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## Obesity Treatment Alternatives: Foods to Surgery

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# OBESITY TREATMENT ALTERNATIVES: FOODS TO SURGERY

A Thesis

Submitted to the Graduate Faculty of the  
Louisiana State University and  
Agricultural and Mechanical College  
in partial fulfillment of the  
requirements for the degree of  
Master of Science

In

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By

Brooke Erwin Bayham  
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## ABSTRACT

The purpose of these studies was to explore the roles of dietary strategies and bariatric surgery in obesity treatment. The breakfast study was a randomized, crossover trial used to evaluate the role of egg proteins, and a retrospective chart review was conducted to obtain comparative information about two different bariatric surgeries.

The breakfast study included 20 subjects who were randomized to receive an egg breakfast (EB) or a cereal breakfast (CB) matched for energy density and macronutrient composition but different protein quality for one week. Following a washout period, each subject was crossed over to receive the opposite breakfast for one week. The EB resulted in lower cumulative lunchtime food intake ( $p=0.05$ ), reduced hunger on day 1 ( $p=0.001$ ), greater feelings of fullness on days 1 and 7 ( $p=0.02$ ), and decreased desire to eat on day 1 ( $p=0.03$ ). Acylated ghrelin was lower on day 1 of the EB compared to the CB ( $p=0.005$ ) but not on day 7. PYY was greater at 120 minutes ( $p=0.006$ ) and 180 minutes ( $p=0.001$ ) on day 1 and at 180 minutes on day 7 ( $p=0.03$ ) after the EB.

The bariatric surgery studies examined 835 Roux-en-Y gastric bypass (RYGB) patients and 766 vertical sleeve gastrectomy (VSG) patients. Study one focused on patients diagnosed with type 2 diabetes (T2D). The acute effect bariatric surgery had on resolving T2D was measured by calculating the number of patients who discontinued their hypoglycemic medication use post-operatively. Upon discharge, 95 of the 123 (77.2%) RYGB patients and 107 of the 139 (77.0%) VSG patients had been taken off their medication. Eight weeks post-operatively, 30 of the 38 (~79%) RYGB patients and 59 of the 71 (83%) VSG patients with follow-up data remained off medication. Study two examined differences in weight loss, early post-operative surgical complications, and insurance coverage between RYGB and VSG patients. RYGB

patients lost more weight at one and two years ( $p<0.001$  for both). There was no significant difference in the percentage of weight loss or complications in insured versus self-pay patients. RYGB patients experienced a higher incidence of major complications than VSG patients ( $p<0.001$ ).

## CHAPTER 1

### INTRODUCTION

When energy intake exceeds energy expenditure, the positive energy balance leads to the storage of excess energy as fat<sup>1</sup>. The abundance of food in the current environment combined with increasingly sedentary lifestyles contributes to positive energy balance<sup>1</sup>. Genetics also play a role in body fat regulation<sup>1</sup>. The genetic makeup of modern man has not significantly changed since the era of the hunter-gather society<sup>1, 2</sup>. During that time, humans ate copiously when food was abundant and were able to store excess energy as fat for times when food was unavailable<sup>1</sup>. This genetic predisposition to store fat combined with behavioral and environmental factors may explain why many individuals are growing obese.

Obesity, a disease of excess energy stored as adipose<sup>1, 3</sup>, has become an epidemic in the US<sup>4, 5</sup>. Approximately 1/3 of the adult population is considered obese<sup>6</sup>. The World Health Organization (WHO) divides obese individuals into three classes: class I (BMI = 30-34.9 kg/m<sup>2</sup>), class II (BMI = 35.0-39.9 kg/m<sup>2</sup>), and class III (BMI  $\geq$  40 kg/m<sup>2</sup>)<sup>7, 8</sup>. Individuals within class III are morbidly obese which indicates they are at least 100 pounds overweight<sup>3</sup>. If current obesity trends continue, data from the National Health and Nutrition Examination Study (NHANES) project that 51.1% of all adults in the US will be obese by 2030<sup>5</sup>, and global projections surpass one billion people by 2030<sup>9</sup>.

Not only is obesity linked to a harsh social stigma<sup>10</sup>, but it is also linked to many co-morbid conditions such as cardiovascular disease<sup>11, 12</sup>, hypertension<sup>11-13</sup>, diabetes<sup>11, 12</sup>, obstructive sleep apnea<sup>11-13</sup>, certain cancers<sup>12</sup>, and degenerative joint disease<sup>3, 12, 13</sup>. According to one prospective study of over 4500 obese patients, the most common co-morbidities were



hypertension (55.1%), obstructive sleep apnea (48.9%), diabetes (33.2%), and asthma (23.1%)<sup>14</sup>. More than 50% of these patients had at least two co-morbid conditions<sup>14</sup>. Even without any existing co-morbid conditions, obesity increases the risk of mortality<sup>15</sup>. In 2000, approximately 360,000 deaths were obesity-related<sup>11</sup>. Because obesity increases the risk of other diseases, healthcare costs for obese individuals exceed those of normal weight individuals<sup>16</sup>. In 2008, obesity-associated medical costs were estimated to be \$147 billion dollars<sup>16</sup> and are projected to reach \$960 billion dollars in the next two decades<sup>5</sup>.

The World Health Organization (WHO) and National Institutes of Health (NIH) clinical guidelines for obesity suggest obese individuals should reduce their energy intake and increase their energy expenditure to induce a 10% weight loss<sup>17, 18</sup>. Diets of different macronutrient compositions have been found to result in similar weight loss of 7% after 6 months<sup>19</sup>, and a diet that follows a 25% caloric restriction has been shown to result in a 10% weight loss at 24 weeks<sup>20</sup>. Dietary strategies that decrease hunger and increase satiety may be useful for individuals following a reduced-energy diet. Holt *et al*<sup>21</sup> tested the effect of several foods on their ability to induce satiety and found that eggs have twice as much satiety-inducing capability as ready-to-eat breakfast cereals<sup>22</sup>. Eating a daily breakfast, especially one that is high in protein, has been shown to reduce ghrelin<sup>23</sup>, increase peptide YY<sup>24</sup>, and reduce energy intake for the remainder of the day<sup>25</sup>. Thus, eating high-protein foods such as eggs for breakfast may enhance weight loss.

Engaging in physical activity can increase energy expenditure and lead to a reduction in weight and body fat<sup>26</sup>. Exercise also plays a role in the prevention of weight gain<sup>26</sup>. Pharmacologic agents such as orlistat can be used in combination with lifestyle modifications to augment weight loss and aid in weight loss maintenance<sup>27</sup>. However, of all the obesity treatment

alternatives available, bariatric surgery is the most effective treatment for morbid obesity<sup>8, 28</sup>. Numerous studies have found that clinically significant weight loss can be achieved through bariatric surgery within one to two years and can be maintained over time<sup>29</sup>. If attempts to lose weight through diet, exercise, and obesity drugs fail, individuals may seek bariatric surgery to lose weight and to improve or resolve any co-morbidities.

### **Justification**

Because obesity currently affects 1/3 of the US adult population, and the number of obese adolescents and children is also increasing, obesity treatment alternatives need to be examined for their effectiveness in inducing and maintaining weight loss. Dietary approaches to obesity may be the safest method for weight management, but few studies show diets that result in significant maintenance of weight loss. Dietary strategies for weight loss that individuals can easily follow over time are needed. Bariatric surgery appears to result in significant weight loss, but most studies focus on the more established gastric bypass. Few studies examine large samples of a newer bariatric operation, the vertical sleeve gastrectomy.

### **Research Questions**

1. Does protein quality affect food intake and satiety in overweight adults?
2. Does the vertical sleeve gastrectomy resolve diabetes as effectively as the Roux-en-Y gastric bypass?
3. Does the vertical sleeve gastrectomy result in similar weight loss to the Roux-en-Y gastric bypass?
4. Does the vertical sleeve gastrectomy result in fewer or greater complications than the Roux-en-Y gastric bypass?

5. Does payment method (i.e. insurance or self-pay) influence weight loss in vertical sleeve gastrectomy patients and Roux-en-Y gastric bypass patients?

## **Objectives**

1. To determine if consuming a breakfast with high quality protein is associated with increased satiety and decreased food and energy intake at lunch.
2. To determine if the vertical sleeve gastrectomy is as effective as the Roux-en-Y gastric bypass in resolving diabetes.
3. To determine if the vertical sleeve gastrectomy results in similar weight loss with a similar or lower complication rate than the Roux-en-Y gastric bypass and if insurance reimbursement affects weight loss.

## **Hypothesis**

1. A breakfast containing greater protein quality will decrease food intake and increase satiety in overweight adults more than a breakfast with lower protein quality.

## **Limitations**

1. The breakfast study did not measure GLP-1 following breakfast or lunch.
2. The breakfast study had a small sample size (n=20).
3. The breakfast study only showed an acute effect of each breakfast.
4. The bariatric surgery studies were based upon information from a retrospective chart review.
5. The bariatric charts had limited follow up so long-term results were not obtained.
6. The bariatric charts lacked laboratory data to show changes in glucose, insulin, cholesterol and triglyceride levels, and vitamin levels.

## **Assumptions**

1. The information contained in the bariatric charts was accurate and reliable.

## **Definitions**

1. National Health and Nutrition Examination Survey (NHANES): a continuous program that collects information about the nutrition and health status of the US population using a complex, multi-stage probability sampling design
2. Body Mass Index (BMI): body weight (kg) divided by height (m<sup>2</sup>) used as a measurement to classify weight status
3. Obesity: BMI  $\geq 30$  kg/m<sup>2</sup>
4. Morbid obesity: BMI  $\geq 40$  kg/m<sup>2</sup>
5. Satiety index score (SIS): score that measures a food's satiating capabilities
6. Branched chain amino acid (BCAA): amino acids with an aliphatic side chain; include the amino acids leucine, isoleucine, and valine
7. Jejunio-ileal bypass (JIB): one of the first bariatric procedures used to induce weight loss but was discontinued because it resulted in severe complications
8. Roux-en-Y gastric bypass (RYGB): a bariatric procedure involving the creation of a small gastric pouch combined with a gastrointestinal bypass which excludes the duodenum and the proximal jejunum
9. Vertical sleeve gastrectomy (VSG): a bariatric procedure involving a subtotal gastric resection of the fundus and body to create a long, tubular gastric conduit along the lesser curve of the stomach
10. National Institutes of Health (NIH): the medical research agency of the United States
11. World Health Organization (WHO): the authority for health within the United Nations system which manages global health issues and the health research agenda

12. Excess weight: mid-point in the range of ideal body weight as defined by the 1983 Metropolitan Life Insurance Tables for a medium frame subtracted from initial weight
13. Excess weight loss (EWL):  $[\text{Weight loss (lbs)}/\text{Excess weight (lbs)}]*100$
14. Type 2 diabetes (T2D): chronic disease in which blood glucose levels are elevated as a result of insulin resistance with or without a defect in insulin secretion by the pancreatic beta cells
15. Homeostatic Model Assessment (HOMA): model used to quantify insulin resistance and beta-cell function
16. American Society for Metabolic and Bariatric Surgery (ASMBS): society created to advance the science of bariatric surgery whose goal is to improve the treatment of obesity and obesity-related diseases through the understanding of metabolic surgery
17. Glucagon-like peptide 1 (GLP-1): peptide hormone produced by the L cells which is released in response to meal intake and may act as physiological regulator of food intake by suppressing appetite after the consumption of food
18. Peptide YY (PYY): peptide hormone produced by the L cells which is released in response to meal intake and may act as physiological regulator of food intake by suppressing appetite after the consumption of food
19. Acylated ghrelin: orexigenic hormone secreted primarily in the stomach which plays a role in appetite regulation by inducing hunger

## CHAPTER 2

### REVIEW OF LITERATURE

Obesity has become a nationwide epidemic over the past few decades<sup>5, 13, 30, 31</sup>. No state had a prevalence of obesity greater than 15% in 1990, but only two decades later in 2010, no state had a prevalence less than 20%<sup>30</sup>. Currently, 36 states have an obesity prevalence greater than or equal to 25%<sup>30</sup>. The morbidly obese population doubled between 2000 and 2005<sup>11</sup>, and data from the 2007-2008 National Health and Nutrition Examination Survey (NHANES) has shown that 33.8% of the United States (US) adult population is obese<sup>32</sup>.

