The Effects of Laparoscopic Gastric Bypass Surgery on Patients with Obstructive Sleep Apnea

by

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ABSTRACT

Roux-en-Y Gastric bypass (RYGB) surgery is widely accepted as the most successful treatment of obesity, and has also been shown to eliminate a number of comorbidities associated with excess body weight including Obstructive Sleep Apnea (OSA). Despite such favorable effects, few studies have systematically examined the effect that the surgery has on health-related indices of obese patients being treated concomitantly for OSA. The purpose of this research was to examine these effects when patients were compliant with OSA treatment. This study was a prospective, within-subjects’ design, and was part of a larger, single-center pilot study. Participants included six females who presented for RYGB and were diagnosed with OSA, which was being treated with CPAP therapy prior to surgery. They completed a series of study visits at postoperative follow up. The subjects completed a series of questionnaires at each visit, and anthropometric data were measured. Other assessments included blood lipid profiles, spirometry testing, and polysomnography. OSA treatment compliance of all participants was monitored closely, and those who were non-compliant (<50%) were excused from the study. Analyses showed LRYGB to impart significant loss of body weight (and BMI), neck circumference, and improvement in SAQLI scores, total cholesterol, and AHI in the immediate (up to 6 month) postoperative period. However, our analysis did not reveal any statistically significant changes in triglyceride, HDL cholesterol, or LDL cholesterol concentrations, or in spirometric indices of lung function postoperatively. Our results have demonstrated that bariatric surgery imparts a pronounced improvement in the health-related indices outlined in the study, and that are sustained over time in the immediate postoperative period.
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And to my fiancé Joe, thank you for your love and words of encouragement at the times when I have needed them the most.
CHAPTER 1

Introduction
Obesity has become an increasingly serious epidemic in the United States since the 1980’s. Prevalence of the condition escalated from 22.9% between 1988 and 1994 to 34% in 2008 [1, 2]. There are a number of comorbid conditions associated with obesity including diabetes mellitus, cardiovascular disease, cancer, obstructive sleep apnea, and other metabolic abnormalities [2-10]. A recent report stated that the cost of obesity has reached nearly 300 billion dollars per year, and overweight and obesity have been shown to increase the rate of several common adverse medical conditions, resulting in a remarkable economic costs to society [11].

Obstructive sleep apnea is a disorder that is closely linked to obesity, and prevalence of both conditions is increasing in tandem [12-17]. Sleep apnea is a condition characterized by recurrent incidences of upper airway obstruction during sleep, which are caused by increased upper airway collapsibility [18]. Epidemiological studies continue to show that Obstructive Sleep Apnea (OSA) is also associated with a number of other comorbid cardiovascular conditions including hypertension, coronary artery disease, myocardial infarction, congestive heart failure, and stroke [4, 19-24].

Bariatric surgery (typically, gastric bypass surgery) is widely accepted as the most successful treatment of obesity and has also been shown to eliminate a number of comorbidities (including OSA) associated with excess body weight. The number of bariatric surgeries performed each year is expected to continue rising as obesity remains a chronic health concern in the United States [25]. Although bariatric surgery has been shown to help attenuate, if not resolve, obstructive sleep apnea in addition to promoting significant weight loss, the degree to which it may affect both conditions when they occur concomitantly is not completely clear. The purpose of the study proposed herein is to demonstrate the health-related effects of gastric bypass surgery in obese patients with OSA.
CHAPTER 2

Review of the Literature
2.1 Obesity

Obesity, defined as the accumulation of excessive body fat, is classified by having a body mass index (BMI) of $\geq 30 \text{ kg/m}^2$. The BMI is a calculation used to estimate an individual's amount of body fat and is calculated using weight in kilograms divided by height in meters squared. Four classes of obesity have been established based on BMI and are depicted in Table 2.1.

<table>
<thead>
<tr>
<th>Class of Obesity</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild obesity (Class 1)</td>
<td>30-34.9 kg/m$^2$</td>
</tr>
<tr>
<td>Moderate obesity (Class 2)</td>
<td>35-39.9 kg/m$^2$</td>
</tr>
<tr>
<td>Morbid/severe obesity (Class 3)</td>
<td>40-49.9 kg/m$^2$</td>
</tr>
<tr>
<td>Super morbid obesity (Class 4)</td>
<td>$\geq 50 \text{ kg/m}^2$</td>
</tr>
</tbody>
</table>

Table 2.1 Classes of obesity. Classes of obesity are determined by BMI and are divided into four categories [26].

The life expectancy of a severely obese individual (Class 3) is reduced by 5 - 20 years when compared to that of a non-obese individual and as a result, obesity is now known as one of the major causes of preventable death in the United States. In fact, nearly 280,000 deaths each year are the result of “overnutrition”, a rate that is second only to smoking [27]. According to data from the CDC in 2008, nearly 72 million Americans were obese, and the number is expected to continue rising [2]. Women are more likely to be obese than men, and individuals of African American, Native American, and Hawaiian descent are more prone to this disease. As the prevalence of obesity becomes greater, so does the risk for other chronic disease including cardiovascular disease, some cancers, diabetes mellitus and hypertension. In addition, obesity often predisposes and increases presence of other comorbidities such as obstructive sleep apnea and other breathing disorders, likely due to the increased neck circumference and central adiposity associated with the obese population [4, 5, 10, 28, 29]. A linear
relationship between the degree of obesity and the risk of developing one or more of these comorbidities has been documented in recent literature [4].

Although BMI is the standard measurement for obesity, it is a suboptimal indicator of body composition, and even less appropriate when measuring body fat distribution [7]. Obesity-related comorbidities such as Obstructive Sleep Apnea (OSA) and metabolic conditions (glucose intolerance, hyperinsulinemia, diabetes, hypertriglyceridemia, and hypertension) are often the result of undesirable body fat distribution, where upper/central body fat is greater than fat deposition in the lower extremities. As a result, other anthropometric measurements such as neck circumference can be more useful than BMI to determine disease risk, especially when there is concern of sleep related disorders [7]. A neck circumference of < 37 cm in men and < 34 cm in women indicates that these individuals are less likely to be overweight or obese, while persons with a neck circumference greater than these values may require further examination to address risk factors associated with abdominal obesity [7].

In addition to neck circumference, the Mallampati score (MS) is another valuable clinical assessment used to evaluate risk of OSA. There are four MS classes (1 - 4) that use tongue size to compare visibility of the uvula, hard palate, soft palate, and tonsils. As MS increases, visibility of anatomical structures of the oral cavity becomes attenuated [30]. Assessment of MS is both simple and noninvasive, and according to one study can independently predict presence and severity of OSA [31]. Another study examined nasal patency, MS, neck circumference, and BMI to determine risk factors associated with OSA. Participants underwent a diagnostic polysomnogram (PSG), which revealed a significant relationship between MS and apnea hypopnea index (AHI; a measure of OSA severity). MS scores of three or greater indicated a higher prevalence of OSA, suggesting that MS scores can be clinically indicative of risk of developing the syndrome
The previous studies indicate that patients with risk factors described above, in addition to MS scores of three or more, should undergo further testing to evaluate the presence of OSA.

2.2 Obesity-Related Healthcare Costs

Along with obesity-related complications comes an increased cost for society to pay for the medical fees associated with the disease. The National Obesity Education Initiative of the National Heart, Lung, and Blood Institute and the National Institute of Diabetes and Digestive and Kidney Diseases held the first expert panel on the identification, evaluation, and treatment of overweight and obesity in adults in 1995 in order to address guidelines of care for the 97 million Americans who were overweight or obese [32]. The estimated cost attributable to obesity and its related diseases have reached nearly $100 billion annually in the United States, and of this, approximately $51.6 billion are the medical costs related to diseases associated with the epidemic [32]. Nearly 3% of the obese population was morbidly/severely obese (Class 3) in 2000 and this accounted for nearly 20% of the total expenditures related to total medical expenditures that year [5, 6]. Clearly, the link between obesity and increased health risks poses an additional threat of inflated medical care and disability costs in the United States, and these costs will continue to increase with the growing population of obese Americans.

2.3 Obesity-Related Comorbidities

Obesity predisposes a number of comorbid conditions as a result of excess body weight and increased waist circumference including hypertension, dyslipidemia, type 2 diabetes, coronary heart disease, stroke, osteoarthritis, obstructive sleep apnea, impaired respiratory function, and some cancers [3, 5, 9, 10, 12, 33-35]. Obesity
contributes to cardiovascular risk as a result of its impact on dyslipidemia, hypertension, glucose intolerance, inflammatory markers, and obstructive sleep apnea/hypoventilation [4, 20-24, 33]. Thus, the altered metabolic profile that is characteristic of obese persons causes a variety of changes in cardiac structure and function, largely because of the accumulation of adipose tissue [33]. As such, obesity can predispose multiple cardiac complications including coronary heart disease, heart failure, and sudden death as a result of excess body weight [33].

Pathophysiologic complications and shortened longevity as a result of obesity are often related to pulmonary health. Excess body weight can reduce the capacity an individual has for exercise because of the increased amount of energy required to complete normal daily activities. Obese individuals are unable to increase oxygen consumption enough to compensate for their excess body fat, thereby subsequently limiting cardiopulmonary function [36].

Obesity can also have multiple effects on respiratory function, including variations in respiratory mechanics, reduced respiratory muscle strength and endurance, suboptimal pulmonary gas exchange, and less control of breathing [37]. Ultimately, these effects can manifest as suboptimal values for pulmonary function tests [37]. It is likely that these changes in lung function are caused by extra adipose tissue in the chest wall and abdominal cavity [37]. Anatomic and functional alterations of the pharyngeal airway that are associated with central obesity (body fat localized around the abdomen) are also more prominent in obese persons, thus contributing to the development of OSA [20]. BMI’s that exceed 30 kg/m², MS scores of three or four, small or receding mandible structure, and poor head or neck movement can all be risk factors associated with airway obstruction and OSA in the obese population. Furthermore, OSA may itself
predispose individuals to worsening obesity because of sleep deprivation, daytime somnolence, and disrupted metabolism [20].

