydroxyvitamin D value compared to Caucasian patients pre-surgery.

A review of the literature indicates both obesity and low serum 25-hydroxyvitamin D values are more common in African American women than in Caucasian women (Coney et al.,
The relationship between body fat and serum 25-hydroxyvitamin D in women is complex; it seems to depend on both race/ethnicity and age. Specifically, the relationship between body fat and serum 25-hydroxyvitamin D is stronger in Caucasians than in African-Americans of all ages (Looker, 2005). In addition, there is a difference in 25-hydroxyvitamin D levels by age within race; a significant relationship among younger black women was found, but no relationship among older black women. The difference in strength by age was also observed in white women, although the relationship only remained statistically significant in older white women, aged 50 plus (Looker, 2005). The relationship between body fat and serum 25-hydroxyvitamin D status in blacks is not clear (Wortsman et al., 2000). Skin synthesis of vitamin D has been estimated to account for the majority of vitamin D in the human body (Holick, 2009; Holick & Chen, 2008). Thus, it may be possible that body fat has a lesser impact in blacks because there is less vitamin D formed in the skin to sequester.

Correlation Between 25-Hydroxyvitamin D and Percent Excess Weight Loss After Surgery

Results in this present study also show that there is a correlation between the percentage of excess weight loss and 25-hydroxyvitamin D values after surgery. This positive correlation shows that as percent excess weight loss increases, 25-hydroxyvitamin D increases. Based on these results, it can be explained that as the patients’ decreased in body fat percentage they are able to absorb vitamin D in their bodies more easily. Another explanation hypothesized by researchers suggests that as patients become more physically active due to lower percent of body fat 25-hydroxyvitamin D increases. Physical activity has been shown in past research to improve 25-hydroxyvitamin D levels (Brock et al., 2010; Hintzpeter et al., 2008; Hirani et al., 2009). One
can assume these patients were also taking their recommended vitamin D₃ supplementation to help maintain higher levels of 25-hydroxyvitamin D values.

Many associated studies looking at the relationship between vitamin D and obesity are available. Research shows that a person with a normal BMI compared to an obese BMI will have a higher 25-hydroxyvitamin D level. In a research study composed in 2003 obese subjects with BMI’s ranging from 30.07-58.22 kg/m² were compared to normal/overweight subjects with a BMI range of 18.03-29.9 kg/m². Serum 25-hydroxyvitamin D was significantly lower in obese compared with non-obese subjects (23.5 ng/mL compared to 30.5 ng/mL) (Parikh et al., 2003). It has also been found that an increase of 1 kg/m² in BMI was associated with a decrease of 1 nmol/L in 25-hydroxyvitamin D (Lagunova et al., 2011). Vitamin D is more easily absorbed in a normal BMI person due to lower amounts of belly fat or visceral obesity as vitamin D appears to be absorbed by the fat tissue and can be more easily released into the blood stream with less fat (Wortsman et al., 2000).

An additional study examined 41 patients undergoing Roux-en-Y gastric bypass surgery and compared them to healthy non-obese subjects matched for age, sex, race/ethnicity and season of 25-hydroxyvitamin D drawn. Among the obese subjects 61% had a 25-hydroxyvitamin D level below 50 nmol/l versus 12% in the non-obese group (Goldner et al., 2008). The results from this study are aligned with prior research findings.

This information agrees with the present study proving that as percent body fat decreased, 25-hydroxyvitamin D values increased.

25-Hydroxyvitamin D and Body Weight

This analyses addressed the research question will 25-hydroxyvitamin D level increase as body weight percent decreases among men and women who have had bariatric surgery at six and
twelve months? Results of this study show that as body weight percent decreased, 25-hydroxyvitamin D level increased. It was also found in this study that as body weight percent decreased, it can predict the patient’s 25-hydroxyvitamin D level. This information was determined by performing a linear regression model to assess the relationship between the 25-hydroxyvitamin D level and the body weight decrease percentage at six months and twelve months post-surgery. The linear regression equation can predict the patients increased 25-hydroxyvitamin D level with a percentage of variance. After performing the linear regression, the r-square (percentage of variance) was higher in the first six months (12%) then in the second six months (7%). This means that the percent of body fat influences the 25-hydroxyvitamin D level 12% in the first six months and 7% from six to twelve months post-surgery. It has been determined in many studies that as percent body fat is lower, 25-hydroxyvitamin D is higher (Fish et al., 2010; Parikh et al., 2003).