Weight is affected by a combination of genetic, behavioral, and environmental factors<sup>33</sup>. Behavioral factors include diet composition and exercise, and environmental factors include where a person lives, works, and socializes<sup>33</sup>. Although genetics do play a role in some obesity-related diseases, the human genome has not changed enough to completely explain the rise in obesity<sup>33</sup>. The “thrifty gene” hypothesis states that the body’s process of storing calories as fat during abundance in the days of early humans may now be working to our disadvantage<sup>34</sup>. Food is now readily available, and current lifestyles are more sedentary and less labor-intensive compared to the hunter-gatherer era<sup>2</sup>. In addition, when the amount of adipose tissues changes, the body’s desire to maintain energy homeostasis resists weight change<sup>31</sup>. Thus, the lifestyle followed by many individuals leads to a positive energy balance in which more calories are consumed than expended on a daily basis.

Because obesity increases the risk of co-morbidities and mortality, effective strategies should be utilized to induce weight loss. Currently, obesity treatment options include diet, exercise, behavioral modification, anorectic drugs, and bariatric surgery<sup>27, 35</sup>. Non-surgical approaches to obesity typically result in minimal weight loss, and over long periods of time, may

result in weight regain<sup>15, 28</sup>. However, many individuals attempt to lose weight through diet and exercise<sup>26, 36</sup> before undergoing more drastic measures such as bariatric surgery. Also, individuals must be morbidly obese to be clinically eligible to undergo bariatric surgery. A study that examined weight loss diets in over 800 subjects showed that all the diets produced an average weight loss of four kilograms after two years regardless of macronutrient composition<sup>19</sup>. Thus, calorie restriction appears to be the most important factor for dieting and not macronutrient composition<sup>19, 27</sup>. A study examining the chronic effect of caloric restriction showed that a diet that restricted normal caloric intake by 25% resulted in ~10% weight loss at 24 weeks<sup>20</sup>. However, adherence to a low kilocalorie diet can be difficult to maintain over time so using dietary strategies that decrease hunger and increase satiety may improve weight loss efforts<sup>37, 38</sup>.

One easily adaptable strategy that may improve weight loss efforts is to eat a daily breakfast<sup>39</sup>. Body mass index (BMI) and breakfast consumption are negatively correlated<sup>40</sup>. Although breakfast eaters have been shown to have a higher daily energy intake, they have been shown to have lower BMIs than breakfast skippers<sup>40-42</sup>. Because breakfasts differing in macronutrient composition have not been shown to affect lunchtime energy intake differently<sup>43</sup>, individuals should consider consuming breakfast foods known to increase satiety. Eggs, a common breakfast food, have been found to have a 50% greater satiety index scores (SIS) than ready-to-eat cereal<sup>21</sup>. Eggs have been shown to increase satiety and decrease lunchtime energy intake<sup>22</sup>. When individuals ate eggs daily for breakfast in addition to following a reduced calorie diet, they reduced their BMI and waist circumference more than individuals who ate an isocaloric bagel breakfast<sup>37</sup>. They also displayed greater dietary restraint and had greater reductions in hunger than bagel breakfast eaters<sup>37</sup>. In contrast, cross-sectional data from NHANES has shown that individuals who consume ready-to-eat cereals have lower BMIs than

meat and egg breakfast eaters<sup>40</sup>. However, these results may indicate that eating eggs can be a marker of other dietary indiscretions. Thus, including eggs as part of a daily breakfast may induce greater results in a weight loss regimen.

High-protein diets appear to result in greater reductions in weight because protein increases satiety and thermogenesis, reduces loss of lean body mass, and promotes body fat loss, and improves glycemic control<sup>44</sup>. Individuals who increased their protein intake at breakfast had decreased postprandial ghrelin concentrations<sup>23</sup> and thus decreased hunger<sup>23, 45</sup>. Increased intake of protein, especially higher quality proteins, has been shown to enhance weight loss<sup>44, 46, 47</sup>. Consuming more protein also leads to an increased intake of the branched chain amino acid (BCAA) leucine<sup>46</sup>. The satiating effect of eggs may possibly be due to the high quality of egg proteins which are rich in leucine and has been implicated in inducing satiety<sup>44, 47, 48</sup>. Leucine promotes protein synthesis and regulates insulin release and signaling<sup>49</sup>. A study by Layman *et al*<sup>46</sup> compared a moderate protein diet and a high carbohydrate diet with different amounts of leucine ( $9.89 \pm 0.19$  g and  $5.39 \pm 0.10$  g, respectively) over a 10-week period. Subjects in the protein group lost more weight and body fat but less lean body mass than the carbohydrate group although the differences were not significant<sup>46</sup>. However, this suggests that leucine acts as a metabolic regulator, and through its actions in insulin and glucose, can preserve lean muscle while reducing body fat.

Several drugs have been developed to treat obesity through weight reduction<sup>50</sup>. Orlistat prevents ~30% of fat absorption when taken with a meal<sup>27</sup>, but it only produces an average weight loss of 2.9 kg at 12 months<sup>27, 50</sup>. Anti-obesity drugs such as rimonabant and sibutramine produced a weight loss between 3-5 kilograms in six months to one year, but they have been withdrawn from the market due to adverse side effects<sup>27, 50</sup>. Because few anorectic drugs are



available on the market, and many people struggle to lose a clinically significant amount of weight through diet and exercise, they may elect to undergo bariatric surgery.

The first bariatric operation, the jejuno-ileal bypass (JIB), was performed in 1954; however, it resulted in severe complications including hepatic and renal failure<sup>51</sup>. Several years later, Dr. Edward Mason's observations led to the development of the gastric bypass, an operation that resulted in significant weight loss but less severe complications than the JIB<sup>52</sup>. In 1994, Wittgrove and Clark introduced the laparoscopic technique for the gastric bypass which has been shown to have certain advantages over the previously used open method<sup>28, 51</sup>. Surgeons conduct a Roux-en-Y gastric bypass (RYGB) by first creating a small gastric pouch 20-30 milliliters in volume. The duodenum and proximal jejunum are bypassed, and a Roux limb 75-105 centimeters long reroutes the distal jejunum and ileum to the pouch<sup>11</sup>. The RYGB is a restrictive and malabsorptive procedure that induces weight loss through a combination of food restriction and malabsorption<sup>51</sup>.

The vertical sleeve gastrectomy (VSG), a much newer bariatric operation, was originally the first step in the biliopancreatic diversion with duodenal switch<sup>13, 53, 54</sup>. To decrease the risk of surgical complications and mortality in super obese individuals, individuals would first undergo the sleeve gastrectomy which was later followed by a second step<sup>13, 55</sup>. However, the weight loss and co-morbidity resolution achieved with the VSG alone has prompted the use of the VSG as a primary procedure<sup>13, 55</sup>. The sleeve gastrectomy entails a resection of the greater curvature of the stomach which creates a tubular stomach and preserves the pylorus and part of the antrum<sup>11</sup>. The VSG is a restrictive procedure that induces weight loss through the restriction of food intake<sup>51</sup>. Because part of the stomach is removed, gut hormones are also affected and may be a

potential mechanism aiding in weight loss<sup>56</sup>. Currently, the VSG accounts for less than 5% of all bariatric procedures in the US<sup>53, 57</sup>.

The number of bariatric operations performed annually increased 900% between 1998 and 2004<sup>58</sup>. In spite of this significant increase, only 1% of clinically eligible patients undergo a bariatric operation each year<sup>11</sup>. According to criteria established by the National Institutes of Health (NIH), an individual must be morbidly obese ( $\text{BMI} \geq 40 \text{ kg/m}^2$ ) or have a  $\text{BMI} \geq 35 \text{ kg/m}^2$  with a serious co-morbid condition such as cardiopulmonary disease or diabetes to be eligible for a bariatric operation<sup>35</sup>. Today, the laparoscopic gastric bypass comprises the majority of bariatric operations in the US<sup>14, 59</sup>.

Bariatric surgery appeals to morbidly obese individuals because it has been shown to result in clinically significant, sustainable weight loss. The average BMI for individuals electing to have bariatric surgery is greater than  $40 \text{ kg/m}^2$ <sup>60-62</sup>. The RYGB has been shown to result in an average excess weight loss (EWL) of  $50.2 \pm 6.5\%$  at six months post-operatively<sup>56</sup>, and has reached  $\sim 70\%$  at one year<sup>56, 62</sup>. One long-term study showed that RYGB patients can maintain an EWL of 49% 14 years post-operatively<sup>29</sup>. Similarly, the VSG has resulted in an average excess weight loss ranging from  $\sim 39\%$  to  $\sim 56\%$  at six months<sup>56, 63</sup>,  $49\%$  to  $\sim 70\%$  at one year<sup>56, 62, 63</sup>, and  $\sim 68\%$  at two years post-operatively<sup>64</sup>. Average excess BMI loss one year post-operatively for the RYGB and VSG is 70.1% and 55.3%, respectively<sup>65</sup>. Currently, limited data exists in the literature describing long-term weight loss produced by the VSG<sup>66</sup>.

Bariatric surgery also has also been shown to improve or resolve co-morbid conditions such as diabetes significantly more than non-surgical options<sup>67, 68</sup>. Several studies comparing the RYGB and VSG demonstrated that both surgeries comparably resolve hypertension,

dyslipidemia, obstructive sleep apnea, and type 2 diabetes (T2D)<sup>69</sup>. One prospective study that followed 608 morbidly obese patients for 14 years after gastric bypass surgery showed surgery is the most effective treatment for maintaining normal plasma glucose concentrations in individuals with T2D or impaired glucose tolerance<sup>29</sup>. Although diabetic medications help control blood glucose levels, they may not prevent the progression of the disease which leads to microvascular complications including retinopathy, nephropathy, and neuropathy. T2D may also lead to cardiovascular disease which accounts for 70% of the deaths in individuals with T2D in the US<sup>68</sup>.

The VSG has similar efficacy to the RYGB in T2D remission<sup>70, 71</sup>. The RYGB and VSG resolved T2D in approximately 85% of subjects (n=91) in one study at one year post-operatively<sup>70</sup>, and a study comparing the VSG and RYGB in 90 patients found no significant differences in diabetes control between the two operations at one and two years<sup>71</sup>. Both surgeries appear to result in early, dramatic improvements in glycemic control and Homeostatic Model Assessment (HOMA) indices that are maintained post-operatively<sup>72</sup>. However, conflicting ideas remain on the efficacy of the VSG because the proximal small intestines are not excluded<sup>72, 73</sup>. Lee *et al* demonstrated greater T2D resolution in RYGB patients compared to VSG patients at 12 months (93% and 47%, respectively) which they attributed to the exclusion of the duodenum<sup>73</sup>. In contrast, Nocca *et al* found that more VSG patients discontinued taking diabetic medication than RYGB patients<sup>74</sup>. Bariatric surgery can also effectively improve or resolve many other conditions in the majority of patients<sup>55, 61, 69, 75, 76</sup>, and it can also decrease the risk of mortality by 35% compared to morbidly obese individuals who do not undergo obesity surgery<sup>14, 15</sup>.

Studies have shown low overall mortality rates following bariatric surgery ranging from 0.1% to 1.5%<sup>57, 59, 77</sup>. Thirty-day mortality rates appeared to be less than 0.2% for all bariatric

operations<sup>57, 59</sup>, and less than 2% specifically for RYGB<sup>78</sup>. The mortality rate for VSG patients appears to be less than 1%<sup>12, 13, 79</sup>. According to data of over 66,000 surgeries from the American Society for Metabolic and Bariatric Surgery (ASMBS) Centers of Excellence, the three predominant causes of mortality were pulmonary emboli, cardiac complications, and sepsis/infection<sup>59</sup>.

Common minor complications identified by the ASMBS include atelectasis, dehydration, diarrhea, dumping syndrome, esophageal reflux, pneumonia, nausea and vomiting, and infection<sup>80, 81</sup>. Common major complications include cardiopulmonary issues such as cardiac arrest, deep venous thrombosis, pulmonary embolism and respiratory arrest or failure, gastrointestinal (GI) bleeds or leaks, small bowel obstruction, anastomotic stricture, ulcer at the anastomosis or in the GI tract, and wound dehiscence or infection<sup>80, 81</sup>. Complications experienced by patients appear to be dependent on the type of surgery and the surgeon's experience<sup>78</sup>. A review of 3,464 gastric bypass cases found wound infections, anastomotic leaks, gastrointestinal tract hemorrhages, bowel obstructions, and pulmonary emboli were the most common complications occurring in the early post-operative period<sup>82</sup>. Studies report differing overall total complication rates in RYGB patients. Sjostrom *et al*<sup>83</sup> and Carrodeguas *et al*<sup>84</sup> reported a complication rate of 13% in 1164 patients and 31% in 1291 patients, respectively, as well as differing major complications. Complication rates vary in VSG patients and range from 0% to 23.8%<sup>66</sup>. The most common complications patients encounter with the VSG appear to be gastrointestinal bleeds<sup>13, 66</sup> and gastrointestinal leaks<sup>12, 13, 66</sup>.