2.4 Obesity and Health-Related Quality of Life

Adverse physical function secondary to weight gain has long been a concern for clinicians and other practitioners. However, a diminished health related quality of life as a result of excess weight has broadened the spectrum of obesity-related consequences due to the fact that an obese person is unable to live a full and active life. Empirical evidence consistently reveals that consequences of obesity are not limited to poor physical health alone, and that functional capacity and quality of life are severely impacted as a result of increased body weight.

One’s Health-Related Quality of Life (HRQOL) encompasses emotional, physical, social and subjective emotions of well-being [3]. Subjective assessment of medical and health-related outcomes is important because it evaluates the impact of specific diseases on ones’ life, provides information beyond medical treatment, and helps practitioners to understand why patients’ attitudes differ throughout the disease population. In addition, HRQOL assessments can help to evaluate the effects of treatment and influence clinical dimension, service provision, health care expenditures, and public policy [3].

It is widely accepted that obesity reduces HRQL, and a number of studies have been published exploring this relationship. For example, Stewart and Brook (2007) found that excess weight was related to diminished ability to function (such as walking, climbing stairs, working, and playing sports), pain, anxiety, poor health perception, and reduced activity compared to people of healthy weight. The authors also concluded that as more weight accumulated, level of functioning was reduced [38]. An ongoing national
survey of obese people in Sweden found that obesity was associated with high levels of anxiety and depression, in addition to poorly-perceived quality of life [39].

2.5 Obesity-Related Psychopathology

Current research indicates that there is a potential link between obesity and depression, and it has been estimated that 10% of obese population are also depressed [40]. According to Faith et. al. (2002), depression is one of the most common psychiatric disorders among obese patients seeking outpatient care, and its presence may result in poor treatment compliance and health outcomes, thereby hindering weight loss attempts [35, 41]. Furthermore, data have shown that the obesity itself can exacerbate depressive symptoms, and children/adolescents who are depressed during childhood have a greater likelihood of obesity during adulthood [42, 43]. Thus, severity of one’s depression may indicate the strength of the relationship between adult-onset obesity and early depression.

Numerous other studies have investigated the connection between obesity and depression. For example, Wadden et al. (1988) investigated outcomes in 128 obese women who underwent 48 weeks of behavioral intervention including diet alone, diet in addition to aerobic exercise, diet and strength training, or a combination of all three. The investigators assessed effects on body composition, resting metabolic rate, and depression. In addition to weight loss (approximately 15.1 pounds), it was found that mean scores on the Beck Depression Inventory (BDI, a tool used to assess clinical indicators of depression) were also reduced significantly between baseline and week 48. Follow-up evaluations were conducted one and three years after treatment, and it was found that increases in BDI paralleled weight regain. These results indicate that
depression can improve with weight loss, but may also predispose rebound weight-gain in individuals who have persistent symptoms [44].

Sherwood et al. (1999) also examined the role that depression plays in weight loss. In the study, 444 women diagnosed with binge eating disorder were assigned behavioral interventions that focused on diet and/or exercise. Although these treatments were found to reduce binge eating and promote significant weight loss, the effects appeared to be moderated by the presence of depression, suggesting that behavioral interventions are not as effective in people who are depressed, and that treatment of depression may be necessary in order to effectively promote weight loss in patients with psychopathology related to disordered eating [45].

Other evidence suggests that the link between obesity and depression may be moderated based on severity of obesity. For example, data from National Health and Nutrition Examination Survey demonstrated an association between class of obesity and presence of depression in adolescents (aged 15 – 19). Those who had healthy weights in relation to height were less likely to be depressed than obese subjects in the 95th to 100th percentile, where rates ranged from 20% (boys) to 30% (girls) [46].

In addition to being depressed, obese people may also be more likely to demonstrate disordered eating patterns such as Night Eating Syndrome (NES) [47-50]. NES is a syndrome characterized by morning anorexia, evening hyperphagia, insomnia, and conscious nocturnal ingestions [50-55]. Individuals with this syndrome are thought to have abnormal circadian rhythm, occurring with disruption to normal sleep-wake cycles. This in turn can cause hormonal imbalances that may contribute to both depression and aberrant eating behavior [56]. Data have shown that when matched for weight and age, individuals with NES are found to be more depressed than those without NES [49]. It
should also be noted that night eaters become progressively more depressed throughout the day as hyperphagia intensifies, and it is thought that the abnormal circadian patterns they experience can result in increased prevalence of depression and therefore cause disordered eating patterns including morning anorexia, evening hyperphagia, and nocturnal ingestions [56].

2.6 Bariatric Surgery

The most successful medical treatment for obesity is bariatric surgery. This procedure involves reducing the size of the stomach and/or changing the path food takes through the digestive system, and can result in up to 50-70% loss of body weight [57]. As the obesity epidemic escalates, the number of candidates for bariatric surgery continues to rise. The incidence of bariatric surgery increased from 13,386 procedures in 1998 to 121,055 in 2004 [4-6, 29]. It is estimated that nearly 220,000 took place in 2010 [29]. Medicare guidelines state that in order to qualify for bariatric surgery, it must be “medically appropriate” and the surgery must be “performed to correct an illness that caused the obesity or was aggravated by the obesity” [1].

Although some may view surgical intervention for obesity as an excessive health risk, it should be noted that interventions with other more conventional strategies are often ineffective. Patients who have undergone weight loss following surgery can expect to lose approximately 60% of excess body weight on average, which greatly exceeds outcomes for those who rely on more traditional weight loss strategies [46]. When these latter methods of weight loss (such as low calorie diets or physical activity) are utilized to treat obesity, weight regain usually occurs, and maintenance of weight loss after utilization of these methods is somewhat rare [1]. For example, consumption of a low calorie diet (where total energy intake is lower than total energy expenditure) can result in a loss of up to 8% of excessive body weight over a six-month period, but it is likely
that this weight will be regained after one year [1, 32]. Physical activity is also sometimes used as a primary weight loss method of treatment for obesity. However, results are very modest and on average only 2-3% loss of body weight results when diet is not incorporated [5]. Physical activity is primarily essential for weight maintenance and is most effective when a combined with diet and behavioral therapy. Although many obese individuals have attempted conventional weight loss methods such as the aforementioned, the obese population as a whole is seldom successful with long-term weight management that does not have a surgical component. While research has shown that weight loss as a result of bariatric surgery can be maintained for up to sixteen years postoperatively, in contrast, rebound weight gain after traditional mechanisms occurs as rapidly as between six and twenty four months [5].

Surgical intervention is most often the result of failed attempts at conventional weight loss strategies, and is currently the most effective and durable treatment for the clinically obese. Numerous studies have demonstrated that comorbidities of obesity are significantly improved or eliminated after bariatric surgery and that the surgery elicits superior health-related outcomes when compared to those of other conventional treatments [4-6, 29].

Bariatric surgical procedures are typically classified as either restrictive, malabsorptive or a combination of both [29]. Restrictive procedures elicit reduced energy intake by significantly decreasing the stomach’s capacity, while malabsorptive procedures involve reducing the size of the functional small intestine, which in turn causes nutrient malabsorption, resulting in pronounced weight loss. Types of gastric bypass surgery include Roux-en-Y gastric bypass (RYGB), vertical banded gastroplasty, gastric banding, and bileopancreatic diversion and duodenal switch.
RYGB is a procedure that incorporates restriction and malabsorption and achieves greater weight loss and resolution of comorbidities, when compared to other bariatric surgical techniques such as gastric banding (Figure 1) [29, 58]. The RYGB involves restricting caloric intake by reducing the stomach’s capacity to 20-30 mL (about one ounce), and entails reconfiguration of the small bowel, which subsequently causes reduced energy absorption. Studies have shown that this surgery also results in reconfiguration of neuronal and gut hormones related to energy balance, thereby facilitating even more weight loss [58]. RYGB is currently used more frequently in the United States than any other bariatric procedure, and is referred to as the “gold standard” because of its successful treatment of obesity [29, 58].

In a systematic review and meta-analysis of 22,094 patients who had undergone bariatric surgery, Buchwald et. al (2004) analyzed postoperative effects on diabetes, hyperlipidemia, hypertension, and OSA. Though the authors reported that OSA had resolved in more than 80% of participants, only a few of the studies used included objective measurements (i.e. number of apneas and/or hypopneas), making these results difficult to interpret. The extracted bariatric surgery literature is copious on this subject and concludes that a substantial majority of patients who undergo bariatric surgery not only succeed in weight loss but also experience marked improvement of other comorbid conditions [8].
Figure 2.1. Roux-en-Y gastric bypass. In a Roux-en-Y gastric bypass, the stomach is made smaller by creating a small pouch at the top of the stomach using surgical staples or a plastic band. The smaller stomach is connected directly to the jejunum, bypassing the rest of the stomach and the duodenum. (Adapted from [59]).

2.7 Complications of Bariatric Surgery

Common complaints following bariatric surgery include nausea, vomiting, diarrhea, constipation, and gastroesophageal reflux [19]. An individual diet plan is created to help minimize complications and will note tolerance of specific foods and appropriate serving sizes. The diet must advance postoperatively from clear liquid, to full liquid, then to pureed foods, and finally to a regular diet as tolerated [60]. Protein intake is strongly encouraged to promote healing of the gastrointestinal system. Special attention must also be given to vitamins and minerals (especially calcium, folate, iron, fat-soluble vitamins A, D, E, and K, and vitamins B₁ and B₁₂) because of the malabsorption associated with surgical weight loss [25, 60].
It is important for the surgery candidate to understand that treatment should not stop postoperatively. Bariatric surgery will cause malnutrition, and a team of health care professionals is required to monitor changes the body will undergo following surgery. Percentage of body fat, anemia, and vitamin and mineral levels must be closely monitored to prevent potentially serious conditions [60]. Behavioral modification and lifestyle changes are necessary to experience the benefits of bariatric surgery and to improve quality of life postoperatively.