In other related literature the relationship between serum 25-hydroxyvitamin D, anthropometric measurement and percent body fat of 90 young women was examined. Approximately 59% of subjects were 25-hydroxyvitamin D insufficient (≥29 ng/ml), and 41% were sufficient (≥30 ng/ml). Strong negative relationships were present between serum 25-hydroxyvitamin D and computed tomography measures of visceral and subcutis fat and dual-energy x-ray absorptiometry values of body fat. In addition, weight, body mass, and imaging measures of adiposity at all sites were significantly lower in women with normal 25-hydroxyvitamin D concentrations than women with insufficient levels (Kremer, Campbell, Reinhardt, & Gilsanz, 2009). This study is related to the present study showing the same results. As body fat was lower, 25-hydroxyvitamin D was higher.
The relationship between body fat content and 25-hydroxyvitamin D was studied in 410 healthy black and white women. The BMI range was from 17-30 kg/m². Percent of body fat was measured by a DXA scan. The levels of 25-hydroxyvitamin D decreased as total body fat increased. When analyzing the group by quartiles of total body fat, the mean 25-hydroxyvitamin D level in the group with less than 31% total body fat was 56.6 nmol/L, the group with 32-37% total body fat was 52.6 nmol/L, the group with 38-42% total body fat was 50.8 nmol/L, and the highest group of total body fat was over 42% with a 25-hydroxyvitamin D average of 44.2 nmol/L. These results suggest that total body fat is another influence on 25-hydroxyvitamin D levels besides other well-known variables like race, season and vitamin D dietary intake. This study indicates that it is the adiposity, not simply the body mass, that influences the 25-hydroxyvitamin D level (Arunabh, Pollack, Yeh, & Aloia, 2003). It is clear that the greater the body fat, the less likelihood of reaching optimal 25-hydroxyvitamin D. Body fat should be taken into consideration when assessing the oral vitamin D supplementation for patient’s pre and post-surgery as well as individuals not preparing for bariatric surgery.

The present study shows that as body weight percent decreases, 25-hydroxyvitamin D increases. Serum 25-hydroxyvitamin D was also predicted by body weight percent decrease. Knowing a patient’s body fat percentage can help in predicting the supplementation of vitamin D₃ that a patient should be given prior to and post bariatric surgery.

**Relationship between 25-hydroxyvitamin D status, calcium and PTH**

When assessing the relationship between 25-hydroxyvitamin D, calcium and PTH post-surgery at the six and twelve month time frames, a relationship was not identified until twelve months post-surgery. The results show that there was a negative significant relationship between
25-hydroxyvitamin D and PTH. The correlation showed that as 25-hydroxyvitamin D was lower when PTH was higher. The study results also showed that there was a significantly positive relationship between PTH and calcium. As PTH increased, calcium increased as well.

An inverse relationship between 25-hydroxyvitamin D and PTH is well established from past research (Steingrimsdottir et al., 2005). The serum level for 25-hydroxyvitamin D corresponding with the PTH inflection point has been interpreted as indicative of optimal calcium homeostasis and proposed as a marker of 25-hydroxyvitamin D sufficiency (Chapuy, Preziosi, & Maamer, 1997; Dawson-Hughes, Harris, & Dallal, 1997). A protection mechanism for the body for the maintenance of calcium homeostasis, in the setting of declined absorption of calcium, is the elevation of PTH, which directly causes an increased production of 1,25-dihydroxyvitamin D (calcitrol) and an increase in calcium reabsorption from the bone. Calcitriol improves both the absorption of calcium in the intestines and the bone-resorptive effects of PTH on the bone (J. M. Johnson et al., 2006).