## Journal Articles

Of the three articles presented as part of this thesis, one has been published, one is under review, and the other is soon to be submitted. The objective of the egg breakfast article was to determine whether high protein quality eaten at breakfast affects satiety and food intake at lunch. The objective of the two articles on bariatric surgery was to compare the vertical sleeve gastrectomy to the Roux-en-Y gastric bypass in terms of weight loss, diabetes resolution, the incidence of major and minor complications, and the effect of insurance coverage on weight loss and complications.

The first article, “Superior Quality of Egg Protein Results in Increased Satiety,” compared the effect an egg breakfast containing high quality protein had on satiety and food intake compared to a ready-to-eat cereal breakfast matched for energy density and macronutrient composition. It has been submitted to the *American Journal of Clinical Nutrition*. Bayham *et al* found that the egg breakfast reduced cumulative lunchtime intake, decreased acylated ghrelin post-breakfast, and increased PYY post-breakfast. The egg breakfast also improved the HOMA index in individuals who had greater insulin resistance prior to the study.

The second article entitled “Early Resolution of Type 2 Diabetes Seen after Roux-en-Y Gastric Bypass and Vertical Sleeve Gastrectomy” has been published in *Diabetes Technology and Therapeutics*. Bayham *et al* found that both operations equally resolved T2D in obese adults, but the vertical sleeve gastrectomy had a significantly lower rate of overall complications in individuals with T2D. At eight-weeks post-operatively, approximately 79% of RYGB and 83% of VSG patients remained off their diabetes medication.

A third article, “Sleeve Gastrectomy Results in Less Weight Loss but Fewer Major Complications than the Roux-en-Y Gastric Bypass” will be submitted to the *Annals of Family Medicine*. Bayham *et al* found that the RYGB resulted in greater weight loss at one and two years than the VSG, but the VSG resulted in fewer major complications than the RYGB.

## CHAPTER 3

### **BREAKFAST CONTAINING EGG PROTEINS INDUCES GREATER SATIETY COMPARED TO A BREAKFAST WITH LOWER PROTEIN QUALITY**

Data from the 2007-2008 National Health and Nutrition Examination Survey (NHANES) showed that 68% of adults in the United States (US) are overweight or obese<sup>32</sup>. Consuming less energy than needed for weight maintenance is the cornerstone of weight loss treatment. However, long-term compliance following a reduced energy diet is challenging<sup>85</sup>. Hence, additional supportive strategies are needed. Researchers are currently investigating nutritional approaches to reduce food intake. Foods differ in their ability to reduce hunger and increase satiety<sup>21</sup>. Breakfast foods with high satiety index scores (SIS) induce a greater feeling of fullness compared to those with lower SIS and are also negatively correlated with energy intake at lunch<sup>85</sup>. Therefore, higher SIS breakfasts may help in reducing food intake during a day.

Eggs, a common breakfast food, have a 50% greater SIS than ready-to-eat (RTE) cereal<sup>21</sup>. An egg breakfast (EB) results in greater feelings of satiety and decreased energy intake at lunch<sup>22</sup>. When habitual EB eaters follow a reduced calorie diet, they reduce their BMI more than those who eat an isocaloric bagel breakfast<sup>37</sup>.

Incorporating eggs in the diet may supplement weight loss efforts by inducing satiety and increasing compliance with a reduced-calorie diet. Eggs are protein-rich and contain high concentrations of the branched-chain amino acid (BCAA) leucine<sup>44</sup>. Leucine plays a role in insulin signaling and glucose metabolism<sup>44, 86</sup>, and it has been shown to decrease food intake and body weight<sup>48</sup>. A mouse model of diet-induced obesity demonstrated that increasing dietary leucine reduces inflammation in the adipose tissue and improves glucose tolerance when consuming a high-fat diet<sup>87</sup>. Previous studies that compared the effects of an EB to a bagel breakfast did not match them for macronutrient composition, and the EB had a greater amount of

protein<sup>22,37</sup>. It was unclear if the satiating effect of the EB was due to greater protein quantity or the better quality of egg proteins.

Here we tested the hypothesis that an EB will induce greater satiety than a RTE wheat cereal breakfast (CB) with lower protein quality but similar energy density (ED) and macronutrient composition. Thus, by matching the protein quantity, we determined if the breakfast containing higher quality protein increased satiety and reduce food intake. The satiating effects of the breakfasts was assessed at the beginning and end of two, one-week periods by hunger and satiety ratings from questionnaires, food intake at lunch, and satiety hormone concentrations. Secondly, we determined changes in indices of glycemic control in response to EB and CB consumption.

## **Methods**

This study was approved by the institutional review board at Pennington Biomedical Research Center. Written informed consent was obtained from the subjects prior to the initiation of study procedures.

### Eligibility Criteria

Individuals were screened over the telephone to determine their eligibility including having a BMI  $\geq 25$  and  $\leq 60$  kg/m<sup>2</sup>, being between 18 and 60 years of age, and having lost no more than 5% body weight in the three months preceding the study. Those who qualified came to the clinic for a screening visit which included a history and physical examination to determine eligibility. Individuals with an unstable cardiac condition; major systemic illness; history of drug abuse or eating disorder; uncontrolled diabetes or hypothyroidism; familial hyperlipidemia; an allergy, sensitivity, or dislike of eggs, soy, or wheat; those attempting to lose weight; or those with an eating disorder were excluded from the study.



## Subjects

Of the 56 subjects who screened for the study, 20 meet eligibility criteria to enter the intervention trial. Subjects were randomized into two groups. One subject withdrew from the study and was subsequently replaced. The data collected for the withdrawn subject was discarded. Group 1 consumed the EB during the first test week and the CB during the second test week, and group 2 consumed the CB during the first test week and the EB during the second test week. Subjects completed the study on individual timelines and were not assessed as groups.

## Procedures

In this randomized, crossover trial, each subject received two diets in random order. Nine subjects were randomized to receive the EB, and 11 subjects were randomized to receive the CB during the first test week. On day one, subjects reported to the clinic following a 12-hour fast and were provided with breakfast at 8:00 AM which they were required to consume completely. The EB was similar to the CB in weight (g), caloric content, and macronutrient composition (described below and in Table 1). An intravenous line was placed in each subject's forearm before breakfast to collect blood samples until 120 minutes after consuming lunch. Subjects remained in the clinic and were given a standardized lunch 180 minutes after they consumed breakfast. A questionnaire assessed their satiety and hunger before and after breakfast and lunch (described below). To avoid unintentional impact on food intake, the subjects were told the purported aim of the study was to determine the effect of breakfast on blood glucose and insulin, blood hormones and blood pressure. Subjects came to the clinic for the next six days at 8:00 AM in a fasting state to eat the same breakfast consumed on day one. No blood samples were collected and lunch was not provided on days 2-6. On day seven, the blood tests and questionnaires were repeated and food and water intake were measured following lunch. After

the first test week, the subjects underwent a two-week washout period in which they consumed their usual pre-study breakfasts. Following the washout period, they returned for the second test week, and the cycle was repeated with the opposite breakfast.

### Breakfast and Lunch

The EB contained two scrambled eggs, 120 ml skim milk, two slices of Holsum® thin white bread, 5 g of butter, and 18 g of Smuckers® strawberry jam. The CB contained 1.5 cups of Special K® ready-to-eat cereal, 200 ml Silk® original soymilk, one slice of Natural Grain “Wheat n’ Fiber”® bread, 13 g of butter, and 10 g of sugar-free strawberry jam. The breakfasts were matched for ED and macronutrient composition but differed in the Protein Digestibility Corrected Amino Acid Score (PDCAAS)<sup>88</sup>, leucine content, and glycemic load (Table 1). A standardized lunch consisting of lemon sage chicken, wild rice, mixed vegetables, a white dinner roll, canned pears, salted butter, 1% milk, and water was provided *ad libitum*. The amount of food and water consumed was covertly weighed both before and after the subject was served.

Table 1. Energy density, macronutrient composition, and protein score of the breakfasts		
	Egg breakfast	Wheat breakfast
Weight (g)	291	293
Energy (kcal)	400	398
Energy density (kcal/g)	1.37	1.36
Carbohydrate (%)	43.1	44.8
Fat (%)	36.0	35.4
Protein (%)	20.2	19.8
Protein (g)	12.5	13.7
PDCAAS <sup>1</sup>	100	42
Leucine (g)	1.77	0.48
Glycemic load	24	30.8
<sup>1</sup> Protein Digestibility Corrected Amino Acid Score		

## Measures

**Demographic characteristics** – Age, race, and sex were self-reported. Height and weight were measured with light clothing and no shoes during the screening visit prior to the initiation of study procedures. BMI was calculated as  $\text{kg/m}^2$ <sup>89</sup>. Weight was also measured on days one and seven of each test week.

**Blood chemistry** – Blood samples were taken from the subject in a fasting state before breakfast was consumed (0 minutes) and were subsequently analyzed to determine fasting serum glucose, serum insulin, peptide YY (PYY), acylated ghrelin, and serum leucine. The Homeostatic Model Assessment (HOMA) index of insulin resistance was calculated as previously described<sup>90</sup> using fasting glucose and insulin levels. Blood samples were also taken 30, 60, 120, and 180 minutes after breakfast and 120 minutes after lunch to repeat the assessments of the satiety-related hormones, PYY and acylated ghrelin. To assess serum leucine concentrations, blood samples were taken 60 and 300 minutes after breakfast.

**Questionnaire** – A visual analog scale (VAS) was used to measure hunger and satiety as previously described<sup>91</sup>. It consisted of lines which subjects were asked to mark corresponding to their feelings for each question from 0 (not at all) to 100 (most imaginable). The following questions were given to the participants using questionnaires presented electronically before and after breakfast and lunch: 1) How hungry do you feel at this moment?, 2) How full does your stomach feel at this moment?, 3) How strong is your desire to eat at this moment?, 4) How much food do you think you could eat at this moment?, and 5) How satisfied do you feel at this moment?

## Statistics

Data were summarized as counts and percents for categorical variables and as means and standard deviations for continuous variables. Student's t-test was employed to assess the significance of the difference between EB and CB with respect to (1) change in each of the five VAS question during the time increment from 30 minutes to 180 minutes post-breakfast, (2) the lunch cumulative energy intake in kcal (day1 + day 7) from fat, carbohydrate, protein and total consumption, (3) changes in acylated ghrelin and PYY concentrations, respectively, across time (0, 30, 60, 120 and 180 minutes post-breakfast) during day 1 and day 7 of EB and CB breakfasts, and (4) change in acylated ghrelin and PYY concentrations, respectively, during the time increment between 30 minutes and 180 minutes post-breakfast during day 1 and day 7. Statistical analyses were all carried out using SAS<sup>®</sup> 9.2 (SAS Institute, Inc, Cary , NC 27513). Statistical significance was declared for  $p \leq 0.05$ .

## **Results**

A total of 20 subjects completed the study [female (75%), African American (70%), mean age 40.7 years, and mean BMI  $\geq 30$  kg/m<sup>2</sup> (Table2)].

Table 2. Baseline characteristics of participants on day 1 of each breakfast*		
	Group 1	Group 2
<i>n</i>	9	11
Male:Female	3:6	2:9
White:Black	2:7	4:7
Age, years	41.7±14.4	39.9±14.0
Weight, kg, EB	100.3±13.9	106.0±20.6
Weight, kg, CB	99.6±13.5	105.7±19.9
BMI, kg/m <sup>2</sup> , EB	35.7±2.8	39.4±9.3
BMI, kg/m <sup>2</sup> , CB	35.6±2.9	39.1±9.2
* Age, weight, and BMI given as mean ± standard deviation		

### Total Food and Energy Intake at Lunch

Subjects had a significantly lower cumulative lunchtime energy intake (kilocalories) consumed at lunch on days 1 and 7) during the EB week ( $p=0.05$ ; Figure 1). The difference between the two breakfasts in food and energy intake was not significant individually on day 1 or day 7. Although the differences were not statistically significant, subjects consumed fewer calories from carbohydrate and protein ( $p=0.06$ ; Figure 1) during the EB test week.