2.8 Bariatric Surgery and Cardiovascular Risk

Dyslipidemia (defined as abnormal blood-lipid concentrations, often requiring use of antihyperlipidemic medications) is strongly associated with excess body weight and is diagnosed among 18-74% of individuals preparing for bariatric surgery [61-69]. It has been established that bariatric surgery helps to reduce cardiovascular risk and reduce the prevalence of dyslipidemia from anywhere between 4% and 100% [61, 64, 67, 69-72]. Bariatric surgery has been shown to decrease total cholesterol, LDL-C and triglycerides, while increasing HDL-C, thus minimizing cardiovascular risk and decreasing the need for antihyperlipidemic medications [72, 73].

2.9 Cost Effectiveness of Bariatric Surgery

It is widely accepted that bariatric surgery can result in significant weight loss and in turn resolve a number of comorbid conditions. Despite these facts, the cost effectiveness of the procedure remains unclear. In one study, 3,651 severely obese patients who underwent surgery were matched to a control subject that had no intervention. The patients were matched for age, gender, geography, health status and baseline medical costs. Participants were predominantly female, and mean age was 44 years. Comorbid conditions among the patients included hypertension, high cholesterol, and diabetes.
Costs were analyzed for six months prior to surgery, the cost of surgery itself, and postsurgical care for an average of 18 months. Prescription drugs, doctors’ visits, and hospitalization were included in the analysis and compared to claims for the control patients who didn’t present for surgery. Results indicated that insurance companies experienced return on investment 25 months following laparoscopic surgery (average cost of $17,000). However, after “open” (i.e. non-laparoscopic) surgeries, (costing an average of $26,000), it took about 49 months for the companies to “break even”. It should also be noted that cost savings of bariatric surgery are also expected to increase as surgical technology (i.e. robotic-assisted and minimally-invasive technique) improves and surgeons gain more experience with the procedure [74].

2.10 Obstructive Sleep Apnea (OSA)

OSA is a disorder of the pharyngeal (upper) airway that results in consistent disruption of breathing during sleep. The presence of five or more disruptions that last ten seconds or longer per hour of sleep, in addition to daytime sleepiness results in a diagnosis of the syndrome [47, 57, 58, 75, 76]. The severity of OSA is typically classified using the Apnea Hypopnea Index (AHI) [47] where values of 5 -14, 15-29, and > 30 indicate mild, moderate and severe OSA, respectively [75]. The word apnea refers to pauses in breathing during sleep, while hypopnea can be defined as a momentary reduction of respiratory flow or a moderate cessation of air flow [75, 77]. Together, these disruptions produce arousals, fragment sleep, and are frequently associated with oxygen desaturations [77]. OSA not only compromises pulmonary function by affecting the airways of the respiratory system, but has also been demonstrated to cause weight gain as a result of poor sleep, altered glucose metabolism, and imbalances to hormones that regulate energy balance (i.e. leptin, ghrelin, and orexin) [78]. Furthermore, untreated,
OSA can lead to other complications including pulmonary and systemic hypertension, myocardial infarction, stroke, and premature death [4, 22, 23, 28, 77, 79-83].

2.11 Diagnosis of OSA

Diagnostic polysomnography (PSG) is the most common method for diagnosis of OSA. During a laboratory-based PSG, the patient spends the night at a nocturnal clinical setting (sometimes called a Sleep or PSG Laboratory) where physiological characteristics such as air flow through nasal passages, oxygen saturation, abdominals, chest wall movement, and body position are monitored by sleep technicians while the person is asleep [75]. In cases where the diagnostic PSG reveals the presence of OSA, the patient will subsequently undergo a Positive Airway Pressure titration test, in order to determine the best course of nocturnal treatment.

2.12 Treatment of OSA

OSA is typically treated with nocturnal, continuous positive airway pressure (CPAP). This therapy is the most commonly used positive airway pressure device, and is the result of numerous research studies and technological advances [77]. The first report of CPAP therapy involved five patients being treated by Sullivan and colleagues [81]. The OSA patients were treated with a homemade device using a vacuum-cleaner blower motor and some tubing, and the investigators noted that the positive airway pressure that was produced resulted in pneumatic splinting of the upper airway, which resulted in increased functional capacity and decreased upper airway edema.

Therapeutically, CPAP works by providing a consistent distending pressure to offset the collapse of the oropharynx (resulting from negative thoracic pressure upon inspiration), which is characteristic in OSA patients. A CPAP machine produces continuous 20 to 60 L/minute flow using a fan or turbine at a set pressure [77]. This
airflow then creates a 4 to 20 cm H\textsubscript{2}O pressure delivered to a mask or nasal prongs through flexible tubing. This pressure remains constant during inhalation and exhalation, and provides no mechanical assistance to the patient. The CPAP machine must be able to provide enough airflow so that strong inhalation does not create a large enough drop in pressure to alter the pneumatic splinting process. So long as the machine is properly titrated, the occurrence of respiratory events during sleep is greatly reduced and effective treatment may even completely resolve sleep disordered breathing [77].

Over the past two decades, marked improvements have been made in CPAP machine technology. Machines are lighter, quieter, and many allow for compliance monitoring. Traditionally, the positive pressure was delivered with a nasal mask or nasal pillows, but technology has advanced to include full-face masks or oronasal masks for patients who are accustomed to breathing through the mouth. PAP machines are now available as continuous positive airway pressure (CPAP) or autotitrating positive airway pressure (APAP) [77]. APAP works in a similar way as CPAP, except that it measures a patient’s inhalation and exhalation on a breath-by-breath basis, and automatically adjusts the system’s in/out air pressure in response to the sleeper’s varying needs. Because rapid weight loss (such as that observed after bariatric surgery) facilitates physiologic changes in upper-airway structure, an auto-titrating device can adjust the therapeutic pressure level in a more timely/appropriate manner (thereby increasing user comfort), and may be more efficacious for use in this population [84].

Despite improvements in PAP therapy, compliance to treatment has been relatively low when addressed in the literature, ranging from only 30-60%. Barriers to compliance described by participants in one study included “the process of having to put a mask on every night”, aesthetic issues with mask/headgear use, inconvenience of having to use a machine to sleep, and daily routines that were disrupted by CPAP. To
address compliance issues and promote treatment adherence, it has been suggested that tailored interventions recognizing individual experiences, beliefs, and perceptions of treatment can improve treatment adherence and optimize outcomes [85].

Treatment of OSA with PAP has been shown to resolve daytime sleepiness and improve quality of life, alertness, cognitive function, and also to reduce cardiovascular risk [75, 77]. In addition, previous studies have demonstrated that in OSA patients, treatment with PAP therapy alone, or in combination with weight-loss intervention, can effectively reduce BMI [80, 82].

2.13 Prevalence of OSA in Obese Persons

OSA is prevalent in 4% of the general population. It is also more prevalent in men than women, most likely because women usually have less adiposity surrounding the neck and abdomen [34]. Fat deposits in these areas decrease the size of the airways and increase airflow resistance, which causes breathing cessation [34]. There is a clear link between body mass and OSA, and studies have demonstrated that a 10% increase in a typical individual’s bodyweight (~ 6 kg) over four years makes one’s risk of developing OSA is six times higher than if weight was maintained [75]. Consequently, OSA is estimated to affect 71 - 77% of the obese population and up to 91% of persons presenting for bariatric surgery [28, 57, 58, 76, 83].

Despite the increased prevalence of the syndrome, it is estimated that between 60% and 80% of Americans with OSA are not diagnosed [34]. BMI has been strongly correlated with OSA, and obesity is the only truly reversible risk factor of the syndrome [57, 58, 79, 83]. Thus, the prevalence of the syndrome is likely to increase as the obesity epidemic continues. Furthermore, since OSA is known to increase risk of complications for patients during the perioperative period routine screening for OSA should be included.
as a component of preoperative evaluation for surgical procedures [83]. This is particularly important for bariatric surgery patients, as OSA is often under-diagnosed in this population [86].

2.14 OSA, PAP Therapy, and Weight-Loss

Obesity is the most significant preexisting factor of OSA because of the anatomical and neuromuscular changes that occur in the body as a result of excess body weight, including BMI, neck circumference, retroglossal space, and distribution of fat [28, 75, 87]. Central obesity typically results in fat distribution to the abdominal area, upper body, and neck, and is most often associated with OSA [87]. It results in a smaller width inside the airways. Airway volume is decreased as central obesity becomes more severe and results in decreased expiratory lung volume. In addition, visceral adiposity provides a plentiful source inflammatory cytokines and adipokines, factors which can impede pharyngeal collapsibility and significantly lessen the control one has of breathing [58, 75].

Patients who do not receive and/or comply with PAP therapy often experience difficulty with weight loss for a number of reasons, including abnormal hormonal regulation and reduced physical activity resulting from increased daytime sleepiness [87]. It is likely that when left untreated, OSA may perpetuate obesity, and while some research has shown that in OSA, PAP therapy reduces BMI [69, 71], other data have not confirmed these effects [87]. Since only 20% - 40% of OSA patients are compliant with PAP therapy it is difficult to assess the true effects of weight-loss intervention, combined with PAP therapy, on weight loss [78].

One research study suggests that treatment compliance supplemented by substantial weight loss can result in significant reduction of OSA severity [80]. The study
included 39 treatment compliant patients who underwent diet counseling or gastroplasty. Patients here were considered “compliant” if they wore their machine at least 50% of the time. After one year of CPAP therapy in addition to weight loss, AHI was significantly lower than baseline and was correlated with a reduced BMI. Four patients with weight loss ranging from 29 to 94 kilograms were successfully weaned from CPAP after a PSG without the treatment device demonstrated marked improvement in breathing during sleep [80]. Results concluded that successful weight loss could alleviate OSA severity when the individual also remains compliant with CPAP therapy.

CPAP treatment has also been shown to facilitate weight loss, independent of nutrition intervention. A study by Loube, Loube, and Erman (1997) investigated weight loss as a secondary effect of OSA treatment. No intervention was conducted, although patients were encouraged to attempt weight loss [82]. CPAP compliance or noncompliance was determined by a self-report, and subjects were considered compliant when the machine was worn at least four hours per night. Twenty-one patients were compliant to CPAP treatment and 11 were not. A comparison of the compliant versus noncompliant groups showed that those individuals who wore a CPAP at least four hours each night were more likely to lose at least 4.5 kg throughout the study’s duration than those who did not. Short term weight loss can in fact result from CPAP treatment of obese individuals with OSA, which can increase motivation for treatment compliance [82].