PTH values in previous studies show that out of 127 patients at one year following gastric bypass surgery 21% had an elevated PTH value and a normal 25-hydroxyvitamin D value (Fish et al., 2010). In a related study looking at two different groups, one with long limb gastric bypass and the other group with short limb gastric bypass, PTH was measured post-surgery on a total of 243 patients. Elevated PTH was found in 88.9% of patients with a low 25-hydroxyvitamin D (<30 ng/mL). When looking at patients with a normal 25-hydroxyvitamin D value, 42.1% had an elevated PTH value (J. M. Johnson et al., 2006).

In the present study the results show that one year post-surgery if the 25-hydroxyvitamin D value was lower the PTH value is higher. This shows the same results as these related studies discussed. The elevated PTH level is protecting the body for the maintenance of calcium
homeostasis. This shows that the body is compensating for the lack of calcium resorption and is taking calcium from the bones. With the results from this study showing that as the patients were farther away from their initial surgery their 25-hydroxyvitamin D decreased and PTH increased is concerning because this can result in osteopenia, osteoporosis, and ultimately osteomalacia over time.

**Summary**

Rates of obesity have progressively increased over the last two decades. It is now clear that 25-hydroxyvitamin D deficiency is associated with obesity. Before global screening began for 25-hydroxyvitamin D deficiency after bariatric surgery, 25-hydroxyvitamin D deficiency was infrequently reported and typically not checked with lab work until many years after bariatric surgery (Goldner et al., 2008). After looking at factors that affect 25-hydroxyvitamin D and how to improve values, it is important to check 25-hydroxyvitamin D, calcium and PTH on all morbidly obese patients with routine labs before and after bariatric surgery to maintain in normal range and keep bariatric surgery patients nutritionally sound. Determining the amount of prescribed vitamin D taken through lab work can ensure that patients comply with advice from doctors and that dosages prescribed match vitamins purchased.
The purpose of this ex post facto study was to examine the link between serum 25-hydroxyvitamin D, body mass index (BMI), and percent of excess weight loss after laparoscopic bariatric surgery among morbidly obese men and women at a Midwest bariatric center. This chapter will conclude the study, delineate the limitations to this study, and provide recommendations for future research.

Conclusions

It has been well documented that 25-hydroxyvitamin D deficiency is an ongoing issue for morbidly obese bariatric surgery patients. It is important to take into account 25-hydroxyvitamin D deficiency before surgery when evaluating the impact bariatric surgery has on 25-hydroxyvitamin D values. The observed correlation between 25-hydroxyvitamin D values and BMI before surgery may suggest that increasing degrees of obesity are risk factors for more severe 25-hydroxyvitamin D deficiencies. In the present study as a patient lost a higher percent of their body weight post-surgery, their 25-hydroxyvitamin D value increased. The present study also investigated if differences existed between 25-hydroxyvitamin D levels based on gender,
race/ethnicity and the type of surgery (Roux-en-Y gastric bypass or gastric band) the patient received at the three different time frames (prior to surgery, between baseline and six months post-surgery and between six and twelve months post-surgery). It was concluded the only significant difference examined was between Caucasian (77) and African-American (18) patient’s 25-hydroxyvitamin D levels prior to surgery. African-American patients had a much lower baseline average of 25-hydroxyvitamin D levels.

It can be concluded as well that a patient’s percent of excess weight loss can predict the patient’s 25-hydroxyvitamin D value. This can help determine more accurately the vitamin D₃ supplementation that a patient should be taking based on the percent of weight they have lost.

Also determined in this study, serum 25-hydroxyvitamin D levels did not have a significant relationship with PTH and calcium until one year post-surgery. At one year, as 25-hydroxyvitamin D was lower, PTH was higher and as PTH increased, calcium did as well.

Bariatric surgery has become increasingly more popular over the last couple decades. The data found in this study suggests that it is important to test morbidly obese bariatric surgery patient’s before surgery to determine their 25-hydroxyvitamin D values to prevent problems after bariatric surgery caused by further deficient 25-hydroxyvitamin D values.

Limitations

As the reader examines the results of this study, several limitations must be considered.

- There are many variables that can affect 25-hydroxyvitamin D other than what was examined in this study. These variables include the type of medications the patients were taking, the time of year the 25-hydroxyvitamin D value was
checked, the vitamin D intake from food and how much 25-hydroxyvitamin D can be affected by caffeine.