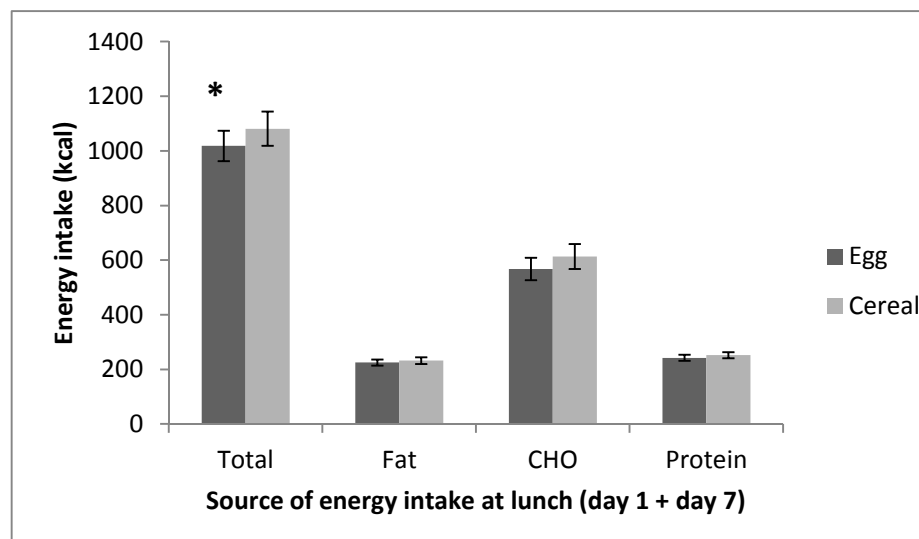


Figure 1. Cumulative total energy intake (kcal) at lunch ( $p=0.05$ ) and energy intake from fat, carbohydrate, and protein in egg breakfast versus cereal breakfast.

### Hunger and Satiety Following Breakfast

To measure the acute effect of each breakfast, the difference between VAS scores at 30 and 180 minutes post-breakfast was determined (Table 3). After consuming the EB on day 1, subjects felt significantly less hungry before eating lunch than on day 1 of the CB ( $p=0.002$ ). The EB also induced a greater feeling of fullness before eating lunch compared to the CB on day 1 ( $p=0.02$ ) and day 7 ( $p=0.02$ ). The EB resulted in a decreased desire to eat before lunch on day 1 ( $p=0.03$ ), and on day 7, subjects felt they could not eat much food at lunchtime ( $p=0.03$ ). Although there was no difference in hunger at 180 minutes following the EB on day 1 or day 7,

the CB increased hunger scores on day 7. The EB did not significantly affect hunger, fullness, desire to eat, or satisfaction after lunch was consumed.

Table 3. Acute effect of egg and cereal breakfasts on change in VAS score from 30 minutes post-breakfast and 180 minutes post-breakfast between day 1 and day 7			
	VAS Question	Day 1 p-value	Day 7 p-value
1	How hungry do you feel at this moment?	0.002*	0.245
2	How full does your stomach feel at this moment?	0.048*	0.019*
3	How strong is your desire to eat at this moment?	0.028*	0.173
4	How much food do you think you could eat at this moment?	0.213	0.029*
5	How satisfied do you feel at this moment?	0.409	0.077
*Significance at $p < 0.05$			

### Satiety-Related Hormones, Glucose, and Insulin

High concentrations of acylated ghrelin, the active form of ghrelin, are associated with hunger<sup>92</sup> and are typically high before a meal<sup>4</sup>. Accordingly, acylated ghrelin concentrations were greatest before breakfast and decreased 30 minutes post-breakfast. Subsequently, acylated ghrelin concentrations increased up to 180 minutes post-breakfast. Compared to the CB, acylated ghrelin concentrations were significantly lower 180 minutes following the EB on day one ( $p=0.005$ ; Figure 2). To measure the acute effect of each breakfast, the difference between ghrelin concentrations at 30 and 180 minutes post-breakfast was determined. On day one of the EB, acylated ghrelin remained significantly reduced before lunch ( $p=0.03$ ; Figure 3) but not on day seven (Figure 4).

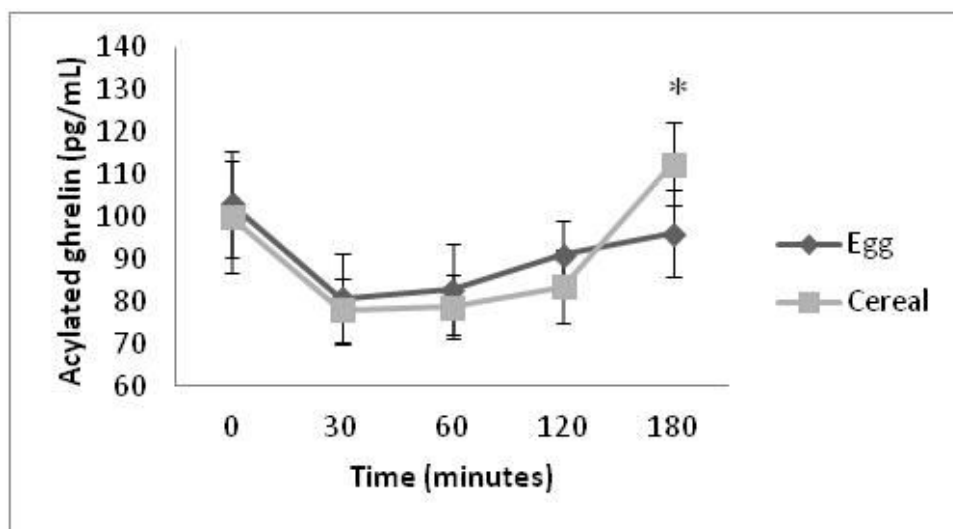


Figure 2. Acylated ghrelin concentrations on day 1 of the egg and cereal breakfasts were different at 180 minutes ( $p=0.005$ ).

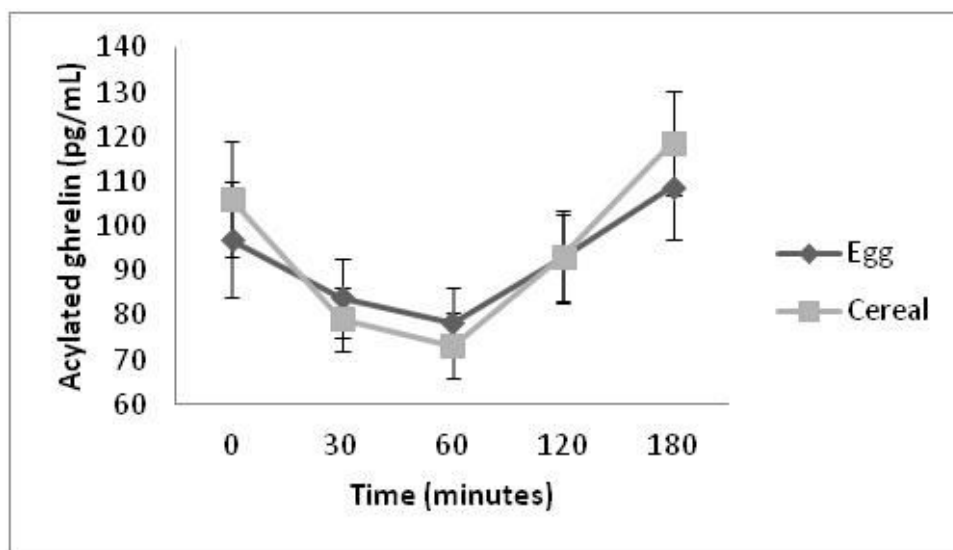


Figure 3. Acylated ghrelin concentrations on day 7 of the egg and cereal breakfasts were not different.

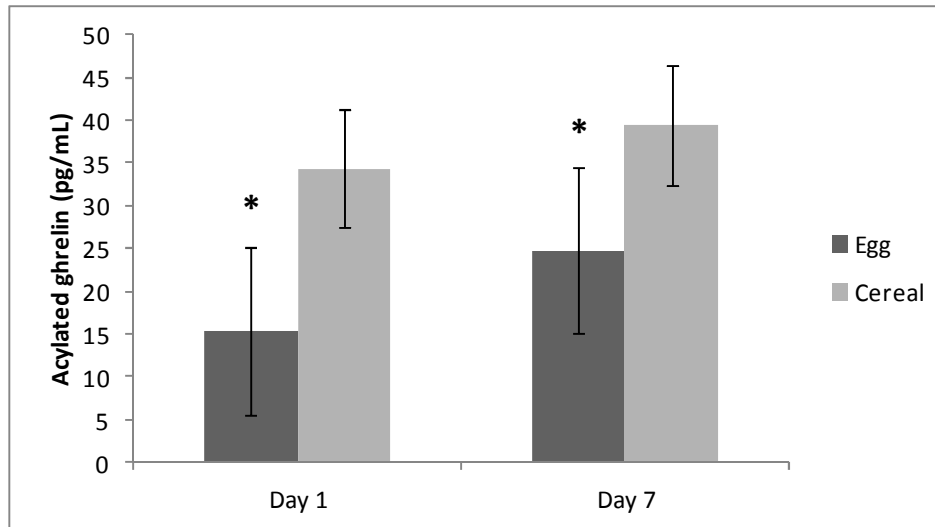


Figure 4. The rise in acylated ghrelin occurring from 30 minutes post-breakfast to 180 minutes post-breakfast on days 1 and 7. The EB significantly decreased acylated ghrelin in day 1 ( $p=0.03$ ) but not on day 7.

Higher concentrations of PYY are associated with satiety, and following a meal, PYY concentrations typically increase<sup>4, 93</sup> as they did in this study. PYY concentrations were lowest before breakfast but increased post-breakfast and reached their peak after lunch on days 1 and 7 for both breakfasts. PYY concentrations were significantly greater during the EB week on day one 120 minutes and 180 minutes ( $p=0.006$  and  $p=0.001$ , respectively; Figure 5) post-breakfast and on day seven 180 minutes post-breakfast ( $p=0.03$ ; Figure 6). The difference between PYY concentrations at 30 and 180 minutes post-breakfast were significantly increased before lunch on day one and day seven of the EB ( $p<0.001$  and  $p=0.005$ , respectively; Figure 7).



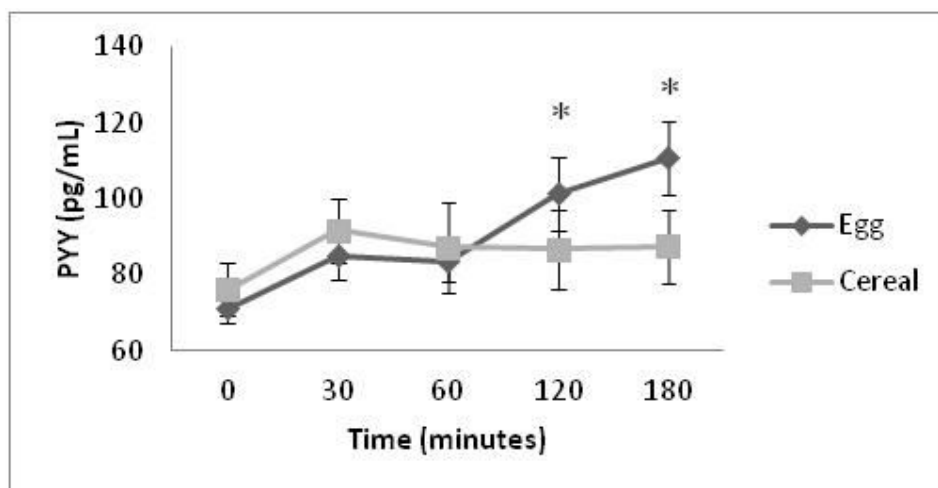


Figure 5. PYY concentrations on day 1 of the egg and cereal breakfasts were different at 120 minutes ( $p=0.006$ ) and 180 minutes ( $p=0.001$ ).

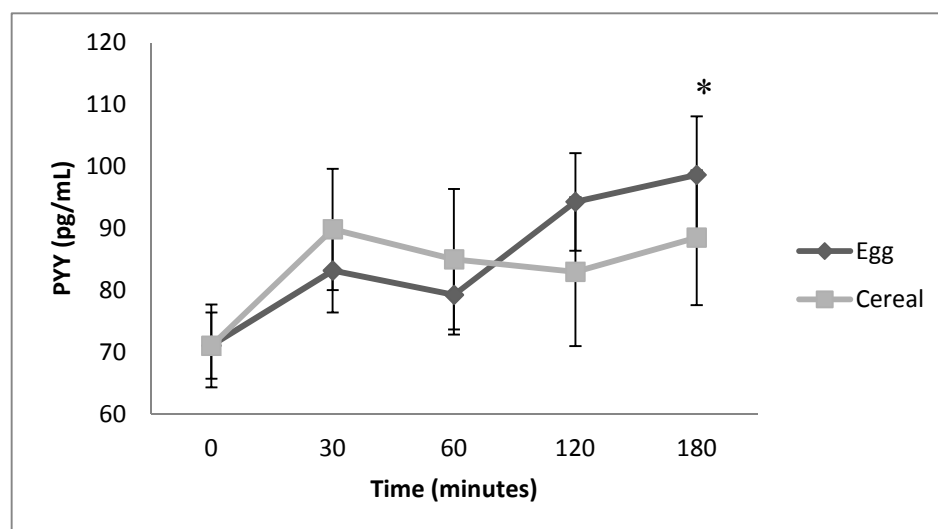


Figure 6. PYY concentrations on day 7 of the egg and cereal breakfasts were different at 180 minutes ( $p=0.03$ ).