In another study, effects of OSA treatment on exercise-induced weight loss were examined. Here, the authors determined that treated, compliant individuals (i.e. those who wore the CPAP mask for ≥ 5 hours sustained modest reductions in BMI, while those that were not treated failed to demonstrate any loss of weight. These results provide
further evidence that CPAP treatment/compliance plays an important role in weight loss for individuals with OSA [88].

In contrast, Redenius and colleagues (2008) found that CPAP usage was not associated with weight reduction. Here, participants (n = 97) were classified as compliant when CPAP was used ≥4 hours for ≥70% of nights [75]. Subjects in the control group (n = 45) either received no OSA treatment or were noncompliant (i.e. used CPAP <4 hours <70% of nights). After one year, there was no significant difference in body weight between the compliant and control groups. In contrast to other data, this study showed that CPAP treatment compliance did not necessarily promote weight loss [87]. Further exploration is necessary to determine the effect PAP treatment has on weight loss in OSA patients.

2.15 OSA and Depression

It has been suggested that depression is a major cause of disease burden, and is the result of OSA pathology and/or symptoms. Although prevalence studies have indicated elevated rates of depression in individuals with OSA both clinically and throughout the community, symptoms common to both conditions such as fatigue, drowsiness, lack of energy, and irritability pose a challenge when distinguishing the severity of both depression and OSA [89, 90].

Depressed mood, loss of interest, and reduced motivation are complaints of patients with OSA when untreated. Acker et al. (2010) assessed occurrence of major depressive symptoms of patients with untreated OSA for twelve months [91]. In the study, 1260 patients with an AHI >9 were screened for depression using self-administered questionnaires. Scores of ≥14 on the BDI or ≤13 on the WHO were designated as significant depressive symptoms. Results showed that 27.9% of patients
with untreated OSA were significantly depressed. Of those depressed patients, 46.2% were mild, 35.9% moderate, and 17.9% severe.

Another study examined the presence of depressive symptoms in OSA patients, prior to initiation of CPAP therapy and found depression to be highly correlated with the incidence of disordered breathing, as well as the BMI of the patients [90]. Further research is necessary to determine if compliance with treatment will resolve depression associated with OSA.

2.16 OSA and Bariatric Surgery

It has been estimated that up to 70% of all obese patients have OSA [79]. As OSA is a prominent comorbidity of obesity, it is important to understand the impact that weight loss surgery has on OSA. Dixon, Schachter, and O’Brien (2001) examined changes in sleep disturbance and obesity following bariatric surgery [92]. One year after surgery, 123 patients were asked to complete the same questionnaire and assessment that occurred before surgery. Information gathered came from self-report, and patients were also asked to report any treatment being used for OSA, including PAP therapy. Results indicated that 59% of men and 45% of women had sleep disturbances, with no differences in daytime sleepiness. The best clinical indicator of OSA was waist circumference, and average weight loss after 12 months was 48 percent. There was notable improvement in all questions upon follow up and snoring was reduced to 14%, compared to 82% preoperatively. According to the sleep questionnaire, preoperative self-reported prevalence of OSA was 33% and reduced to 2% twelve months after LAGB surgery. In addition, self-reported daytime sleepiness was reduced in 90% of participants, and reports of poor sleep quality in 94% of participants, one year postoperatively. The authors concluded that weight loss surgery should be considered
for obese individuals suffering from OSA and that substantial weight loss can improve obesity related sleep disorders [92]. However, it should be noted that the results from this study relied solely on patient’s self-reported (subjective) assessment of severity of symptoms, and did not include any objective measurements of OSA, such as results from PSG and/or AHI.

Persistence of OSA after surgical weight loss was assessed by Lettieri and colleagues (2008) [78]. Twenty-four patients underwent a PSG prior to bariatric surgery and again one year postoperatively. Weight loss was compared to BMI, OSA, and CPAP requirements. ESS and snoring were also variables of the study. Following surgery, average BMI dropped by 35% (50 ± 10.4 to 32.1 ± 5.5 kg/m²). AHI also decreased by 49% in 22 of the 24 subjects (47.9 ± 33.8 to 24.5 ± 18.1). Although bariatric surgery was found to reduce AHI and lessen severity of the syndrome, the majority of patients one year postoperatively were still found to have OSA. It should be noted however that in this study, only six individuals were compliant with treatment at the follow up visit and the authors did not assess differences in weight loss outcomes between compliant and non-compliant subgroups [78].

Although there is a substantial amount of literature suggesting that bariatric surgery can resolve OSA, true diagnostic measurements of the syndrome (gathered from PSG’s, such as AHI) are often non-existent. Additionally, most studies fail to include compliance intervention or quantification as part of study design. Further research is needed in order to elucidate the true effects of bariatric surgery on OSA and weight loss, and should account for differences in patients’ compliance with PAP treatment. Furthermore, it is important that subsequent studies quantify OSA severity using standardized criteria (i.e. AHI) as opposed to subjective measurements of sleep quality or self-reported usage of prescribed PAP therapy.
CHAPTER 3

Methods
3.1 Specific Aim

The purpose of this research was to examine the effects of laparoscopic Roux-en-Y gastric bypass (LRYGB) surgery in obese patients with OSA.

3.2 Hypothesis

Obese patients being treated for OSA will demonstrate improvements in health-related indices that are sustained over time following LRYGB.

3.3 Study Design

The study was a prospective, within-subjects’ design, and was part of a larger, single-center pilot study (designed to examine the effects of bariatric surgery on morphologic and hormonal markers of OSA).

Obese subjects (n = 10) pending laparoscopic, Roux-en-Y gastric bypass surgery (LRYGB) with concomitant referral for pulmonology and sleep medicine consultation were evaluated for obstructive sleep apnea (OSA). In addition to routine care and treatment (which included prescription of a PAP breathing machine for use during sleep), those with a diagnosis of OSA were asked to participate in a series of additional study visits (Visits A – D) during six months of subsequent, post-operative follow up (Figure 3.1). More details on specific procedures are outlined in sections below. At each visit, subjects were asked to complete a series of questionnaires and assessment of body composition. Other health indicators, including measurements of anthropometrics (height and weight), neck circumference, blood lipids and/or, results from spirometry testing and/or polysomnograms, were monitored and/or collected throughout the study. In addition, all participants were placed on a comprehensive monitoring and intervention plan (using ResTraxx monitoring software), in order to maximize compliance (section 2.9). Patients who consistently demonstrated poor compliance (< 70%) during the preoperative period were excused from further participation in the study.
Figure 3.1 Study design. Study candidates with a diagnosis of OSA were asked to participate in a series of study visits during six months of subsequent, postoperative follow up.
3.4 Methodology

The protocols detailed herein were approved by Institutional Review Boards at both Summa Health System and Youngstown State University (Appendices A and B). The study resulted from a joint effort of Summa’s Bariatric Care Center (BCC, Akron City Hospital 95 Arch Street, Suite 240), and Respiratory, Critical Care and Sleep Associates (LLC) (RCSA, Akron City Hospital, 95 Arch Street, Suite 210), and included collaboration with personnel from Youngstown State faculty who hold Scientific Staff affiliation within Summa’s Department of Surgical Research. Whenever possible, study visits were scheduled to coincide with subjects’ pre-existing, postoperative-care/routine-care office visits at RCSA/BCC, as the proximity of these two offices significantly decreased the burden of travel time/costs to the subject, and likely minimized the overall attrition that might have otherwise occurred.

The study timeline and assessment schedule are depicted in Figure 3.2. Briefly, after giving informed consent, subjects were asked to complete a set of study-related assessments at four separate times throughout a seven month time period (once directly prior to their bariatric surgery, then at three months and six months postoperatively).
Figure 3.2 Study timeline. After giving informed consent and Visit A, study participants were asked to complete a series of assessments for the study at four separate visits, which took place over a seven-month period. Visit B took place directly prior to the candidate’s bariatric surgery, and visits C and D occurred at three months and six months postoperatively.

3.5 Subjects

Ten Caucasian obese women (BMI > 34.9 kg/m2) between the ages of 18 and 75, who were pending laparoscopic Roux-en-Y gastric bypass surgery and had probable OSA, were recruited for the study. Specifically, we recruited patients who presented to the BCC for evaluation for surgical weight loss, and had probable OSA (as assessed by the surgeon).

3.6 Telephone Screening and Informed Consent

Patients were referred for an initial sleep medicine evaluation (SME, which took place at RCSA as part of their normal, routine medical care). At this time, they were also briefly informed (by BCC staff) about the proposed study. Patients who expressed an interest in the study were then contacted (via telephone) by research staff so that the patient’s interest and eligibility could be confirmed, at which point they were asked to meet with the research staff immediately following their scheduled SME.
At the initial SME, the sleep medicine physician referred the patient for a diagnostic polysomnogram (PSG) in order to diagnose the presence of OSA (see detailed description below). After completion of the SME, a member of the study team then escorted the patient to the research office to review the study's procedures and to complete informed consent (Appendix C). Completion of informed consent at this time allowed the research staff access to pertinent medical information so that continued eligibility could be assessed (i.e. the presence of OSA, as indicated by a review of the results from the diagnostic PSG, per the direction of the sleep medicine physician).

3.7 Diagnosis of OSA for Continuation of Eligibility

All participants underwent a routine-care PSG in order to test for the presence of OSA. Procedures for this test are detailed under section 3.11.3. In short, if results from the PSG indicated a positive OSA diagnosis, then the physician confirmed continued eligibility, and prescribed an auto-titrating PAP machine (APAP) with ResTraxx (see section 3.10) and participants proceeded with the baseline and postoperative assessments. If participants did not have a confirmed diagnosis of OSA, a member of the research team made contact via telephone in order to excuse them from further study participation. All participants continued to receive routine, follow-up care (as medically indicated) regardless of eligibility/participation in the research study.

3.8 Study Visits

Table 3.1 lists a summary of assessments that were completed/recorded at the time of study visits at baseline and the postoperative time points. “Routine Assessments” refer to those indices that were measured as a part of routine, day-to-day care, ordered by the bariatric surgeon or by the sleep medicine physician at follow-up appointments. “Ancillary Testing” refers to those assessments that were not taken routinely, and were
being obtained for study use only. Further information regarding Routine and Ancillary Testing assessments is detailed in sections 3.11 and 3.12.