- The effect exercise has on vitamin D was not taken into consideration.
- Hormonal regulation/imbalance effects were not examined in relation to vitamin D levels.
- It has been reported that vitamins produced in the United States have contained the incorrect amount of the vitamin listed on the labels; therefore, it is hard to determine if the supplements prescribed actually matched the dosage consumed.
- A low number of gastric band patients compared to gastric bypass patients made it impossible to compare the surgeries and how 25-hydroxyvitamin D would be affected by a specific procedure alone.
- The group of patients studied was mostly Caucasian women that had gastric bypass surgery.
- PTH was not measured consistently among patients before surgery; therefore the data could not be used in this study.
- The time frame for a patient to have surgery was not standardized.

**Recommendations for Future Research**

Based on the results of the present study, additional research on the link between serum 25-hydroxyvitamin D, body mass index (BMI), and percent of excess weight loss after laparoscopic bariatric surgery among morbidly obese men and women should be conducted to fulfill the many factors associated with the ongoing issue of 25-hydroxyvitamin D deficiency.
There are many suggestions for future research. The sample size in this study was small with a lack of diversity in ethnicity/race. It would have been supportive in this study to see if there were differences in the type of surgeries (gastric band vs. gastric bypass) in regards to 25-hydroxyvitamin D level prior to surgery, six months or twelve months post-surgery. Due to the small sample of gastric band patients a significant difference was not measured. Also, due to the small sample size there was not a significant difference between genders and race/ethnicity in relation to 25-hydroxyvitamin D levels six and twelve months post-surgery. The sample size included mostly Caucasian women that received gastric bypass surgery. In the future it will be important to have more comparable numbers when it comes to demographics and types of bariatric surgery.

The patients participating in this study were prescribed vitamin D₃ supplementation to take daily. The surgeon prescribing the supplementation could not routinely watch each patient take the vitamin D₃ supplement. The results could be skewed if the patient’s involved did not take the supplementation as they were told. In future research if this can be better monitored it would be helpful for a more accurate result.

This already obese population should also be compared to overweight and normal BMI populations to provide more detailed information on how much BMI or percent of total body fat can affect a person’s 25-hydroxyvitamin D level. This study was limiting in that the morbidly obese population was the only population assessed. In future research it will be essential to compare the different ranges of weight to have a better recommendation on the amount of supplementation of vitamin D₃ required based on BMI/total body fat for all populations. It will be especially significant for patients that will be having or have had bariatric surgery.
The amount of vitamin D the patient’s received from their food intake was not assessed in this study therefore was not taken into consideration when collecting the data. In future research monitoring vitamin D from food intake prior to surgery and post-surgery to assess the effects on 25-hydroxyvitamin D levels will help with more accurate results. The researcher would also recommend taking into consideration the medications that each patient was on pre and post-surgery to assess if it affects their 25-hydroxyvitamin D level. It is also suggested in future research to monitor the time of year 25-hydroxyvitamin D levels were drawn, as sun exposure plays a major role on 25-hydroxyvitamin D levels.

It would have been helpful to have each patient’s PTH level pre-surgery to determine if it was affected in a significant way after bariatric surgery. The PTH level was not collected due to all patients involved not having it measured before their bariatric surgery. The results only included the difference in PTH between six and twelve months post-surgery. If this level is obtained prior to surgery in future studies it may show a more significant difference in PTH levels and help with recommendations on calcium and vitamin D₃ supplementation to keep levels in optimal range and prevent bone health issues post bariatric surgery.

This study examined the time periods of prior to bariatric surgery, six months and one year post bariatric surgery. It will be important in future research to examine patient’s post bariatric surgery for 1-5 years or longer, measuring the same blood values. This research will support long-term bone health and bariatric patients nutritional health overall as they are further away from their bariatric surgery.
Summary