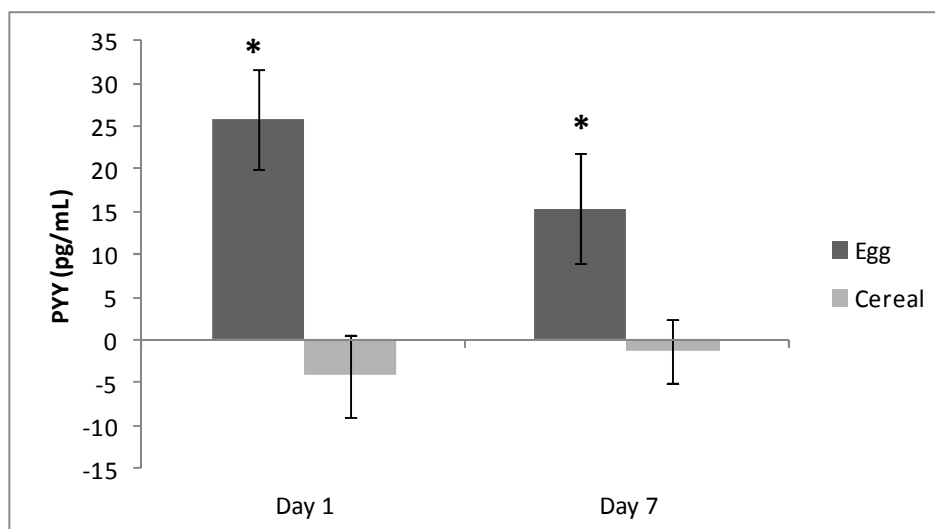


Figure 7. The change in PYY occurring from 30 minutes post-breakfast to 180 minutes post-breakfast on day 1 and 7. The EB increased PYY significantly more than the CB on day 1 ( $p<0.001$ ) and day 7 ( $p=0.005$ ).

There were no significant differences in serum glucose, insulin, or leucine concentrations between the EB and the CB. However, at the end of the EB week, subjects with leucine concentrations in the top 50<sup>th</sup> percentile before breakfast had a significant improvement in their HOMA index for insulin resistance in one week compared to subjects in the bottom 50<sup>th</sup> percentile for leucine ( $p=0.03$ ). Subjects in the top versus bottom 50<sup>th</sup> percentiles for leucine had an average difference of  $-0.51\pm1.51$  and  $0.63\pm0.93$ , respectively, in their HOMA index on day 7 of the EB. This effect was not observed on day 7 of the CB week.

## Discussion

Because adherence to a low calorie diet can be difficult to maintain over time, dietary strategies that decrease hunger and increase satiety may promote compliance and enhance weight loss<sup>37, 38</sup>. Eggs have a high satiety value<sup>21</sup>, and thus previous research hypothesized that consuming an EB would increase satiety and reduce caloric intake at lunch compared to an isocaloric bagel breakfast<sup>22</sup>. As hypothesized, egg intake at breakfast was associated with greater

satiety and significantly lower energy intake during their subsequent meal and for all meals in the next 24 hours<sup>22, 25</sup>. A follow-up study of longer duration compared the effects of the two same breakfasts (an EB and a bagel breakfast matched for ED) on weight loss<sup>37</sup>. Compared to the bagel breakfast, the EB significantly increased weight loss and reduced waist circumference in individuals following a reduced calorie diet. However, the EB had no significant effect on weight loss and waist circumference on individuals not following a reduced calorie diet; therefore, including eggs as part of a daily breakfast appears to induce greater results to a weight loss regimen.

Increased intake of protein, especially those of higher quality, enhances weight loss<sup>44, 46, 47, 49</sup>. The satiating effect of eggs may possibly be due to the high quality of egg proteins which are rich in leucine, a branched chain amino acid (BCAA) implicated in inducing satiety<sup>48, 49, 94</sup>. Vander Wal *et al* matched the breakfasts for ED but not macronutrient composition<sup>22, 37</sup> so the protein quantity as well as the protein quality was slightly higher in the egg breakfasts in these studies; therefore, it was unclear if eggs induce satiety due to the quantity or quality of protein. To determine the satiating effect of an EB, the two breakfasts compared in this study were nearly identical in ED and macronutrient composition and protein quantity but differed in the quality of protein. The breakfasts included a primary source of protein from either eggs or wheat which have PDCAA scores of 100 and 42, respectively,<sup>88</sup> as well as differing leucine content of 8.5% and 6.8%, respectively. Because the two breakfasts were nearly identical, the effect of the EB on reducing lunchtime food intake was not as pronounced as previously observed<sup>22</sup>. Nevertheless, the higher quality of egg protein appears to significantly affect satiety, lunchtime energy intake, and satiety-related hormones.

Previous research showed that when dieters consumed an EB daily, they lost significantly more weight and display greater dietary restraint and reductions in hunger than bagel breakfast eaters<sup>37</sup>. In contrast, cross-sectional data from NHANES III showed that individuals who consumed RTE cereals and other types of wheat-based breakfasts had significantly lower BMIs than those who consumed meat and eggs for breakfast<sup>40</sup>. Meat and egg breakfast eaters were also shown to have the highest daily energy intake of all the breakfast groups included in the analyses<sup>40</sup>. While a precise explanation for this discrepancy is unknown, a possible reason may be that egg intake is a marker of other dietary indiscretions. For instance, males with the highest egg intake reported greater daily energy intake, greater saturated fatty acid intake, and a 5-fold greater consumption of bacon than males with the lowest egg intake although their BMIs were similar<sup>95</sup>. Bacon intake correlated with egg intake in males ( $r=0.35$ ) and females ( $r=0.21$ )<sup>95</sup>. Greater weekly egg consumption was positively associated with a less healthful diet, and males with greater egg consumption were more likely to consume whole milk, red meat, and bacon<sup>95</sup>. Therefore, the positive association of eggs with BMI may be due to the accompanying foods such as bacon that are associated with egg intake. If eggs are consumed without such high fat-high energy accompaniments, they may influence BMI differently. However, the present study was not designed to test this hypothesis.

Diets high in protein appear to result in greater reductions in weight because protein increases satiety and thermogenesis<sup>49, 96</sup>, reduces loss of lean body mass, promotes body fat loss, and improves glycemic control<sup>49</sup>. Recently, studies showed no particular advantage of dietary macronutrient composition, including greater protein intake in long-term weight loss or maintenance<sup>19</sup>. However, this study did not consider protein quality.

Whey, soy, and gluten proteins appear to be equally effective at reducing hunger by mediating the endocrine response in the postprandial state<sup>97</sup>. A breakfast containing 25% whey elicited the greatest response in glucagon-like peptide 1 (GLP-1) and insulin<sup>94</sup> possibly because it has the highest leucine content which increases protein quality<sup>47</sup>. High protein intake leads to greater consumption of the BCAA leucine<sup>44, 49</sup>. Layman *et al*<sup>46</sup> compared a moderate protein diet and a high carbohydrate diet with different amounts of leucine ( $9.89 \pm 0.19$  g and  $5.39 \pm 0.10$  g, respectively) over a 10-week period. Subjects in the protein group lost more weight and body fat but less lean body mass than the carbohydrate group although the differences were not significant<sup>46</sup>. In the present study, although the EB contained three times the amount of leucine than the CB (1.77 g and 0.48 g, respectively), no difference was found in serum leucine between the EB and CB. The breakfasts may not have contained the amount of leucine needed to change serum leucine concentrations in the fed state.

Leucine intake may influence metabolism in other ways as well. Leucine regulates phosphorylation events in the insulin signaling cycle that ultimately leads to the activation of the initiation complex and the promotion of protein synthesis<sup>49</sup>. Leucine also stimulates the pancreas to release insulin and modulates the intracellular insulin signals occurring in skeletal muscle and adipose tissue<sup>49</sup>. This suggests that leucine acts as a metabolic regulator, and through its actions in insulin and glucose, can preserve lean muscle while reducing body fat. BCAA concentrations, including leucine, are elevated in obesity<sup>98</sup>, and increased levels are correlated with insulin resistance<sup>99</sup> which suggests that leucine is a biomarker for abnormal carbohydrate metabolism. Yet, leucine supplementation improves glycemic control<sup>87</sup>. While there were no differences in the group mean for serum leucine, those in the top 50<sup>th</sup> percentile for serum leucine showed a significant improvement in insulin resistance. Also those in the top 50<sup>th</sup> percentile for HOMA

index (higher insulin resistance) had significantly higher serum leucine and showed an improvement in HOMA index. These data suggest that while an EB may influence satiety via leucine-independent pathways, EB/leucine may improve insulin resistance.

No differences were found between the top and bottom percentiles for serum leucine on ghrelin or PYY (data not shown). On day 1 of the EB, the subjects' decreased hunger was reflected by the significant decrease in acylated ghrelin concentrations post-breakfast. Consuming the EB significantly increased postprandial PYY concentrations up to 3 hours following breakfast on both days 1 and 7 which suggests that eggs are more satiating than cereal in spite of the fact that they contained the same amount of protein. Thus, protein quality may have a greater effect on satiety than protein quantity.

This study had some limitations. The breakfasts were designed to resemble typical breakfasts and inordinate manipulations to the ingredients were avoided. Consequentially, although the two breakfasts were closely matched for ED and macronutrient composition, the glycemic load for the EB and CB was 24 and 30.8, respectively. Although it is unlikely that glycemic load is responsible for the differences in satiety, the contribution of this small difference on the favorable effect of the EB on satiety is unknown. Similarly, the role, if any, of different types of lipids or other protein sources, including animal proteins, is unknown. GLP-1, an anorectic hormone secreted in response to dietary proteins, was not measured. A dose response of satiety to egg quantity is also unknown. Future studies should examine whether protein quantity and quality work synergistically together to reduce appetite.

In summary, this study matches the breakfasts for energy density and macronutrient composition to compare the effect of protein quality on measures of satiety. Eggs appear to affect satiety by decreasing acylated ghrelin and increasing PYY up to four hours following breakfast.

These effects were seen despite the closely matched breakfasts. The protein quality does appear to affect satiety although this effect may be independent of leucine. Although serum leucine concentrations did not correlate with measures of satiety, they do appear to be associated with an improvement in glycemic control following just one week of a daily EB. Therefore, due to the superior quality of proteins, eggs may provide a useful adjunct in weight management because they increase satiety. The satiating role of other foods with higher protein quality should be determined. Developing strategies to use foods as appetite suppressants may have considerably greater appeal compared to the use of anorectic drugs which may have several undesirable side effects.

## CHAPTER 4

### EARLY RESOLUTION OF TYPE 2 DIABETES SEEN AFTER ROUX-EN-Y GASTRIC BYPASS AND VERTICAL SLEEVE GASTRECTOMY<sup>100</sup>

In 2007-2008, approximately 72.5 million adults in the United States were considered obese. Data from the 2007-2008 National Health and Nutrition Examination Survey showed an overall obesity prevalence of 33.8% and a combined overweight and obesity prevalence of 68.0%<sup>32</sup>. Compared with individuals with a normal body mass index (BMI) of 18.5–24.9 kg/m<sup>2</sup>, individuals with a BMI of 30 kg/m<sup>2</sup> or more increase their risk of obesity-related diseases<sup>101</sup> such as cardiovascular disease, hypertension, certain cancers, and type 2 diabetes (T2D)<sup>12</sup>.

More than 8% of the U.S. population is affected by diabetes<sup>102</sup>. T2D accounts for the majority of diagnosed cases of diabetes in adults, whereas type 1 diabetes only accounts for 5%<sup>102</sup>. T2D can be treated with diet, oral hypoglycemics, or insulin therapy. Between 2007 and 2009, 58% of adults with diabetes reported taking oral hypoglycemic, 12% reported taking insulin, and 14% reported taking insulin and oral hypoglycemic<sup>103</sup>. The average direct medical costs of an individual diagnosed with diabetes are more than double those of an individual without diabetes<sup>103</sup>. Typically, diet and other strategies such as behavioral modification and exercise result in only limited weight loss, which is usually not maintained<sup>72</sup>.

