Sleeve Gastrectomy Compared to Gastric Bypass as a Treatment for Type 2 Diabetes in those with a BMI < 35

Caitlyn Suelter

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Sleeve Gastrectomy Compared to Gastric Bypass as a Treatment for Type 2 Diabetes in those with a BMI < 35

Abstract

Background: Thirty million people in the United States have diabetes, of which, nearly 90% are considered overweight or obese. Bariatric surgery, with the two most popular types being sleeve gastrectomy (SG) and gastric bypass (GB), is currently indicated as a treatment of type 2 diabetes (T2D) in those with a BMI > 35. However, recent studies have shown bariatric surgery to be an effective treatment in those with BMI < 35. Therefore, the aim of this systematic review was to determine if SG is comparable to GB for treating T2D in those with a BMI < 35.

Methods: An exhaustive literature search was completed using the following search engines: CINAHL-EBSCOhost, Web of Science, and MEDLINE-PubMed, and the following search terms: bariatric surgery, type 2 diabetes, and BMI < 35. The quality of relevant articles was assessed using the GRADE Working Group guidelines.

Results: A total of 2 studies met specific inclusion criteria and were included in this systematic review. Both studies were randomized controlled trials. One study of 60 overweight or non-morbidly obese adults with T2D found GB to be superior to SG in regards to treating T2D. The other study consisted of 64 overweight or non-morbidly obese adults with T2D and found that there was no significant difference in the remission or improvement of T2D between SG and GB.

Conclusion: Whether GB is superior to SG remains unclear; however, SG may be a reasonable alternative to GB. Other studies with larger sample sizes, longer follow-ups, and the use of non-surrogate outcomes are needed to elucidate the differences in SG and GB for treating T2D in those with a BMI < 35.

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Capstone Project

Degree Name
Master of Science in Physician Assistant Studies

Keywords
Bariatric surgery, BMI < 35, type 2 diabetes, sleeve gastrectomy, gastric bypass

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Sleeve Gastrectomy Compared to Gastric Bypass as a Treatment for Type 2 Diabetes in those with a BMI < 35

Caitlyn Suelter, MS

A Clinical Graduate Project Submitted to the Faculty of the

School of Physician Assistant Studies

Pacific University

Hillsboro, OR

For the Masters of Science Degree, August 11, 2018

Faculty Advisor: Patrick J. Boyle, MD

Clinical Graduate Project Coordinator: Annjanette Sommers, PA-C, MS

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Biography
Caitlyn Suelter grew up in Colorado where she majored in Dietetics and minored in Biomedical Sciences at Colorado State University. After completion of her undergraduate degree, she stayed at CSU to complete a master’s degree in Nutritional Science. During her graduate studies, her research focused on the association between pressure to be thin and adolescent weight change. She was asked to present her findings at a conference and was subsequently published in the peer-reviewed medical journal, *Pediatric Obesity*. After completing her graduate degree, she began PA school at Pacific University. Caitlyn has a strong interest in type 2 diabetes and body weight, and how they are interrelated.
Abstract

Background: Thirty million people in the United States have diabetes, of which, nearly 90% are considered overweight or obese. Bariatric surgery, with the two most popular types being sleeve gastrectomy (SG) and gastric bypass (GB), is currently indicated as a treatment of type 2 diabetes (T2D) in those with a BMI > 35. However, recent studies have shown bariatric surgery to be an effective treatment in those with BMI < 35. Therefore, the aim of this systematic review was to determine if SG is comparable to GB for treating T2D in those with a BMI < 35.

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Conclusion: Whether GB is superior to SG remains unclear; however, SG may be a reasonable alternative to GB. Other studies with larger sample sizes, longer follow-ups, and the use of non-surrogate outcomes are needed to elucidate the differences in SG and GB for treating T2D in those with a BMI < 35.

Keywords: Bariatric surgery, BMI < 35, type 2 diabetes, sleeve gastrectomy, gastric bypass
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Table 1: Quality Assessment of Reviewed Studies

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<th>Description</th>
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<tr>
<td>SG</td>
<td>Sleeve gastrectomy</td>
</tr>
<tr>
<td>GB</td>
<td>Gastric bypass (single anastomosis or Roux-en-Y)</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index (kg/m²)</td>
</tr>
<tr>
<td>RYGB</td>
<td>Roux-en-Y gastric bypass</td>
</tr>
<tr>
<td>GLP-1</td>
<td>Glucagon-like peptide-1</td>
</tr>
<tr>
<td>A1c</td>
<td>Glycosylated hemoglobin A1c (%)</td>
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<tr>
<td>T2D</td>
<td>Type 2 Diabetes Mellitus</td>
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<tr>
<td>FBG</td>
<td>Fasting blood glucose (mg/dL)</td>
</tr>
<tr>
<td>AUC</td>
<td>Area under the curve</td>
</tr>
<tr>
<td>OGTT</td>
<td>Oral glucose tolerance test</td>
</tr>
<tr>
<td>HDL</td>
<td>High density lipoprotein cholesterol</td>
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<tr>
<td>GERD</td>
<td>Gastroesophageal reflux disorder</td>
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<td>RCT</td>
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</table>
Sleeve Gastrectomy Compared to Gastric Bypass as a Treatment for Type 2 Diabetes in those with a BMI < 35

BACKGROUND

There are 30.3 million people in the United States who have diabetes, of which, 88% are considered overweight or obese as defined by a body mass index (BMI) of ≥ 25.¹ Current therapies for T2D include lifestyle interventions, such as diet and exercise, glucose lowering medications, and bariatric surgery.