In summary, it is crucial to test 25-hydroxyvitamin D values pre-operatively and continuously post-operatively to help maintain a normal level. Normalization of 25-hydroxyvitamin D values after bariatric surgery is difficult to achieve due to not knowing the degree of surgery induced restriction and malabsorption. Clinicians and dietitians working with morbidly obese bariatric surgery patients need to be aware and focus on factors that can affect a patient’s 25-hydroxyvitamin D value. It is important to initiate screening for 25-hydroxyvitamin D deficiency pre-operatively and adjust the dose post-operatively based on 25-hydroxyvitamin D values along with PTH and calcium values. With continued, larger and more specific research we can pinpoint the amount of vitamin D₃ supplementation to prescribe uniquely to each patient. This will help morbidly obese bariatric patients be at more of a normal 25-hydroxyvitamin D level to be in a better position pre bariatric surgery for bone and overall health.
Bibliography


National Heart Lung and Blood Institute (2000). The practical guide identification, evaluation, and treatment of overweight and obesity in adults (pp. 88).


Appendix A
Institutional Review Board Documentation
Community Health Network

Jenna, I have reviewed your research proposal and have determined it to be exempt from IRB oversight. You may begin your data collection. Any changes made to the project will need to be approved by the IRB prior to implementation.

Please notify the IRB when you have completed your data analysis.

Sincerely

Beth Wilson
Administrative Assistant, IRB
Community Health Network
1500 N. Ritter Ave
Indianapolis, IN 46219
Office: (317) 355-4522
Fax: (317) 355-6102 or 351-7813
E-mail: bwilson@ecommunity.com
Appendix B
Institutional Review Board Documentation
Ball State University

Please note that Ball State University IRB has published the following Board Document on IRBNet:

Project Title: [301195-1] VITAMIN D STATUS OF MORBIDLY OBESE BARIATRIC SURGERY PATIENTS AT THE COMMUNITY BARIATRIC CENTER
Principal Investigator: Jenna Doerffler, Bachelor of Science in Dietetics

Submission Type: New Project
Date Submitted: January 24, 2012

Document Type: Exempt Letter
Document Description: Exempt Letter
Publish Date: February 1, 2012

Should you have any questions you may contact John Mulcahy at jmulcahy@bsu.edu.

Thank you,
The IRBNet Support Team
Appendix C
CITI Completion Certificate

COLLABORATIVE INSTITUTIONAL TRAINING INITIATIVE (CITI)
SOCIAL & BEHAVIORAL RESEARCH - BASIC/REFRESHER CURRICULUM COMPLETION REPORT

LEARNER: Jenna Walker (ID: 2084047)
DEPARTMENT: Dietetics
EMAIL: jndoerffler@bsu.edu
INSTITUTION: Ball State University
EXPIRATION DATE: 01/02/2017

SOCIAL & BEHAVIORAL RESEARCH - BASIC/REFRESHER: Choose this group to satisfy CITI training requirements for Investigators and staff involved primarily in Social/Behavioral Research with human subjects.

COURSE/STAGE: Refresher Course/2
PASSED ON: 01/03/2014
REFERENCE ID: 11742782

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<th>REQUIRED MODULES</th>
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For this Completion Report to be valid, the learner listed above must be affiliated with a CITI Program participating institution or be a paid Independent Learner. Falsified information and unauthorized use of the CITI Program course site is unethical, and may be considered research misconduct by your institution.

Paul Braunschweiger Ph.D.
Professor, University of Miami
Director Office of Research Education
CITI Program Course Coordinator

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To whom it may concern,

I give Jenna Doerfler-Walker permission to review patient records [2008-2010] at Community Bariatric Clinic. Only files that have on record signed informed consent will be accessed. It is Community Bariatric Clinic’s surgery protocol to have patients sign a consent form prior to their bariatric surgery stating that lab information may be used for research studies. Patients are free to waive informed consent if they chose without prejudice. If you have any further questions please contact me at jusab@ecommunity.com.

Best Regards,

Jane Wilson Usab
Bariatric Program Administrator
Community Bariatric Surgeons
7250 Clearview #100
Indianapolis, IN 46256
APPENDIX E
Authorization for the Release of Health Information for Research

Community Hospital Indianapolis
Community Hospital North

Informed Consent Statement for Participation in a Clinical Research Study

This is NOT the consent for your surgery

Title of Research Study: Bariatric Outcomes Longitudinal Database (BOLD) Research Study

Surgeon: Keenan Berghoff, M.D.