Bariatric surgery is the most effective tool for substantial weight loss and long-term weight maintenance in the obese population and far surpasses nonsurgical obesity treatments<sup>104</sup>. For example, a lifestyle intervention program reported an initial weight loss of 8.6% at 1 year, and at 4 years, the individuals maintained a weight loss of 4.7%<sup>15</sup> compared with individuals who underwent gastric bypass and had an average weight loss of 32% at 1–2 years and 25% at 10 years<sup>27</sup>. The laparoscopic technique for Roux-en-Y gastric bypass (RYGB) was introduced in

<sup>100</sup>Reprinted by permission of Diabetes Technology and Therapeutics



the early 1990s<sup>68</sup> and has become the most widely used bariatric operation<sup>72</sup>. Improvements in glycemic control have been seen in RYGB patients postoperatively before substantial weight loss has occurred<sup>29, 72</sup>. The vertical sleeve gastrectomy (VSG), a newer bariatric procedure than the RYGB, was originally performed as the first step in a two-step procedure leading to either a RYGB or a biliopancreatic diversion with a duodenal switch in superobese patients (see Appendix B)<sup>12, 13, 70, 104, 105</sup>. However, several studies have indicated that the laparoscopic VSG can act as a stand-alone procedure and be as effective as the RYGB in initiating weight loss and resolving T2D<sup>70, 72, 104</sup>. The VSG has provided promising results as a primary operation<sup>15</sup>, although nationwide it accounts for only 7.6% of bariatric operations<sup>106</sup>.

Several studies have compared the effect of the RYGB to the VSG in diabetes patients; however, these had a maximum of 91 subjects and focused on follow-up data at 1 or more years<sup>71, 73, 74, 104</sup>. One of the most remarkable features of the RYGB is rapid diabetes resolution before significant weight loss<sup>29, 68</sup>. Only one of the studies comparing glucose metabolism following RYGB and VSG in patients concentrated on the early postoperative period of 1–3 months; the study concluded that both operations led to improvements in glucose homeostasis, but it only had 13 RYGB patients and 14 VSG patients<sup>72</sup>. The current study compared a much larger group of diabetes subjects taking medications who were operated on by the same two surgeons with over 120 patients in both surgical groups. Because there has been a focus on the early resolution of diabetes prior to significant weight loss with both the RYGB and VSG, the goal of this retrospective study was to compare the respective efficacy of the two surgeries in resolving the need for hypoglycemic medication in the first 2 months postoperatively.

## Methods

Between 2002 and 2010, obese patients with T2D ( $n = 262$ ) on hypoglycemic medication underwent either the RYGB ( $n = 123$ ) or the VSG ( $n = 139$ ). All data were obtained from the surgeons' office and recorded retrospectively. The surgeon provided a timeline that requested the patient return for follow-up visits at 2 weeks, 2 months, 6 months, and annually for 5 years; however, according to the surgeons, many patients discontinue follow-up at 2 months if they do not develop any complications.

### Diabetes Medication

All preoperative medications were recorded for each patient. Follow-up data were used to determine if the patient resumed, discontinued, or changed medications postoperatively. T2D resolution was defined as no longer requiring diabetes medication following surgery. Because routine fasting blood glucose measurements were not taken, improvement in T2D control was defined as a reduction in the number of diabetes medications taken postoperatively. Combination therapy was defined as taking both insulin and an oral hypoglycemic medication.

### Complications

Every complication occurring during or following surgery for each patient was recorded. The total number of complications was determined for the hospital stay and upon discharge for both operations. RYGB patients had longer hospitalizations with more records of temperatures and vital signs, routine urinalysis, and complete blood count, notation of cholelithiasis on operative reports, and routine chest X-rays that were not routinely performed in VSG patients. Thus, atelectasis, anemia, elevated blood pressure, fever, hematuria, and cholelithiasis were removed from the analysis because they were more likely to be recorded as complications in the

RYGB group compared with the VSG group. The remaining complications were separated into major and minor categories based on the judgment of the surgeons. Once these adjustments were made, the incidence of overall major and minor complications was determined. Table 4 lists all major and minor complications included in the analyses.

Table 4. Complete List of Complications for Both Operations Used in the Data Analyses	
Major Complications	Minor Complications
<ul style="list-style-type: none"> <li>• Gastrointestinal leak</li> <li>• Anastomotic stricture</li> <li>• Small bowel obstruction</li> <li>• Hernia</li> <li>• Small bowel incarceration</li> <li>• Gastrointestinal bleed</li> <li>• Hypotension</li> <li>• Cardiac ectopy</li> <li>• Bradycardia or Tachycardia</li> <li>• Hypoxemia</li> <li>• Pneumonia</li> <li>• Pneumothorax</li> <li>• Pouch laceration</li> <li>• Azotemia</li> <li>• Heart failure</li> <li>• CO<sub>2</sub> narcosis</li> <li>• Ventricular bigeminy</li> <li>• Pulmonary venous congestion</li> <li>• Septicemia</li> <li>• Shock</li> <li>• Anastomotic ulcer</li> <li>• Mesenteric venous thrombosis</li> <li>• Hematemesis</li> <li>• Peptic or Perforated ulcer</li> <li>• Deep vein thrombosis</li> <li>• Pulmonary embolus</li> <li>• Adhesions</li> <li>• Fistula</li> <li>• Guillain-Barre syndrome</li> <li>• Pancreatitis</li> <li>• Small bowel intussusception</li> <li>• Necrotic small bowel</li> <li>• Perforation</li> </ul>	<ul style="list-style-type: none"> <li>• Gout</li> <li>• Nausea and vomiting</li> <li>• Dehydration</li> <li>• Hypokalemia</li> <li>• Hematoma</li> <li>• Hyper/Hypoglycemia</li> <li>• Ileus</li> <li>• Anastomotic edema</li> <li>• Elevated hepatic transaminases</li> <li>• Gastroparesis</li> <li>• Abdominal wall abscess</li> <li>• Malnutrition</li> <li>• Gastritis</li> <li>• Dumping syndrome</li> </ul>

(Table 4 continued)

<ul style="list-style-type: none"> <li>• Omental torsion</li> <li>• Blind pouch syndrome</li> <li>• Death</li> </ul>	
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### Statistical Analysis

All data were analyzed using a  $\chi^2$  distribution. A *P* value of  $< 0.05$  was considered statistically significant.

### **Results**

Although patients were given a schedule to follow, many were noncompliant, and therefore there was great variability in the timing of follow-up visits.

### Demographics

Age, weight, and BMI are given as mean  $\pm$  SD values (Table 5). Race was not recorded for 49 RYGB patients and 30 VSG patients. There were no significant differences in the patient demographics when comparing the two surgical groups.

Table 5. Pre-operative Characteristics of Study Population According to Operation		
	Roux-en-Y Gastric Bypass	Vertical Sleeve Gastrectomy
n	123	139
Age, years	46.8 $\pm$ 9.5 (18-65)	50.5 $\pm$ 10.3 (18-73)
Weight, kg	137.0 $\pm$ 26.5 (95.9-225.0)	131.3 $\pm$ 29.0 (68.2-235.0)
BMI, kg/m <sup>2</sup>	48.7 $\pm$ 8.1 (37-69.6)	45.8 $\pm$ 9.0 (30.9-72.1)
Sex (% Female)	78.0	66.9
Race (%)		
• White	77.0	89.9
• Black	21.6	7.3
• Hispanic	1.4	1.8
• Other	0	0.9
Data are mean $\pm$ SD values (range) as indicated.		

Table 5 continued

BMI, body mass index.
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Change in Diabetes Medication Usage

Upon discharge, 95 of the 123 (77.2%) RYGB and 107 of the 139 (77.0%) VSG patients had been taken off their diabetes medication. Seventeen of the 26 (65.4%) RYGB patients and 19 of the 32 (59.4%) VSG patients who remained on diabetes medication up to 8 weeks postoperatively showed improvement in their diabetes control by reducing the number of medications taken and were not significantly different. Two RYGB patients who were not taking diabetes medication preoperatively began taking them postoperatively. Patients who reported taking medications postoperatively either remained on the same therapy as preoperatively or switched to another type of therapy (Table 6).

Table 6. Patients Reporting Diabetic Medication Use Post-Operatively		
	Roux-en-Y Gastric Bypass	Vertical Sleeve Gastrectomy
n	28 <sup>a</sup>	32 <sup>b</sup>
No Change <sup>c</sup>	15 (53.6)	21 (67.7)
Combination Therapy → Insulin	5 (17.8)	5 (16.1)
Combination Therapy → Oral Agent	1 (3.6)	4 (13.0)
Oral Agent → Insulin	7 (25.0)	1 (3.2)
Data are number of patients (%). P < 0.05 versus bypass versus sleeve for all rows (one-tailed <i>t</i> test). <sup>a</sup> Two patients who were not on pre-operative medications began taking them post-operatively. They are reported as no change. <sup>b</sup> One patient reported taking medication pre- and post-operatively but the chart did not specify what kind of therapy; therefore, this patient's data is unreported and the percentages were found using n=31. <sup>c</sup> Indicates patient remained on same therapy (oral, insulin, or combination) post-operatively.		

Eight weeks postoperatively, follow-up data were available for 38 RYGB patients and 71 VSG patients. Approximately 79% ( $n = 30$ ) of RYGB patients and 83% ( $n = 59$ ) of VSG patients remained off diabetes medication.

### Incidence of Complications

The overall incidence of major and minor complications was 24.8% and 22.8%, respectively, for RYGB patients and 3.6% and 6%, respectively, for VSG patients ( $P < 0.001$ ). The incidence of complications both perioperatively and after discharge is shown in Table 7.

Table 7. Number of Diabetic Individuals Who Experienced a Complication Due to Surgery				
	Surgery [n (%)]			
	Major Complications		Minor Complications	
	Hospital/Peri-operatively <sup>a</sup>	After Discharge <sup>b</sup>	Hospital/Peri-operatively <sup>c</sup>	After Discharge <sup>d</sup>
Roux-en-Y Gastric Bypass	19 (9.4)	31 (15.3)	20 (9.9)	26 (12.9)
Vertical Sleeve Gastrectomy	1 (0.6)	5 (3.0)	1 (0.6)	9 (5.4)
<sup>abc</sup> $P < 0.001$ for comparison of procedures.				
<sup>d</sup> $P < 0.025$ for comparison of procedures.				

## **Discussion**

Although diabetes medications help control blood glucose levels, they may not prevent the progression of the disease process, which leads to microvascular complications including retinopathy, nephropathy, and neuropathy. T2D may also lead to cardiovascular disease, which, in the United States, accounts for the death of 70% of individuals with T2D<sup>68</sup>. Bariatric surgery appears to be the best method to prevent the occurrence and progression of T2D<sup>29, 68</sup>.

Although this study and the study by Peterli *et al*<sup>72</sup> are the only studies to focus on the early response of T2D to both RYGB and VSG, other studies have evaluated the later response of T2D to these operations<sup>71, 73, 74, 104</sup>. Similar to this study's results, some of these other studies found that VSG has similar efficacy as that reported for T2D remission with RYGB<sup>70, 71</sup>. One found that both RYGB and VSG had a resolution rate of approximately 85% in 91 patients at 12 months postoperatively<sup>70</sup>, and another showed no significant differences in T2DM between the two surgeries at 1 and 2 years postoperatively in 90 patients<sup>71</sup>. Both surgeries appeared to result in early, dramatic improvements in glycemic control that was maintained postoperatively<sup>72</sup>. However, some studies still suggest that RYGB may lead to better T2DM resolution, possibly because of the exclusion of the proximal small intestines from the stream of undigested chyme<sup>73</sup>. For example, one study that compared T2D remission for both operations showed almost a twofold higher remission in RYGB patients compared with VSG patients<sup>73</sup>. In contrast, another study reported greater diabetes resolution in VSG patients compared with RYGB patients<sup>74</sup>. Approximately 76% of VSG patients discontinued their diabetes pharmacologic treatment compared with only 60% of RYGB patients<sup>74</sup>. Similarly, other studies report discontinuation of diabetes medication in the majority of VSG patients<sup>13, 70</sup>.