Table 3.1 Routine Assessments and Ancillary Testing Summary of assessments—“Routine Assessments” refer to those indices that were measured as a part of routine, day-to-day care, ordered by the bariatric surgeon or by the sleep medicine physician at follow-up appointments. “Ancillary Testing” refers to those assessments that were not taken routinely, and were being obtained for study use only. Mallampati score had been a component in the original study design, however was not collected by the study physician and therefore unavailable for analyses.

3.9 PAP Compliance Intervention

Study participants received aggressive compliance intervention in order to maximize their adherence to APAP prescription. Patients who consistently demonstrated poor compliance (< 70%) during the preoperative period (i.e. the month[s] prior to surgery) were excused from further participation in the study. The compliance intervention entailed the following components:

3.9.1 Education

At their initial and follow-up visits with the sleep medicine physician, patients received education with regard to etiology and progression of OSA. The physician also provided a detailed explanation of auto-titrating CPAP therapy and
the importance of treatment adherence. These concepts were also be reinforced by study personnel at subsequent follow-up visits.

3.9.2 Equipment Provision and Support

After the sleep medicine physician prescribed auto-titrating CPAP therapy, participants met with a Respiratory Therapist at Summa’s specialty pulmonary clinic. At that time, they received their APAP machine, and the specialist provided detailed instructions on the use and maintenance of the machine, and Restraxx monitoring device. The specialist also provided a customized mask fit (based on patient preference and recommendations of the sleep physician) in order to ensure proper interface between the patient and the APAP device.

3.9.3 Usage Monitoring/Follow-Up

For the purposes of the study, threshold usage (for therapeutic consideration) was set at 70% of time (Appendix D). Study personnel used ResTraxx to check usage ≥ three times per week. When average weekly usage (i.e. over seven consecutive days) fell below the 70% threshold, the patient was contacted to find out the cause and to reinforce/encourage compliance. In cases where the patient reported difficulties with the equipment or discomfort with the interface, the PAP specialist contacted them in order to resolve the issues. If the patient reported other side effects and/or sustained difficulties with sleeping, the sleep medicine physician followed up. In all cases where usage fell below threshold, study staff maintained contact one to two times weekly until the issues were resolved. Patients who demonstrated compliance above the threshold received bi-weekly phone calls and monthly, mailed correspondence from study
staff to provide encouragement and positive reinforcement, and to proactively manage any related concerns.

3.9.4 Incentive

Patients who successfully maintained enrollment through the duration of the study received financial compensation ($75.00) for their time and effort.

3.10 Resmed APAP Machine/ResTraxx

Participants received a ResMed S8 AutoSet II Auto PAP Machine. This machine includes Easy-Breathe Technology and aH4i Heated Humidifier and is an auto-titrating PAP that delivers therapeutic pressure to the airways in a smooth waveform that is designed to mimic breathing of the individual patient. It further customizes treatment regimens by allowing a choice of three different Expiratory Pressure Relief comfort levels (1, 2, and 3 cm of H2O per breath). In addition, participants received an add-on compliance-monitoring device (ResTraxx). Information collected via the ResTraxx included detailed reports of compliance, daily length of use, leak rate, Apnea Index (AI), Apnea Hypopnea Index (AHI) and Hypopnea Index (HI) incident data, and was reviewed by the Physician Board Certified Sleep Medicine practitioner. The ResTraxx software showed evidence of patients’ compliance (Appendix D) and helped to resolve any issues with the Resmed machine to optimize treatment outcomes.

3.11 Routine-Care Assessments

3.11.1 Anthropometrics

Body weight was measured to the nearest 0.01 kg using a portable, electronic scale (Model # 6856, Detetco). Height and neck circumference were measured to the nearest 0.1 cm using a portable stadiometer (Model #226, Ayrton) or standard tape measure, respectively. For percent excess weight loss
(%EWL) calculations, ideal body weight was considered as the patient’s body weight that corresponded with a BMI of 24.0 kg/m².

3.11.2. Spirometry Testing

These tests took approximately 30 minutes, and were administered by a trained, Respiratory Therapist at Akron City Hospital, according to standard guidelines set forth by that department. The evaluation of spirometry measured the participant’s breathing ability. During a spirometry test the patient takes the deepest breath possible, and then exhales into the sensor as hard as they can for as long as possible (preferably at least 6 seconds). Generally, the test will be preceded by a period of quiet breathing in and out from the sensor to measure tidal volume, or the rapid breath in (forced inspiratory part) will come before the forced exhalation. The maneuver is typically repeated three times to ensure the best results.

Parameters measured during a typical spirometry test include Vital Capacity (VC), Forced Vital Capacity (FVC), Forced Expiratory Volume (FEV) at timed intervals of 0.5, 1.0 (FEV₁), 2.0, and 3.0 seconds, Forced expiratory flow 25–75% (FEF 25–75) and Maximal voluntary ventilation (MVV), sometimes referred to as Maximum Breathing Capacity. All PFTs were reviewed with the assistance of a board-certified pulmonologist.

3.11.3 Polysomnogram (PSG)

This study was administered by a Sleep Technician at a sleep laboratory participating in the Summa Health System network, and was used to detect the presence and severity of OSA symptoms. A PSG is a comprehensive recording of the biophysiological changes that occur during sleep. The study is indicated when a sleep disorder is suspected, and is most often performed at night when most people sleep.
For this test, the patient came to a sleep lab in the early evening, and over the next one to two hours was introduced to the setting, which was designed to mimic a traditional bedroom. Wires for each channel of recorded data led from the patient and converged into a central box, which was then connected to a computer system for recording, storing and displaying the data. Equipment worn by the patient included a finger probe pulse oximeter (SpO₂); apparatus for electromyelograms (EMG) placed at the anterior tibialis muscle and chin sites (used to assess nocturnal muscle movement). Piezoelectric belts worn by the subject measured chest and abdominal movements. Subjects also had electrodes placed on their head in order to measure brain waves (electroencephalogram) and eye movements (electrooculogram). In addition, they had airflow measurements performed by thermistor, and/or pressure transducer. These devices were worn as a cannula underneath the nose during sleep. Cardiac rhythm was measured during the study through use of electrocardiographic electrodes worn on the surface of the skin. During sleep, data was collected and directly observed by the sleep lab technician as the computer monitor continuously displayed multiple channels of data. In most labs the test was completed and the patient discharged home by 7 a.m.

After the test was completed a "scorer" examined the data by reviewing the reports from the PSG in 30-second segments. The score was made up of all of the data collected during the sleep study, and included the following constructs (valuable in the process of assigning AHI): Sleep onset latency, which is the onset of sleep from time the lights were turned off; and normally is less than 20 minutes. Determining "sleep" and "awake" is based solely on the EEG. Patients may believe that they were awake for much of the study when the EEG actually shows they were sleeping; Sleep efficiency: the number of minutes of
Sleep divided by the number of minutes in bed. Normal sleep efficiency is approximately 85 to 90% or higher; *Sleep stages*, which are based on 3 sources of data from EEG, EOG, and chin EMG. From this information each 30-second segment is scored as "awake" or one of 4 sleep stages: 1, 2, 3, and Rapid Eye Movement (REM) sleep. Stages 1–3 are together called non-REM sleep. Stage 3 non-REM sleep is also referred to as "slow wave" sleep because of the large brain waves compared to the smaller brain waves seen in Stage 1 and 2, which are considered "light sleep"; Any breathing irregularities, namely apneas and hypopneas. Apnea is a complete or near complete cessation of airflow for at least 10 seconds followed by an arousal and/or 3% oxygen desaturation; hypopnea is a 50% decrease in airflow for at least 10 seconds followed by an arousal and/or 3% oxygen desaturation; *Arousals*, which are sudden changes in brain wave activity, occur for a number of reasons such as irregular breathing, leg movements, or outside noises. Cardiac rhythm abnormalities, leg movements, body position during sleep, and oxygen saturation during sleep are also included in scoring of the PSG.

After the data from the PSG had been scored, the test recording and the scoring data were sent to the sleep medicine physician for interpretation. The interpretation was done concurrently with the medical history where the physician obtained a comprehensive list of medications the patient was being prescribed, and any other factors that may have affected the PSG’s outcome. All PSGs were reviewed with the assistance of a board-certified sleep-medicine physician.

3.12 Ancillary Testing Assessments

3.12.1 Questionnaires
a. Calgary Sleep Apnea Quality of Life Index (CSAQLI): The Calgary SAQLI is an interviewer-initiated series of questions that assess disease-specific health related quality of life measure. It has been shown to be a highly responsive tool for quality of life measurements in people with OSA. The practitioner-administered questionnaire contains four main domains including: Daily Functioning, Social Interactions, Emotional Functioning and Symptoms [36]. (Appendix E).

b. Bariatric Analysis and Reporting Outcome System (BAROS): BAROS is a self-administered quality of life questionnaire, which assesses several related constructs, including self-esteem, labor/employment, and physical, social and sexual health. Each of the concepts has four choices of answer ranging from negative to positive. The choices involve simple drawings distributed along a line to help the subject select the most appropriate answer. (Appendix F)

c. Beck Depression Inventory (BDI): The Beck Depression Inventory is a self-administered questionnaire used to assess cognitive indicators of depression. Scores on this 21-item scale range from 0 to 63, with a score of 10 used to discriminate between asymptomatic and symptomatic individuals. (Appendix G)

d. Epworth Sleepiness Scale (ESS): The Epworth Sleepiness Scale (ESS) was developed in 1991 as a tool used to assess sleep tendencies, and is often used in clinical practice and research as a quick way to determine one’s subjective sleepiness. The ESS is an eight-item questionnaire that assesses the likelihood of a subject falling asleep in sedentary situations. Subjects rate their self-perceived chance of falling asleep/sleeping on a Likert scale from 0 (never) to 3 (high chance). The total, summed value of responses is the Epworth Score
(ES), which ranges from 0 to 24. A score of eleven or greater indicates elevated daytime sleepiness [93]. (Appendix H)

e. **Night Eating Questionnaire (NEQ):** The Night Eating Questionnaire is a 14-item questionnaire which is used to measure severity of the Night Eating Syndrome (NES) by assessing hunger and craving patterns, portion of calories consumed after supper, difficulty sleeping/staying asleep, nocturnal ingestion, and mood. The NEQ assesses NES based on a 5-point, Likert-type scale, and scores may range from 0 – 52. Previous data have demonstrated the NEQ to be an efficient, valid measure of severity for NES, with a score of 25 or higher defining a night eater [94]. (Appendix I)

f. **Demographic Questionnaire:** Subjects were asked to complete a standard questionnaire designed to obtain demographic information including age, patient-defined gender and ethnicity, as well as basic information regarding educational and current employment status. This data was only to be used for potential statistical analytic groupings, and was administered one time at Study Visit A. (Appendix J)