Bariatric surgery is currently indicated for patients with a BMI > 40, or > 35 with at least one comorbidity (eg, T2D). Two common bariatric surgeries include gastric bypass (GB) and sleeve gastrectomy (SG). SG is a procedure in which part of the greater curvature of the stomach is removed, leaving a smaller pouch. Part of the stomach that is removed during SG contains cells that release the hormone associated with hunger, ghrelin. It is thought that the combination of the decrease in ghrelin and smaller stomach size result in weight loss and subsequent improvement in blood glucose control.

GB is a different procedure in which a smaller pouch is created at the distal end of the esophagus using varying sizes of the stomach, for example, with the lesser curvature of the stomach in a single anastomosis (mini-) GB, or with using the more superior portion of the stomach in the Roux-en-Y GB (RYGB) procedure. During GB, the stomach and part of the small intestine are still intact, but are bypassed, resulting in a change in hormones. Like SG, GB results in a decrease in ghrelin, but additionally an increase in glucagon-like peptide-1 (GLP-1), a satiety hormone. GLP-1 also results in delayed gastric emptying (slower absorption of glucose and other nutrients), glucose
dependent insulin secretion from pancreatic beta cells, suppressed glucagon release from pancreatic alpha cells, and early satiety—all of which contributing to the improvement of T2D. Additionally, after undergoing GB, patients have a much smaller stomach/pouch size compared to SG, further contributing to earlier satiety.

Multiple factors are considered when the patient and provider decide whether bariatric surgery is an appropriate treatment, as well as which type of surgery is best for the patient. The percent of weight lost following GB is typically more than SG. McGuire et al\textsuperscript{2} found mean total weight loss following GB and SG after 12 months to be 114 ± 50 lbs and 74 ± 28 lbs, respectively. Additionally, GB is a more complex surgery, which typically has longer operative and anesthesia time; increased cost due to these factors,\textsuperscript{3} whereas SG does not consist of rearranging the GI tract, but rather decreasing the size of the stomach. By leaving the GI tract in place, this allows for the ability to still undergo certain procedures, eg, endoscopy which can be a helpful diagnostic tool for peptic ulcers, gastric cancer, and etc.

Both GB and SG can result in nutrient deficiencies; however, due to the GI tract rearrangement, it is more common for patients to be deficient in B12, iron, calcium, vitamin D, selenium, and zinc following GB.\textsuperscript{4} The reversibility of the surgery is another important consideration. SG cannot be reversed; however, GB can potentially be reversed. This is attempted when there are significant post-operative complications. One of the common complications following GB is “dumping syndrome”; this can also occur with SG but is much less common. Dumping syndrome consists of nausea, diarrhea, abdominal pain, weakness, dizziness, and even syncope following a meal that is high in glucose and fat. This occurs due to the rapid movement of food into the small
intestine. Late dumping syndrome can occur as well, which is a more serious complication. Late dumping syndrome is when an inappropriate amount of insulin is released from the pancreas due to rapid gastric emptying and subsequent glucose absorption, leading to hypoglycemia.

Studies have shown bariatric surgery to be an effective treatment for T2D in those with a BMI > 35. More recently however, studies have explored bariatric surgery as a treatment for T2D in those with a BMI < 35. For example, separate studies have shown GB and SG to be beneficial in treating T2D in the non-morbidly obese (BMI 30-34.9). Additionally, comparative studies have found SG and GB to have similar improvement rates in glycosylated hemoglobin A1c (A1c) in those with a BMI > 35. However, whether SG is comparable to GB at treating T2D, has not been very well studied in those with a BMI < 35. For this reason, the aim of this systematic review was to determine if SG is comparable to GB at reducing or remitting T2D in patients with a BMI < 35.

METHODS

An exhaustive literature search was completed using the following search engines: MEDLINE-PubMed, Web of Science, and CINAHL-EBSCOhost, and the following search terms: bariatric surgery, type 2 diabetes, and BMI < 35. Specifiers used included studies that were published within 5 years, in the English language, were randomized controlled trials, and were conducted on human subjects. Additionally, only studies that enrolled adults with BMI 25-34.9 diagnosed with T2D (unable to be controlled by lifestyle and/or medical therapies), and compared SG and GB directly were included. Studies were excluded if they were studying other types of bariatric surgery or
were performed on subjects who had a BMI < 25 or > 35. The quality of relevant articles was assessed using the GRADE Working Group guidelines.\textsuperscript{11}

**RESULTS**

A total of 224 articles (including duplicates) were found using the above search engines and search terms. There were 117, 77, and 30 articles that were found using MEDLINE-PubMed, CINAHL-EBSCOhost, and Web of Science, respectively. After screening the 224 articles, 2 articles\textsuperscript{12,13} met the specific inclusion criteria above and were included in this systematic review. See Table 1.