A high preoperative BMI, a previous bariatric operation, and T2D have been shown to be positive predictors for the occurrence of surgical complications<sup>105</sup>. Several case series have reported complication rates less than 10% in VSG patients<sup>12, 105, 106</sup>. Similarly, our study showed an overall complication rate of 9.6% in diabetes patients undergoing VSG. In contrast, RYGB patients appear to be more at risk for postoperative complications. Schauer *et al*<sup>68</sup> found an overall major complication rate of 13.6% and minor complication rate of 24.9% in 191 diabetes patients undergoing RYGB. The current study showed a higher incidence of major complications

in the RYGB group (24.7%), but the minor complication rate (22.8%) was similar to the results of Schauer *et al*<sup>68</sup>. Major complications commonly reported include gastrointestinal leaks<sup>15, 29</sup>, small bowel obstructions<sup>13, 68</sup>, and deep vein thromboses<sup>68</sup>. Minor complications commonly reported include wound infection<sup>13, 29, 68</sup>, nausea and vomiting<sup>68</sup>, and ulcers<sup>68</sup>. The only death reported in this review was a bypass patient with T2D who died less than 6 weeks postoperatively because of a pulmonary embolism. Similarly, other studies have suggested low mortality rates: Basso *et al*<sup>13</sup> reported only two deaths in 300 cases, and Gan *et al*<sup>107</sup> reported no deaths in 378 cases. In spite of the risk of complications, bariatric surgery is associated with decreased overall mortality compared with findings among obese individuals seeking conventional treatment<sup>27</sup>.

Limitations of this study include missing demographic data, which may skew the means for both operations. Another limitation is the lack of laboratory data showing pre- and postoperative blood glucose and hemoglobin A1c levels to confirm improvement in blood glucose control. Follow-up was marginal so long-term maintenance could not be determined. Long-term complications such as osteoporosis and vitamin deficiencies are typically handled by the patient's primary care physician. Because these charts could not be accessed, long-term complications were not recorded so that their prevalence would not be underestimated.

## **Conclusions**

Bariatric surgery appears to be an effective treatment for diabetes. Both the RYGB and VSG appear to give similar early resolution to diabetes prior to significant weight loss in more than half of the operated patients. Many individuals who were unable to discontinue their diabetes medications were able to reduce the number of medications. The risk of complications



also appears to be relatively low, especially in VSG patients. This review supports prior evidence that bariatric surgery is a very successful treatment for obese individuals with diabetes seeking optimal glycemic control. Although our study has limited long-term follow-up, we focused on the question of early diabetes resolution as measured by the ability to stop hypoglycemic medication in a large group of community-operated patients. RYGB and VSG seem to have a similar positive effect on the early resolution of diabetes; however, the rate of complications was less with the VSG. Therefore, the VSG should be considered as a viable option for individuals with T2D seeking weight loss surgery.

## CHAPTER 5

### **SLEEVE GASTRECTOMY RESULTS IN LESS WEIGHT LOSS BUT FEWER MAJOR COMPLICATIONS THAN THE ROUX-EN-Y GASTRIC BYPASS**

Data from the 2007-2008 National Health and Nutrition Examination Survey (NHANES) was used to show that 33.8% of adults in the United States (US) are obese<sup>32</sup>. Bariatric surgery is the most effective therapy for morbid obesity<sup>8</sup>, and its use has increased exponentially over the past decade from approximately 13,400 surgeries in 1998<sup>108</sup> to approximately 220,000 surgeries in 2008<sup>109</sup>. However, only 1% of clinically eligible individuals are using bariatric surgery as a treatment option for morbid obesity<sup>109</sup>. Data from the Bariatric Outcomes Longitudinal Database (BOLD) demonstrated that the majority of individuals seeking bariatric surgery are adults 26-55 years of age (71.2%), females (78.8%), and white (78.1%), and more than half of these individuals undergo the gastric bypass operation<sup>57</sup>. A newer bariatric operation, the vertical sleeve gastrectomy (VSG), has emerged as a one-step procedure from the first step in creating the biliopancreatic diversion with a duodenal switch<sup>13, 54</sup> for super obese patients. Although the VSG accounts for less than 5% of all bariatric procedures performed in the US<sup>57, 59</sup>, it appears to be safe, results in adequate weight loss, and is gaining recognition as a suitable treatment for the morbidly obese patient.

Bariatric surgery has been shown to result in more significant long-term weight loss compared to non-operative methods such as diet and exercise<sup>15, 27, 28, 56, 67</sup>. The average body mass index (BMI) for individuals electing to have bariatric surgery is greater than 40 kg/m<sup>2</sup><sup>61, 62, 76</sup>. Bariatric surgery results in substantial weight loss and improvement or resolution of co-morbid conditions<sup>31, 76</sup> but can be accompanied by complications. The incidence of complications associated with the Roux-en-Y gastric bypass (RYGB) and the VSG is low<sup>3, 53</sup>

which may be due in part to a growth in the experience of surgeons and the introduction of laparoscopic techniques<sup>8, 28, 110</sup>.

Many of the bariatric surgical series have been reported from academic centers<sup>14, 57, 59</sup>, but as the number of bariatric surgeries performed annually continues to rise, community surgeons are performing the operations more frequently. The community surgeon meets with the patient pre-operatively and for several weeks post-operatively. If a patient does not encounter an early serious surgery-related complication, the patient may seek follow-up with their family physician after the first six weeks of the post-operative period for continued care. Although there are guidelines for the pre- and post-operative care of bariatric patients<sup>111, 112</sup>, family physicians should also understand the bariatric operations used, their potential for weight loss, improvement of co-morbid conditions, and the associated surgical complications occurring in the initial post-operative period. The objective of this report is to compare the weight loss and early surgical complications in more than 1600 patients who underwent either the RYGB or the VSG in a private community surgical practice.

## **Methods**

This study was exempted by the institutional review board at Pennington Biomedical Research Center.

### Subjects

We conducted a retrospective chart review of 835 RYGB patients and 766 VSG patients who underwent their operation between 2002 and 2010 by two surgeons in a private community surgical practice. All of the patients met the eligibility criteria for bariatric surgery as defined by the National Institutes of Health<sup>35</sup>. The patients were divided into either insured or self-pay

categories based upon information provided in the chart. We hypothesized that self-pay patients would lose more weight based on their greater personal financial investment in the procedure and maintain better long-term weight loss than individuals who had insurance reimbursement. Because some demographic data were missing, the missing data were subtracted from the group total and the new totals were used to compute percentages for age, sex, race, and insurance coverage.

### Weight Loss

Each patient's weight on the day before or the day of surgery was documented as the patient's baseline weight. Post-operative weights were recorded at the weekly time points on which they were obtained for up to two years. The patients' weights between 26-52 weeks and 78-104 weeks were compared to their baseline weight to determine the percentage of total body weight lost at one and two years. The weight loss in insured and self-pay patients in both surgical groups was also compared.

### Complications

Any event occurring during surgery or within the first six weeks post-operatively was recorded for every patient for both operations. The recorded complications were divided into minor and major categories in consultation with the operating surgeons following the guidelines of the American Society for Metabolic and Bariatric Surgery<sup>3</sup>. The surgical complications in insured and self-pay patients in both surgical groups were also compared.

## Statistical Analyses

A Student's t-Test was used to determine differences in normally distributed data. The  $\chi^2$  distribution was used to determine differences in categorical data. Significance was defined as  $\alpha < 0.05$ .

## **Results**

Age, gender, race, pre-operative weight, pre-operative BMI, and insurance coverage were recorded if available in the patient's chart (Table 8). On average, VSG patients were approximately three years older than RYGB patients. Significantly more white individuals underwent surgery than blacks ( $p=0.025$ ) or Hispanics and other ethnicities ( $p=0.015$ ). Significantly more females underwent surgery than males ( $p=0.004$ ). Baseline weight and baseline BMI were different between the two surgical groups ( $p<0.001$ ).

Table 8. Pre-Operative Demographic Characteristics of Patients in Each Surgical Group			
	Roux-en-Y Gastric Bypass	Vertical Sleeve Gastrectomy	P-value
Age, years	n=829 39.6±10.4 (16-68)	n=764 43.1±11.4 (15-73)	<0.001
Weight, kg	n=805 134.2±27.8	n=761 126.6±29.7	<0.001
BMI, kg/m <sup>2</sup>	n=805 47.9±8.1	n=761 45.1±8.9	<0.001
Gender (%)	n=832	n=766	0.004
Male	17.4	18.5	
Female	82.6	81.5	
Race (%)	n=523	n=577	
White	76.5	88.4	0.025
Black	19.7	8.8	0.015
Hispanic	3.1	1.7	0.015
Other	0.8	1.0	
Insurance coverage (%)	n=688	n=742	<0.001
Insured	90.0	8.2	
Self-pay	10.0	91.8	

Table 8 continued

Age is presented as the mean  $\pm$  standard deviation (range).  
Weight and BMI are presented as mean  $\pm$  standard deviation.

### Weight Loss

There was a significant difference in the percentage of initial weight lost between the RYGB and VSG surgical groups at one ( $p<0.001$ ) and two years ( $p<0.001$ ; Figure 8). At one year, RYGB patients ( $n=158$ ) lost 36.4% and VSG patients ( $n=242$ ) lost 29% of their baseline body weight. At two years, RYGB patients ( $n=39$ ) lost 42.7% whereas VSG patients ( $n=135$ ) lost 30.3% of their baseline body weight.

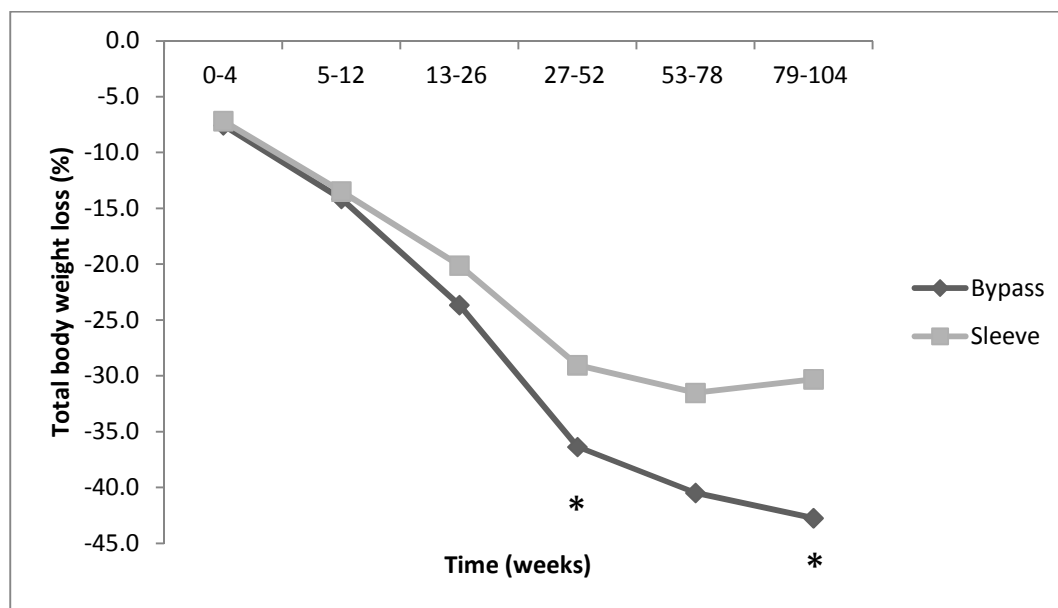


Figure 8. The Roux-en-Y gastric bypass results in greater weight loss at one and two years ( $p<0.001$  for both).

There were no differences in weight loss between self-pay and insured RYGB and VSG patients (Table 9). Self-pay patients in both surgical groups continued to lose weight up to two years. Self-pay VSG patients lost 31% more weight at two years than insured VSG patients, but

this difference was not statistically significant. RYGB patients with insurance coverage continued to lose weight up to two years, but insured VSG patients re-gained almost 8% of their weight at two years.

Table 9. Percentage of Weight Loss between the Roux-en-Y Gastric Bypass and the Vertical Sleeve Gastrectomy at 1 and 2 Years Based upon Payment Method <sup>a</sup>				
	Roux-en-Y Gastric Bypass		Vertical Sleeve Gastrectomy	
	1 year	2 years	1 year	2 years
Insurance	36.7±9.7	45.6±23.4	27.7±10.5	19.8±29.0
Self-pay	34.0±8.0	41.9±27.4	27.0±9.3	28.7±23.5
<sup>a</sup> Mean ± standard deviation				

### Complications

RYGB patients experienced a significantly higher incidence of complications than VSG patients ( $p<0.001$ ). During the peri-operative period in the hospital, 20.4% ( $n=170$ ) of RYGB patients and 1.0% ( $n=8$ ) of VSG patients experienced a complication. In the first six weeks post-operatively, 15.4% ( $n=129$ ) of RYGB patients and 4.2% ( $n=32$ ) of VSG patients experienced a complication. RYGB patients experienced a greater number of the following major complications than VSG patients: stricture ( $p<0.001$ ), gastrointestinal bleed ( $p<0.001$ ), small bowel obstruction ( $p<0.025$ ), and cardiopulmonary complications ( $p<0.001$ ). The incidence of gastrointestinal leaks and thromboembolic complications was not different in the RYGB and VSG operations (Table 10). There were no differences in surgical complications between insured and self-pay patients for either operation.