3.12.2 **Blood Lipid Profile**

The lipid profile consists of a group of tests, often ordered together, to assess one’s risk of heart disease. The lipid profile here included total cholesterol, high-density lipoprotein (HDL-C), low-density lipoprotein (LDL-C), and triglycerides. After a twelve-hour fast, blood samples were obtained by standard venipuncture to the antecubital region. Samples were obtained at Summa Health Care (Akron City Hospital) according to institutional laboratory policy, by a trained medical phlebotomist, and sent to a centralized laboratory for processing.
3.12.3 Body Composition

Body composition (fat and fat-free mass, water) was estimated using single-frequency (50 kHz) bioelectrical impedance analysis (Quantum II Bioelectrical Analyzer, RJL Systems, Clinton, MI) while subjects were in a supine position.

3.13 Data Collection & Analytic Plan

Data were gathered directly from participants for the purposes of the proposed study. End points included scores from questionnaires, compliance/pressure data from Restraxx reports, anthropometric measurement values, and results from PSGs and Spirometry Testing. Data were analyzed using the Statistical Analysis System (SAS Version 9.1, Cary, NC). Demographic and end-point data were conveyed using descriptive statistics (i.e. means and standard deviations), frequencies and percentages. The mixed procedure was used to test for effects of time on the outcome variables (body weight, pulmonary function tests, and apnea-hypopnea indices) to control the probability of type error. Unlike an ANOVA, it can perform analyses inclusive of participants who have with missing data at one or more time points. This strategy has been shown to be particularly advantageous for use in longitudinal bariatric surgery studies [95]. Testing for the fixed effect of time was two-sided and performed at the 5% alpha significance level. When main effects of time included more than two time points, Bonferroni adjustments to the significance level were used for pairwise comparisons between the points [96]. Data from individuals who withdrew or were excused prior to study completion, or for those who completed less than three months follow-up, were not included in the final analysis. Data in the text and figures are given as LS Means ± SEM, unless otherwise indicated.
CHAPTER 4

Results
4.1 Study Participants

A total of 35 women were recruited for the study. Out of these, 22 were screened and found to be ineligible secondary to insufficient AHI per the diagnostic PSG \((n = 18)\) or unwillingness or inability to fulfill the required study protocol \((n = 4)\). Out of the 13 who were enrolled, three were subsequently excused from the study within the first six weeks. One participant was unable to find a mask that was comfortable during sleep, another felt that she was not benefitting from treatment with APAP, and another had atypical sleep habits that made compliance an issue (despite multiple troubleshooting and/or reinforcement efforts on the part of study and support staff). As such, 10 participants had continued enrollment, and at the time of data analysis, six had completed at least three months of post-surgical follow up. Thus, the results detailed herein pertain to this subgroup of six participants (Table 4.1).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (± SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (lbs.)</td>
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<tr>
<td>Age (years)</td>
<td>45 ± 13.4</td>
<td>28 - 60</td>
</tr>
<tr>
<td>Height (in.)</td>
<td>64.5 ± 2.9</td>
<td>60 - 70</td>
</tr>
<tr>
<td>BMI</td>
<td>50.9 ± 6.8</td>
<td>36.7 - 60.3</td>
</tr>
<tr>
<td>% Body Fat</td>
<td>49.2 ± 5.1</td>
<td>48.5 - 54.8</td>
</tr>
<tr>
<td>Neck Circumference (cm)</td>
<td>43.3 ± 6.5</td>
<td>33 - 48</td>
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<tr>
<td>AHI</td>
<td>38.8 ± 26.5</td>
<td>15 - 95</td>
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<tr>
<td>FEV(_1)/FVC</td>
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<tr>
<td>FEV(_1)</td>
<td>110.6 ± 5.6</td>
<td>76 - 124</td>
</tr>
</tbody>
</table>

Table 4.1. Patient baseline characteristics collected at study visits A and B in addition to AHI determined by diagnostic PSG.
4.2 Compliance and ResTraxx Data

Compliance and ResTraxx data (including minutes of usage, leak rate, and pressure at 95th percentile) were monitored regularly for all subjects throughout the course of the study follow-up. Averages were calculated at pre-operative, post-operative, and cumulative (from treatment initiation to six months postoperative) time points and are shown in Table 4.

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Usage (Hours)</th>
<th>Leak Rate (L/Second)</th>
<th>95th Percentile Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Operative Period</td>
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<td>0.02</td>
<td>10.8</td>
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<tr>
<td>Post-Operative Period</td>
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<tr>
<td>Cumulative</td>
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<td>9.3</td>
</tr>
</tbody>
</table>

Table 4.2. Average usage, leak rate, and 95th percentile pressure for pre-operative, post-operative, and cumulative time points. Data are shown as means.
4.3 Body Weight and BMI

A main effect of time was found for body weight ($p = 0.023$, Figure 4.1). Pairwise comparisons revealed differences between zero and three months (302.17 ± 16.1 pounds versus 232.7 ± 16.1 pounds, $p = 0.0079$), and zero and six months (302.2 ± 16.1 pounds versus 207.5 ± 16.1 pounds, $p = 0.0008$), postoperatively, but not between the three and six-month time points (232 ± 16.1 pounds versus 207.5 pounds ± 16.1, $p = 0.2852$).

Figure 4.1. Mean postoperative weight loss (pounds). A main effect of time was found for body weight of participants ($p = 0.023$). In pair-wise comparisons, $\alpha$ indicates significant differences between baseline and three months postoperative, $\beta$ indicates significant differences between baseline and six months postoperative ($p < 0.05$). Data are reported in the text above.
As expected, analysis of BMI yielded a similar pattern for an effect of time ($p = 0.0002$, Figure 4.2) where significant decreases were noted between baseline (50.9 ± 2.1 kg/m$^2$) and both three-months (39.3 ± 2.1 kg/m$^2$, $p = 0.0014$) and six months (34.9 ± 2.1 kg/m$^2$, $p < 0.0001$), but not between the two later time points ($p = 0.2$, data not shown).

Figure 4.2. Mean postoperative Body Mass Index (BMI). A main effect of time was found for BMI of participants ($p = 0.0002$). In the pair-wise comparisons $\alpha$ indicates significant differences between baseline and three months postoperative, while $\beta$ indicates significant differences between baseline and six months postoperative ($p < 0.05$). Data are reported in the text above.
4.4 Percent Excess Weight Loss (%EWL)

For %EWL calculations, ideal body weight was considered as the patient’s body weight that corresponded with a BMI of 24.0 kg/m². A main effect of time was found for %EWL ($p < 0.0001$; Figure 4.3). Significant differences were noted between baseline (0.0 %EWL)) and both three months $22.7 \pm 1.3\%$, $p < 0.0001$) and six months ($31.1 \pm 1.3\%$, $p < 0.0001$), as well as between the latter two time points ($p = 0.0004$).

Figure 4.3. Postoperative percent excess weight loss (%EWL) of participants. A main effect of time was found on %EWL ($p < 0.0001$). In the pair-wise comparisons, $\alpha$ and $\beta$ indicate significant differences between baseline, and three months and sixth months postoperative, respectively ($p$'s $< 0.0001$). $\gamma$ indicates significant differences between three months and six months postoperative ($p < 0.05$). Data are reported in the text above.
4.5 Neck Circumference

Measurements of neck circumference were taken at baseline and six months postoperatively (Figure 4.4) and were significantly decreased between these two time points (43.3 ± 2.2 cm versus 36.2 ± 2.2 cm, \( p = 0.0474 \)).

Figure 4.4. Postoperative neck circumference. A main effect of time was found for neck circumference where values decreased significantly between baseline and six months postoperatively (\( p = 0.047 \), data reported in preceding text).
Significant effects of time were noted for scores on the Calgary Sleep Apnea Quality of Life Index (SAQULI) questionnaire ($p = 0.01$), where pairwise comparisons revealed differences between scores at zero and three months ($4.1 \pm 0.3$ to $5.5 \pm 0.3; p = 0.0080$) and zero and six months ($4.1 \pm 0.3$ to $5.6 \pm 0.3; p = 0.0053$) postoperatively (Figure 4.5). No effects of time were noted for scores on the other questionnaires (Bariatric Analysis and Reporting Outcome System, $p = 0.1972$; Beck Depression Inventory, $p = 0.5266$; Epworth Sleepiness Scale, $p = 0.0777$; Night Eating Questionnaire, $p = 0.9926$; data not shown).

Figure 4.5. Main effect of time on SAQLI Score ($p = 0.01$). In the figure above, pair-wise comparisons with significant differences from baseline to six months are indicated by $\alpha$, while $\beta$ indicates significant differences between baseline and six months following surgery ($p < 0.05$, data reported in preceding text).
4.7 Lipid Profiles

Fasting blood lipid profiles (including total cholesterol, TC; high-density lipoprotein cholesterol HDL; low-density lipoprotein cholesterol LDL; triglycerides, TG) were collected for all participants at baseline and six months postoperatively. Significant differences were found between these time points for TC (170.8 ± 9.3 mg/dL versus 136.5 ± 9.3, mg/dL $p = 0.03$) but not for HDL ($p = 0.999$), LDL ($p = 0.2$), or TG ($p = 0.1$); (Figure 4.6).