Hospital: Community Hospital North

Principal Investigator: Keenan Berghoff, M.D.
7250 Clearvista Drive, Suite 355
Indianapolis, IN 46256

Research Institution: Community Hospital North
Bariatric Services
7250 Clearvista Drive, Suite 355
Indianapolis, IN 46256

Telephone Number: (317) 621-7771

Data Coordinating Center: Surgical Review Corporation
4800 Falls of Neuse Road, Suite 160
Raleigh, NC 27609

Introduction:
You have been asked to take part in a research study being conducted by Community Hospital North, Bariatric Services and Surgical Review Corporation. The study is about bariatric (weight loss) surgery. Before agreeing to take part in the study, it is important that you read and understand the following information regarding the study. Taking part in the research is voluntary. If you decide not to take part in the study you will not be penalized or lose any benefits. You can still have weight loss surgery. You may stop taking part in the study at any time without penalty.

This consent form may contain wording that you do not understand. You should ask your surgeon or coordinator to explain any words or information in this consent form that you do not understand.

IRB Approved
December 22, 2009

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Subject Initials
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Participants in the Study:
- All patients who are having weight loss surgery performed at an American Society for Metabolic and Bariatric Surgery (ASMBS) Bariatric Surgery center of Excellence, including centers which have received Provisional Status designation, will be asked to take part in the study.
- All patients having surgery performed by a surgeon who is a Fellow of the ASMBS will be asked to take part in this study whether or not the surgery is performed at an ASMBS Bariatric Surgery Center of Excellence.

Purpose of the Study:
The weight loss surgery itself is not part of the study. It will be performed in the same way whether or not you agree to take part in the study.

The purpose of this study is to record and compare the long term results and effects of several types of weight loss surgery. By comparing the type of surgery performed and the health of patients for five years after their surgery, we hope to learn:
- what types of patients do best after surgery
- the types of surgery that are most helpful, and
- which types of surgeries remain most helpful after five years.

Because you intend to have weight loss surgery, we would like your surgeon to send us information about your medical condition and your surgery and send us information about your health and weight loss each year for five years following your surgery.

Study Procedures:
If you choose to take part in this study, your surgeon will send health information about you to the Surgical Review Corporation. Information will include:

- Your name (optional)
- Your year of birth
- Your height
- Your weight
- Any prior surgeries
- The date of hospital admission and date of discharge for your weight loss surgery
- The type of weight loss surgery performed
- Your medical condition before, during and immediately after the surgery
- Your health condition and weight following your surgery each year for five years following your weight loss surgery.

In the future, the researchers may ask you to take part in other research studies about weight and weight loss surgery. You do not have to take part in these studies unless you want to. You can take part in future studies at the same time that are are you are taking part in this study.
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If you decide not to have weight loss surgery, or if the surgery does not occur for other reasons, you will no longer be part of this research study.

If you decide not to take part in the study, we will collect demographic information including your year of birth, gender, race, ethnicity, height and weight in a manner that cannot be traced back to you in order to have a record of the general medical condition of the people who have been asked but decided not to take part.

There is currently no expiration date for this study.

Risks of Participating in this Study:
There are no risks of physical harm associated with participating in the BOLD research study. The study does involve possible inconvenience in reporting your medical condition. There is a small risk of emotional distress in the event your medical information is inadvertently disclosed to unauthorized third parties.

Benefits:
Participation in the BOLD research study is not expected to provide any direct benefits to you. We hope the information and knowledge gained from the study will help surgeons improve the way the surgery is performed and better understand the risks and benefits of each type of weight loss surgery.

Compensation:
You will not be paid for participating in the BOLD research study. We assume no obligation to pay any money or provide free medical care in case this research study results in any harm to you.

Confidentiality of Records:
As part of this study, identifiable health information or protected health information ("PHI") about you will be collected and used. The PHI will include demographic information (including your name (optional), year of birth, gender, ethnicity, and race), your medical history including prior surgeries and medical conditions, information regarding your weight loss surgery, and information regarding your medical condition following your surgery.

Your name may be collected at the option of your surgeon. If your name is collected, it will not be disclosed to the researchers and will only be accessed by your surgeon or his/her staff.