Table 10. Incidence of Major Complications among Total Population*		
	Roux-en-Y Gastric Bypass	Vertical Sleeve Gastrectomy
Stricture <sup>1</sup>	26 (3.1)	2 (0.3)
Gastrointestinal Bleed <sup>1</sup>	25 (3.0)	1 (0.1)
Gastrointestinal Leak	4 (0.5)	0 (0)
Small Bowel Obstruction <sup>2</sup>	9 (1.1)	0 (0)
Cardiopulmonary <sup>1</sup>	19 (2.3)	2 (0.3)
Thromboembolic	1 (0.1)	3 (0.4)
* n (%)		
<sup>1</sup> p<0.001		
<sup>2</sup> p<0.025		

## Discussion

Bariatric surgery is the most effective treatment for morbid obesity because it significantly reduces body weight, sustains weight loss, and improves co-morbidities associated with obesity to a greater extent than non-surgical treatments<sup>8, 113, 114</sup>. Individuals typically seek a weight loss operation when other treatment options such as diet, exercise, and behavioral modifications fail to produce substantial or durable weight loss<sup>8, 114</sup>. Obesity decreases life expectancy<sup>28</sup>, but undergoing bariatric surgery can decrease the risk of mortality in the morbidly obese by 35% compared to non-operated controls<sup>14, 15</sup>. This increase in life expectancy appears to be due to the improvement or resolution in obesity-related co-morbidities such as type 2 diabetes, certain cancers, and heart disease<sup>61, 115</sup>.

Lifestyle modification programs report only modest weight loss usually followed by weight regain<sup>27</sup>, and pharmacologic therapies such as orlistat and phentermine produce a weight loss of only 2.9-3.6 kilograms after one year<sup>27, 50, 116</sup>. The RYGB has been reported to result in maximum total body weight loss of 32% at one to two years<sup>15</sup>. Surgical journals express weight loss as a percent of excess weight loss [(weight loss/excess weight)\*100 where excess weight is baseline weight minus ideal weight as defined by the 1983 Metropolitan Life Insurance Tables



for a medium frame]. The RYGB has been shown to result in excess weight losses of 70% at two years, 58% at 5 years, and 55% after ten years<sup>29</sup>. Our retrospective review showed greater total body weight loss at one and two years for RYGB patients, and the VSG patients in our study lost an amount of weight similar to that previously reported for the RYGB<sup>15, 117</sup>. Mean percent excess weight loss reported for VSG patients ranges from 49-62% at one year<sup>62, 63, 65</sup> and up to 68% at two years<sup>64</sup>. The VSG results in considerable excess weight loss at one year in obese patients with lower BMIs<sup>54</sup> and has been favored by surgeons in high-risk populations<sup>118</sup>. Although some weight regain occurs, the excess weight loss exceeds the results of non-surgical treatment options.

This study showed a drastic gap in insurance coverage between the RYGB and VSG surgical groups. Because the RYGB is a more established operation, the percentage of individuals undergoing the RYGB covered by insurance was much greater than the newer VSG. A review of over 66,000 bariatric surgeries between 2005 and 2007 in the US found that ~87% of individuals had private or some other form of insurance whereas almost 6% were uninsured<sup>59</sup>; however, the effect of insurance coverage on weight loss was not discussed. We hypothesized that individuals who paid for their operation would lose more weight than individuals who were covered by insurance. Although there was no statistical difference in weight loss between self-pay and insured patients, self-pay VSG patients had numerically greater weight loss than insured VSG patients at two years. There was no weight loss advantage to self-pay patients in the RYGB group.

Common minor complications identified by the American Society for Metabolic and Bariatric Surgery (ASMBS) include atelectasis, dehydration, diarrhea, dumping syndrome, esophageal reflux, pneumonia, nausea and vomiting, and infection. Common major

complications include cardiopulmonary issues such as cardiac arrest, deep venous thrombosis, pulmonary embolism and respiratory arrest or failure, gastrointestinal (GI) bleeds or leaks, small bowel obstruction, anastomotic stricture, ulcer at the anastomosis or in the GI tract, and wound dehiscence or infection.

The most common of these complications experienced by patients appears to be dependent on the type of surgery and their surgeon's experience. Similar to our study, Carrodeguas *et al*<sup>84</sup> found anastomotic strictures to be the most commonly experienced complication (7.3%) among the 1300 RYGB patients. Gastrointestinal bleeds and cardiopulmonary-related problems were the other top reported complications among RYGB patients in our study. Less than 5% of VSG patients from our study experienced a complication in the first six weeks of the post-operative period. The top three reported complications in the VSG group were thromboembolic-related, strictures, and cardiopulmonary-related adverse events. In contrast, other studies report slightly higher overall VSG complication rates ranging between 5-9% with the most commonly reported complications being GI bleeds and GI leaks<sup>12, 13</sup>. The success of the surgeons in reducing gastrointestinal leaks in our study may be attributable to the operative technique they utilized and have previously published<sup>53</sup>.

Studies have shown low overall mortality rates following bariatric surgery ranging from 0.1% to 1.5%<sup>57, 59, 77</sup>. Thirty-day mortality rates appeared to be less than 0.2% for all types of bariatric surgery and less than 2% specifically for RYGB. The mortality rate for VSG appears to be less than 1%<sup>12, 13, 79</sup>. According to data of over 66,000 surgeries from ASMBS Centers of Excellence, the three predominant causes of mortality were pulmonary emboli, cardiac complications, and sepsis/infection<sup>59</sup>. In our study, two deaths occurred during the initial post-

operative period: one RYGB patient and one VSG patient each died due to a pulmonary embolism.

The limitation of this study was the short duration of follow-up for the majority of patients although the surgeons encourage their patients to adhere to a five-year follow-up regimen. It appeared that the long-term follow up care after the initial six-week post-operative period was performed by the patients' family physician. Our study is one of the first comparative studies with a large number of sleeve gastrectomy patients. The weight loss reported for VSG patients in this study is similar to weight loss reported in previous RYGB studies. Therefore, we feel that the VSG is a viable option for obese patients seeking weight loss surgery. The incidence of complications was much lower in the VSG surgical group, a finding which will hopefully encourage a greater acceptance of bariatric surgery by insurance providers and family physicians. The low mortality rates following bariatric surgery reported in our study and several other studies are evidence that the operations are growing safer as the techniques become more standardized. Overall, bariatric surgical risks appear to be low. Therefore, when conventional treatments for weight loss have failed, obese individuals and their family physicians should consider bariatric surgery in their weight loss discussions. Now that family physicians are becoming more involved in the pre- and post-operative care of bariatric surgery patients, the patients may seek advice from them on surgery selection. Additionally, the VSG should be regarded as an alternative to the RYGB because it is becoming more widely used throughout the US, results in significant weight loss, and is associated with a lower rate of complications.

## CHAPTER 6

### SUMMARY

These three studies have evaluated two of the most commonly used treatment alternatives to combat obesity. An egg breakfast can decrease hunger and enhance feelings of fullness because eggs contain high quality protein. Because consuming an egg breakfast daily increases satiety, individuals following a diet should be encouraged to try this strategy to further promote weight loss. If weight loss cannot be achieved through diet, exercise, or behavioral modification, bariatric surgery is the most effective treatment for obesity. Two bariatric operations, the RYGB and the VSG, both improved or resolved T2D in the early post-operative period in a large percentage of patients. The surgeries also resulted in significant weight loss at one and two years. Complication rates and mortality appear to be low, especially in VSG patients. Therefore, bariatric surgery appears to be a safe, effective tool for weight loss and co-morbidity improvement or resolution.

One randomized trial examining 811 overweight and obese adults following different, calorie-restricted diets up to two years showed that no specific macronutrient composition diet led to greater weight loss than another<sup>19</sup>. The different diets led to similar results because they all restricted daily caloric consumption<sup>19</sup>. However, maintaining a long-term, calorie-restricted diet can be difficult so dietary strategies that increase satiety may be effective tools. Previous research has shown that a breakfast containing protein decreases hunger<sup>23</sup> and increases satiety<sup>45</sup>, but no study has investigated the effect of protein quantity compared to protein quality. Eggs contain the BCAA leucine which increases the protein quality. Despite the fact that the EB was matched with an isocaloric RTE CB for ED and macronutrient composition, the EB led to

significantly lower concentrations of acylated ghrelin and higher concentrations of PYY than the CB and these effects appear to be independent of leucine.

However, individuals with higher serum leucine concentrations displayed greater improvements in their HOMA index for insulin resistance in just one week. Thus, individuals with insulin resistance may benefit from consuming a daily EB because it may potentially prevent the progression to T2D. Individuals who have already been diagnosed with T2D may gain the greatest control through bariatric surgery. Patients who underwent the RYGB returned to normal blood glucose levels before significant weight loss occurred<sup>29</sup>. More than 75% of RYGB and VSG patients were able to eliminate the need for medication in the early post-operative period. More than half were able to remain off medication at eight weeks post-operatively. Thus, these studies are informative in regard to the prevention and treatment of T2D.

Neither breakfast resulted in a decrease in energy intake or body weight at the end of the test week; however, the breakfast study was short in duration, and weight loss is likely if individuals consume eggs for breakfast for a longer duration of time in addition to energy restriction<sup>37</sup>. In contrast, bariatric surgery has been shown to produce significant weight loss that can be sustained over time<sup>29, 66</sup>. The RYGB produced significantly greater weight loss than the VSG at one and two years, but all patients continued to lose weight up to two years post-operatively regardless of the type of operation. Self-pay patients who underwent either operation did not lose more weight than insured patients. Although the RYGB resulted in greater weight loss, it also led to more overall and major complications than the VSG. Mortality from either operation was less than 0.3%.

These studies had several limitations. In the breakfast study, the EB and CB were not matched for other factors that influence satiety such as glycemic index, and the contribution of such factors to the results cannot be accounted for in the study. Also, GLP-1, an anorectic hormone known to increase satiety following a meal, was not measured. The short duration of the study precluded the evaluation of the effect of protein quality on weight loss. The marginal long-term follow-up was the biggest limitation of the bariatric surgery retrospective chart review, but it reflects the reality of a community surgical practice where many patients discontinue care with the surgeon if no major complications arise during the early post-operative period. A greater number of individuals with follow-up two or more years post-operatively would more accurately illustrate the differences between the RYGB and the VSG. The charts also lacked laboratory data that would have provided information on glucose and insulin concentrations, HbA1c levels, lipid profiles, blood pressures, and vitamin levels in bariatric patients. Because the study examining diabetes improvement and resolution lacked these data, diabetes improvement and resolution had been defined as a decrease in the number of hypoglycemic medications taken or the discontinuation of medications taken, respectively.

Future studies pertaining to breakfast consumption should continue to examine the effects of high protein quality on hunger, satiety, and energy intake. The roles of leucine and GLP-1 remain to be examined. Future studies that focus on the effects of bariatric surgery on type 2 diabetes should try to explore the mechanisms involved in the quick improvement seen in blood glucose levels before significant weight loss occurs. The low prevalence of gastrointestinal leaks in the VSG suggest that the surgeon's previously published technique should be more widely adopted<sup>53</sup>.

This thesis contributes to the peer-reviewed literature. First, it demonstrates the role of protein quality in controlling hunger and satiety. Secondly, the bariatric surgery studies are two of the first studies comparing a large group of RYGB and VSG patients and their difference in weight loss, complications, and ability to improve and resolve T2D.

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## APPENDIX A

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Manager, Reprints and Permissions

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Thank you,

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## **APPENDIX B**

### **SLEEVE GASTRECTOMY SURGICAL TECHNIQUE**

The sleeve gastrectomy has been recognized as a viable bariatric surgical procedure in selected patients since 2007.<sup>119</sup> The sleeve gastrectomy is commonly performed via the laparoscopic approach. The greater curvature of the stomach is devascularized, and a sizing dilator is inserted within the stomach and positioned medially along the lesser curve. Using the dilator as a “template,” the antrum, body, and fundus of the stomach lateral to the dilator is resected and removed, leaving a tubular stomach of approximately 90–120 mL in volume. This surgical technique has minimized the risk of gastrointestinal leaks.<sup>53</sup>

## **VITA**

Brooke Bayham was born in Baton Rouge, Louisiana. She received her Bachelor of Science degree in nutrition/dietetics in December 2009 from Louisiana State University. Brooke began a master's program in January 2010 in the Louisiana State University School of Human Ecology with a concentration in human nutrition and food. She is a member of the American Dietetic Association.