Figure 4.6. Blood lipid profiles at baseline and at six months postoperatively. In the pairwise comparisons above, $\alpha$ represents a significant difference between baseline and six-month time points for total cholesterol ($p = 0.03$). No differences were found for other lipid parameters.
4.8 Apnea-Hypopnea Index (AHI), Non-Rapid Eye Movement AH1 (Non-REM AHI), and Rapid Eye Movement AHI (REM AHI)

Data were tested for differences in AHI, Non-REM AHI, and REM AHI, between values measured for each, at baseline and six month time points. The first set of results included all participants \((n = 6, \text{Figure 4.7.1})\), while a second subset \((n = 5, \text{Figure 4.7.2})\) excluded one participant who had a lower overall AHI (< 10 events/hour) but was deemed eligible for the study by Physician Board Certified Sleep Medicine practitioner because of her high REM AHI value. When this subject was included in the analysis, there were trends for differences between time points total AHI \((38.8 \pm 8.6 \text{ events per hour versus } 12.3 \pm 8.6 \text{ events per hour, } p = 0.05)\) and Non-REM AHI \((35.0 \pm 9.2 \text{ events per hour versus } 10.7 \pm 9.2 \text{ events per hour, } p = 0.09)\), respectively. No differences between time points were found for REM AHI \((p = 0.17)\).

The second analysis, which excluded the participant with the lower AHI \((n = 5)\), there was an effect of time on total AHI \((46.2 \pm 8.1 \text{ versus } 14.7 \pm 8.1; p = 0.0254)\) and a trend for an effect of time on Non-REM AHI \((41.8 \pm 9.4 \text{ versus } 12.8 \pm 9.4; p = 0.06)\). No effect of time for REM-AHI in the reduced data set was found \((p = 0.1616)\).
Figure 4.7.1 Main effect of time on AHI (All participants). The data above indicates a trend for effect of time on Total- and Non-REM AHI’s. No significant results were achieved when all patients were included in the dataset ($p$'s > 0.05).
Figure 4.7.2. Main effect of time on AHI (Exclusion): When the patient with the lower AHI was excluded from analysis, a significant effect of time was found for Total AHI (represented by α), and a trend for effect of time was found for Non-REM AHI (p’s < 0.05). Data are shown in the text above.
4.9 Spirometry Testing

There was no effect of time on values from Spirometry testing (FVC, \( p = 0.243 \); FEV\(_1\), \( p = 0.1339 \); and FEV:FVC ratio, \( p = 0.9584 \)); baseline values are shown in Table 3). At six months, values did show some improvement, though differences between the time points did not approach statistical significance (FVC 117.2 ±13.1; FEV\(_1\) 123.2 ± 13.7; and FEV:FVC ratio 104.3 ±11.3).
CHAPTER 5

Discussion
Previous data have consistently reported favorable anthropometric outcomes within one to five years following surgical weight-loss intervention, and it was anticipated that similar results would be apparent in our current research. However, the %EWL we observed at three months postoperatively (average of 22%, range of 17% – 24%) was much less (approximately 23% lower) than that found in a study by Wittgrove and colleagues (1996, [97]), where participants attained anywhere from 14% to 81% EWL. Furthermore, this discrepancy in results was augmented at the six-month time point, where outcomes reported by these previous authors exceeded ours by approximately 31%. At this latter time point, participants in that study had attained a range of 33% to 100% EWL, whereas our current participants’ %EWL only ranged from 25% to 36%.

There are several major differences between the two studies that may account for discord in weight loss outcomes (both net, and range of, %EWL), and as a result, other study outcomes that are known to be associated with changes in body weight. Wittgrove et. al. retained a much larger sample size ($n \geq 65$) and included both men and women. Previous data have shown women to have weight loss outcomes that are inferior to those of men [96], and it may be that the (comparatively) reduced %EWL outcomes observed in the current study results from exclusion of male participants. In addition, patient demographics, including sex, age, and baseline weight/BMI were not reported by Wittgrove et.al. These characteristics, especially presence of a higher baseline weight, may have allowed for a greater %EWL than we observed at the various study intervals.

In the current study, it is notable that although significant changes in net weight occurred between the zero and three month postoperative time points (average loss ~ 69 pounds), our participants did not demonstrate statistically significant decreases between the three and six month postoperative period (average loss only ~ 25 pounds), though their corresponding %EWL was significantly different between these time points.
Perhaps this is because subsequent weight loss became more gradual after the larger initial weight loss occurring between zero and three months. This pattern of initial, accelerated loss, followed by an attenuation of loss, has been noted previously. For example, a similar study conducted by Todiyl and colleagues (2005) at the University of Pittsburgh Medical Center investigated the rate of weight loss following RYGB [98]. Here, a prospectively collected database (including over 3500 patients who underwent RYGB between 1997 and 2004) reported age, gender, BMI, and body weight at baseline. Postoperative weight loss was reported as pounds lost per day. The study’s population was predominantly female, mean age was 41, and baseline BMI was 48kg/m². Average rate of weight loss was highest in the first month postoperatively (1.29lb/day) and by eight months weight loss had stabilized, remaining consistent at approximately 0.22lb/day. The study also found that a larger BMI at baseline was associated with more rapid weight loss at one month, but not at three, six, or twelve months postoperative. We noted a similar pattern in our current study, and found that weight loss was most rapid in the first three months following surgery and became attenuated at the remaining study visits. This information suggests that rate of weight loss in the first twelve months after RYGB can vary depending on baseline BMI, and accounting for such differences may be useful when examining weight loss immediately following bariatric surgery. In addition, because of our small sample size, we were unable to assess independent effects of baseline characteristics, however it should be noted that values for baseline BMI and age of our participants were very similar to those of Todiyl et. al.

Outcomes of our research are also consistent with another study, which reported an average weight loss of 0.5 to 1 pound (0.22 - 0.45 kg) daily for the first three months after bariatric surgery, 0.25 to 0.5 pound (0.11 - 0.22 kg) daily between three and nine
months, and 0.25 pound (0.11 kg) daily thereafter for up to 12 months postoperatively. Furthermore, the authors surmised that weight loss is contingent on baseline body weight status, and that most patients lose about 33 to 44 pounds in the first three months, 55 to 77 pounds by six months, and about 88 to 132 pounds by one year after surgery [99].

Laparoscopic adjustable gastric banding (LAGB) has become a popular bariatric procedure because it elicits considerable weight loss while limiting surgical risk. It has been documented that weight reduction with the LAGB procedure is less pronounced; nonetheless results from this procedure do provide some means for comparison of surgical weight loss outcomes. In one example, a study by Spivak et. al. (2004) examined the effect LAGB on 271 patients [100]. Here, weight was measured at baseline, three, six, nine, twelve, eighteen, and twenty-four months following surgery. Between baseline and three months, information regarding %EWL was not provided, but between three and six months, average %EWL was 16% and increased to 25% between the six and nine-month time period. Results in our study were similar, where participants’ %EWL was greatest a between baseline and three months (22%), and increased by 9% between three and six months to 31%.

A comprehensive review of the current literature pertaining to bariatric surgery, however, has shown that the immediate outcomes following RYGB (three, six, and nine month outcomes) are not reported in the large majority of longitudinal studies, although generalized patterns of weight loss have been outlined. More research is necessary to examine immediate postoperative outcomes in order to understand the rate of weight loss in the more immediate post-surgical period (i.e. in the first 12 months). It is likely that if our study had a longer follow-up time, outcomes would be more consistent with current literature because data after the six month time point would be included in the
analysis. More importantly, our statistical power was likely to be significantly hindered by our abbreviated sample size, though the current study does have the pattern of a larger, initial weight loss followed by attenuated weight change, more consistent with results described in the studies above.

Neck circumference is an important anthropometric assessment that can have a profound effect on respiration. For example, two previous studies, both in male patients who lost weight either by intragastric balloon or diet/lifestyle modification, showed that improvements of OSA symptoms occurred concomitantly with changes to the structure of upper airways and/or neck morphology resulting from decreased fat deposition [101]. As expected, we observed a reduction in neck circumference in our participants that paralleled their concomitant reduction in AHI, providing further evidence that physiological changes in the neck and abdominal area occur as a result of bariatric surgery, and may therefore reduce the severity of OSA in obese patients. Our results were similar to those of a previous study, where craniofacial changes and respiratory quality were examined in seventeen OSA patients following weight loss surgery. Here, neck circumferences of male and female patients were measured preoperatively and at ≥ four months following surgery, in addition to other radiographic measurements used to assess changes in airway capacity. Average baseline neck circumference was 43.35 ± 4.12 cm and was postoperatively reduced to 38.18 ± 2.19 cm [102]. Data from our study were consistent with these findings (and demonstrated slightly greater decreases), where neck circumference in our participants was reduced from 43.28 ± 2.22 cm to 36.18 ± 2.22. Radiographic study assessments in the former study also improved after weight loss, with a reduction in length of the craniocervical junction; increase in velopharyngeal air space, and less space between the hyoid bone and mentum. Although our study did not examine these variables, the previous results outline a
mechanism by which bariatric surgery can viably serve as treatment for OSA and other conditions that result from upper-airway obstruction as a consequence of enlarged neck circumference.

With regard to subjective assessment of quality of life, SAQLI scores for our participants improved significantly each time the questionnaire was administered postoperatively, corroborating a previous report published in 2007 [103]. Here, Lam and colleagues compared the effectiveness of three non-surgical treatments for OSA (sleep hygiene counseling, CPAP therapy, oral appliance) and included 101 subjects with mild to moderate OSA (mean AHI 21.4 events per hour), [103]. In addition, any participants presenting as overweight at baseline were provided with weight loss counseling as an adjunct to treatment intervention. The SAQLI questionnaire was used as one method to measure quality of life after treatment began. Results from the study showed that patients who received CPAP or oral appliance therapy scored significantly higher than conventional counseling for sleep hygiene improvement. Furthermore, a linear relationship was found between changes in AHI and body weight. In our study, average baseline AHI and BMI were substantially higher (average AHI = 38.8 events per hour and BMI 48.1 kg/m²) compared to those in the study by Lam et. al. where corresponding characteristics were lower (average AHI = 19.3 events per hour and BMI 27.3 kg/m²). Despite these differences, both studies show evidence of the relationship between weight loss and improvement in sleep- and health-related QOL, particularly when it occurs in the context of OSA treatment.