By signing this consent form, you are authorizing the Principal Investigator and his employees and agents, employees and researchers at Surgical Review Corporation, and researchers at East Carolina University working with Surgical Review Corporation on this study to use your PHI in connection with this research study and to further disclose your PHI to representatives of the Institutional Review Board affiliated with Community Hospital North, Dr. Keenan Berghoff, agents of the U.S. Food and Drug administration or other U.S. Government agencies, and other authorized persons. Although we will take reasonable steps to protect your identity as much as possible, confidentiality cannot be absolutely guaranteed. Although not likely, it is possible that someone receiving PHI collected under this Consent could potentially re-disclose it, in which the PHI may no longer be protected under the federal rules that govern the use and disclosure of your PHI.
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If results from this research study are published, you will not be identified by name. To help protect your privacy a Certificate of Confidentiality has been obtained from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state or local civil, criminal, administrative, legislative or other proceeding. The researchers will use the Certificate to resist any demands for information that would identify you, except that the Certificate cannot be used to resist a demand for information from personnel of the U.S. Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research study. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

Authorization: 
See Community Health Network Notice of Privacy Practices

Questions: 
Dr. Keenan Berghoff, the Principal Investigator, will be available to answer any questions concerning this research, now or in the future. You may contact Dr. Keenan Berghoff at 317-621-7771. A patient representative who is not associated with this research to whom you may address complaints about this study, as well as questions about your rights as a research participants, is Dale Theobold, MD, PhD, Chairman, Community Hospital Indianapolis, Institutional Review Board, at (317) 355-4522. If you have additional questions, you may contact the Surgical Review Corporation at toll free 866-746-0646.

Costs of the Weight Loss Surgery 
You or your insurance company will be billed for all costs of the weight loss surgery. We assume no obligation to pay any money or provide free medical care for your surgery or for any complications which may result from your surgery.

Costs of Participation in the Research Study 
There are no costs to you or your insurance provider for participating in the BOLD research study. No medical or surgical procedures or tests are performed as part of this study.

Your Rights as a Participant: 
Participating in this study is voluntary. You do not have to take part in this study in order to have weight loss surgery. If you decide not to be in this study or decide to stop participating after it has already started, you may stop at any time without penalty. Your decision not to take part will not affect your medical care in any way.

You have the right to change your mind about permitting us access to your personal health information. If you decide to take away this permission you must notify your surgeon in writing. Any information collected up to the time you take away your
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permission may still be used. Deciding to no longer allow your information to be used in
the study will not result in any penalty or loss to you.

You may choose to withdraw this Consent as provided under the Health Insurance
Portability and Accountability Act of 1996 (HIPAA) at any time after you have signed it
by providing your surgeon with a written statement that you wish to withdraw this
Consent. Your withdraw of this Consent will be effective immediately and your
protected health information can no longer be used or disclosed for research purposes,
extcept to the extent your surgeon has already taken action in reliance on your consent. In
addition, your protected health information received before you withdrew consent may
continue to be used or disclosed in order to preserve the integrity of an ongoing study.

Consent to Participate

Title of Research Study: Bariatric Outcomes Longitudinal Database (BOLD)

I have read all of the above information. This study has been explained to me. I
volunteer to take part in this research study. I have had a chance to ask questions,
and I have received satisfactory answers to the questions regarding areas I did not
understand. I give permission to use my medical information as described in this
consent form. (A copy of this signed and dated consent form will be given to the
person signing this form as the participant or as the participant’s authorized
representative.) I understand that I will not lose any rights to which I am otherwise
entitled.

By my signature I acknowledge receipt of a signed and dated copy of this BOLD
Informed Consent document.

(Print Patient Name)

(Signature of Patient or Patient Legal Representative) Date

Person administering consent: I have conducted the consent process and orally
reviewed the contents of the consent document. I believe the participant understands the
research.

(Print name of person obtaining consent)

(Signature of person obtaining consent) Date

Physician’s Statement: I have offered an opportunity for further explanation regarding
the nature and purpose, the potential benefits and possible risks associated with
participation in this research study and have answered any questions that have been
raised by the individual whose signature appears above.

Date: ____________________ Physician’s Signature: ____________________

iRB Approved
December 22, 2009

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Subject Initials ______