Interestingly, scores on the remaining subjective questionnaire assessments (BAROS, BDI, ESS, and NES) did not change significantly during the postoperative time period. Of note is the fact that one specific, routine question on the BDI uses weight loss as a metric for depression. As bariatric surgery participants in our study continued to
experience weight loss, scores for this question continued to rise, which could have artificially inflated values (as weight loss was intentional, and not a result of depression) at later time points, attenuating decreases that may have otherwise been significant. In addition, it is notable that ESS and NES scores were already relatively low at baseline, thus allowing for little change as the participants experienced weight loss. In general, overall, reduced quality of life was not apparent for the participants, based on low scores of the questionnaires assessed at baseline and as such, would have encountered a “ceiling effect” of sorts, where changes (based on numeric score) would not be perceptible.

It has been previously reported that obesity poses a substantial risk for dyslipidemia, and that obese patients who undergo bariatric surgery sustain subsequent decreases in cardiovascular risk. One study conducted at the Mayo Clinic, Batsis and colleagues (2008, [104]) evaluated the effect of bariatric surgery on metabolic syndrome in a cohort of obese patients (BMI $\geq 35$ kg/m$^2$) by examining the prevalence of metabolic syndrome in patients who underwent RYGB ($n = 180$) compared to nonsurgical patients ($n = 157$), for up to 14 years postoperatively. (According to the American Heart Association and the National Heart Lung and Blood Institute, metabolic syndrome is defined by the presence of increased serum TG levels, low serum HDL-C levels, increased blood pressure, increased fasting plasma glucose, and increased waist circumference [32].) The investigators found significant reductions in BMI (-32%) total cholesterol (-23%), LDL (-35%), HDL (+17%), and TG (-42%) [102].

The pattern of results in the current study paralleled those reported from previous literature. However, here statistically significant effects of time were found for total cholesterol only, and were not achieved for other lipid parameters. In a previous study, Jones and colleagues (1992) examined changes in serum cholesterol at least one year
following RYGB in 36 patients [105]. Average baseline weight was 266 pounds (121 kg) and reduced to 166 pounds (75 kg) at follow up. TC was reduced by 24% and there was a 40% reduction in TG. However, LDL and HDL were not measured at baseline, so changes in these parameters are unknown. Postoperative LDL results in this study were very similar to those of our study (104 mg/dL), although HDL values there were much higher than those in our study (averages of 39 mg/dL vs. 62 mg/dL, respectively).

Although improved lipid profiles following bariatric surgery are well documented, more recent research has shown that outcomes are moderated by demographic characteristics (i.e. age and gender) [72]. Due to our study’s sample size and homogeneity, we were unable control for these, or other potential confounders (such as participant’s use of lipid-lowering medication). Combined with the (relatively) shorter follow-up time, the aforementioned covariates may have imparted notable effects on lipid profiles, and as such, our outcomes should be interpreted with caution.

We found surgical weight loss to exert a pronounced effect on the severity of sleep apnea. In our reduced set of five participants, there was a significant effect of time where AHI decreased by almost 70% at the six-month time point. In parallel, pressure from APAP therapy was reduced by approximately 21%. These results are similar to those reported previously by Letteri et al. (2008) from a study that included 24 bariatric patients who underwent diagnostic PSG prior to surgery and again one year later. Here, AHI decreased from 47.9 ± 33.8 to 24.5 ± 18.1 events per hour (49% decrease), while average CPAP pressures decreased from 11.5 ± 3.6 cm H$_2$O to 8.4 ± 2.1 cm H$_2$O (27%) [78]. Only six patients were noted to be compliant with CPAP therapy at the follow-up visit, although the threshold compliance level and how it was monitored is unknown. To date, there has been little investigation of changes in AHI after a surgical intervention with concomitant compliance monitoring. Further research is necessary to determine
changes in OSA following bariatric surgery when compliance interventions are prioritized into prospective experimental design.

With regard to spirometry, results from our study, though not statistically significant, yielded a pattern similar to that reported in previous literature. For example, results of one study by Thomas and colleagues (1989) found patients who underwent vertical banded gastroplasty, had a small, yet significant increase in FVC of 7% and FEV$_1$ of 6%, though FVC and FEV$_1$ values were normal at baseline, which was also the case in our study. The previous investigation by Thomas et. al. included 28 females and one male, with baseline characteristics that were similar, albeit slightly less, (mean age of 39.3 years and a mean body weight of 126.4 kg) [106] than those of our study participants. Despite the greater body weight and age of our participants, we found no significant effects of time on FEV$_1$ and FVC. Perhaps significant results noted in the previous literature may be attributed to the variation in follow up visits (range of anywhere from two to 66 months postoperative), which may help to explain the inconsistencies in results noted between the studies. With a longer follow up time, participants in the former study may have engaged in lifestyle changes (such as increased physical activity and smoking cessation) that have had favorable effects on lung capacity, and if follow up times were longer in our current study, similar results may have been demonstrated.

Another related investigation by de Souza et. al. (2010) examined spirometric function in sixty-one patients (all female, age 40 ± 8 years, BMI 49 ± 5 kg/m$^2$ and without respiratory disease) [107]. Here spirometry was measured at six and twelve months following RYGB. There were small, albeit insignificant improvements in FEV$_1$/FVC between baseline and six-months, however it should be noted that these variables were already within normal limits at baseline. Improvements in spirometric indices were found
to correspond with weight loss induced by the surgery. In addition, significant improvements at 12 months were established for FVC ($p = 0.020$). Furthermore, improvements in spirometric indices were found to parallel postsurgical weight loss induced, similar to the pattern apparent in our study.

The study by de Souza et. al. suggests that bariatric surgery can exert favorable outcomes on spirometric values, even if pulmonary function is normal at baseline. Patients in our study also had normal, baseline lung function, however despite this fact, results did not show a significant effect of time on spirometric values (although they did improve slightly from baseline values). It may be that a longer follow up time would have showed more significant improvements in lung function, similar to the outcomes described above.

In conclusion, we found that LRYGB surgery elicits loss of body weight (and decreases in BMI), neck circumference, and results in improvements of SAQLI scores, TC, and AHI in the immediate (up to 6 month) postoperative period. However, our analysis did not reveal any statistically-significant changes in TG, HDL, or LDL concentration, or spirometric indices of lung function, although there was a non-significant tendency for improvement of these indices.

As mentioned previously, there were a number of limitations to our study that may have affected outcomes, not the least of which includes a reduction in statistical power secondary to a very small sample size, and the inability to control for potential confounders. Shorter follow up time, compared to other research, and the exclusion of men have also made comparison of our results with those of other studies quite challenging. Although our hypothesis that improvements to health indices would improve more immediately after surgery was correct, the degree to which they were sustained was less than expected when compared to other literature.
Barring the abovementioned limitations it is possible that a more comprehensive study of similar design would have demonstrated results that equate or surpass those reported in other previous studies. Further research in larger, more homogenous sample sizes is needed to elucidate the immediate health-related outcomes of bariatric surgery, in the context of OSA.
REFERENCES


APPENDICES
Appendix A: Approval from Human Subjects Review Committee at Youngstown State University

You forwarded this message on 12/8/2009 2:05 PM.

Pohle-Krauza, Rachael

From: Cathy Bieber Parrott [cbieberparrott@ysu.edu]
To: rjpohlekrauza@ysu.edu; mlmccarroll@ysu.edu; tavolsko@ysu.edu
Cc: Cheryl Coy
Subject: YSU IRB Protocol 65-09
Attachments:

Dr. Pohle-Krauza, McCarroll and Volsko,

Thank you for submitting your protocol entitled "Effects of bariatric surgery on obstructive sleep apnea". A review of the protocol and informed consent using an expedited procedure for courtesy review finds the protocol meets the minimal risk criteria and has adequate protection of human subjects. If this project isn't completed within 1 year, it must be renewed by submitting a progress form. Best wishes for successful completion of your project.

Cathy Bieber Parrott
Chair, YSU IRB
December 8, 2009

Dr. Rachael Pohle-Krauza, Principal Investigator
Dr. Michele McCarroll, Co-investigator
Ms. Terry Volsko, Co-investigator
Department of Human Ecology
UNIVERSITY

RE: HSRC Protocol Number: 65-2010
Title: Effects of Bariatric Surgery on Obstructive Sleep Apnea (BAROSA)

Dear Drs. Pohle-Krauza and McCarroll and Ms. Volsko:

The Human Subjects Research Committee has reviewed the aforementioned protocol using an expedited procedure for courtesy reviews and issued unconditional approval based on professional courtesy recognition of the Institutional Review Board approval action of 11/24/09 by the IRB of Summa Health System.

Any changes in your research activity should be promptly reported to the Human Subjects Research Committee and may not be initiated without HSRC approval except where necessary to eliminate hazard to human subjects. Any unanticipated problems involving risks to subjects should also be promptly reported to the Human Subjects Research Committee.

Sincerely,

Peter J. Kasvinsky
Dean, School of Graduate Studies and Research
Research Compliance Officer

PJk:cc

c: Dr. Janice Elias, Chair
Department of Human Ecology

www.ysu.edu YSU
January 11, 2011

John Zografakis, MD
c/o Rachael J. Pohle-Krauza
Division of Surgical Research & Trauma
3rd Floor Administration
ACH

Dear Dr. Zografakis:

The IFB reviewed the Addition of Key Personnel, submitted on 12/21/10, for the project entitled:

RP#09125  Effects of Bariatric Surgery on Obstructive Sleep Apnea (BAROSA)

These changes were approved on January 10, 2011.

As you know, you must continue to notify the committee of any protocol changes prior to initiation of the changes. You must also provide the committee with documentation of updated risk information, or serious adverse reactions that occur during the course of this project. Please use the RP number when submitting this information to the committee.

Thank you for providing this information to the committee.

Sincerely,

Thomas S. Alexander, PhD, D(ABMLI)
Chair, Institutional Review Board

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Appendices C – J have been removed due to copyright.

Refer to the print version of this thesis.