**Lee et al**

**Study Description**

Lee et al\textsuperscript{12} conducted a double blind randomized controlled trial consisting of 60 subjects with diagnosed T2D. Participants had a BMI within the range of 25.1-34.9, A1c level greater than 7.5%, and had T2D for at least 6 months. Thirty subjects were randomly assigned to either the GB or SG group. Both surgical procedures were done laproscopically. The GB group underwent a single anastomosis (mini-) gastric bypass which has been described in a previous study by Lee and colleagues.\textsuperscript{14} Additionally, Ser et al\textsuperscript{15} previously described the SG procedure used. The primary outcome was remission of T2D, defined as an A1c of \( \leq 6.5\% \) without glycemic therapy at 60 months.\textsuperscript{12}

**Study Results**

Twenty-four participants in each group completed 60-month follow ups; however, all 60 (30 from each group) were included in the primary analysis. The baseline characteristics were similar between both GB and SG groups, including demographic and
anthropometric measurements ($p$ values $> 0.221$). Laboratory values, such as A1c and fasting blood glucose (FBG), were not significantly different at baseline between the groups ($p$ values $> 0.155$). Mean A1c at baseline was 10% (7.5–15). However, serum high density lipoprotein cholesterol (HDL) and fasting C-peptide were significantly different in both groups: HDL was significantly lower in SG group (43 vs 48 mg/dL, $p = 0.017$) and fasting C-peptide was significantly higher in SG group (3.2 vs 2.5 ng/mL, $p = 0.041$).\textsuperscript{12}

At the 60-month follow-up, 18 participants (60%) in the GB group and 9 (30%) in SG group had remission of their diabetes (A1c of $\leq 6.5\%$ without glycemic therapy). Additionally, the mean reduction in A1c was 3.9 in the GB group and 2.8 in the SG group. The area under the curve (AUC) of glucose during the oral glucose tolerance test (OGTT) was significantly improved in both groups, without differences at 60-month follow-up. Additionally, 17\% in GB and 63\% in SG had used oral anti-diabetic medications, and 0\% in GB and 8\% in SG had used insulin.\textsuperscript{12}

Regarding surgical complications, 1 subject in the GB group developed a marginal ulcer, and 2 patients in both GB and SG groups required proton pump inhibitor therapy at 60-months. Five subjects required additional surgical operations, including 1 in the GB group which was converted to RYGB due to intractable bile reflux esophagitis at 48 months following surgery, and 4 subjects in the SG group who had undergone crossover to RYGB because of various reasons (eg, aggravation of diabetes and/or inadequate weight loss, or intractable acid reflux esophagitis).\textsuperscript{12}

\textbf{Yang et al}
Study Description

Yang et al\textsuperscript{13} conducted a randomized controlled trial of 64 subjects with T2D. Participants had a BMI within the range of 28-35, and a diagnosis of poorly controlled T2D after 6 months of medicine therapy defined by an A1c of 7.0\% or greater. Thirty-two participants were randomly assigned to either the GB or SG group. The GB group underwent the RYGB procedure. Both GB and SG were done laproscopically. Yang and colleagues described the surgical techniques in further detail. The primary outcome was T2D remission, defined as an A1c < 6\% without glycemic therapy at 36 months.\textsuperscript{13}

Study Results

Out of the 64 participants, 9 did not complete the 36-month follow up, including 5 in the GB group and 4 in the SG group. At baseline, both groups had similar anthropometric measurements. Additionally, there were no significant differences between baseline A1c, FBG, and C-peptide ($p$ values $> 0.062$), or serum lipid values ($p$ values $> 0.067$).\textsuperscript{13}

At 36-month follow-up, 23 subjects (85\%) in the GB group and 22 subjects (79\%) in the SG group achieved complete remission of their diabetes (A1c < 6.0\% without taking antidiabetic medications). Twenty-five subjects in each group gained successful treatment of their diabetes, which was defined as an A1c $\leq$ 6.5\%. Similarly, 28 in the GB group and 27 subjects in the SG group stopped taking oral hypoglycemic agents and 13 in the SG and 18 in the GB no longer needed insulin injections.\textsuperscript{13}

Regarding surgical procedures: surgical time was significantly longer for the GB group compared to the SG group (104 vs 58 minutes, $p = 0.000$). The mean hospital stay following surgery was significantly longer for the GB group compared to the SG group.
(6.6 vs 5.2 days, \( p = 0.000 \)). In 3 participants, minor complications occurred, which included 1 case of anemia in the GB group and 2 gastroesophageal reflux disorder (GERD) cases in the SG group. All complications were resolved with medications; however, long term treatment with B12 and iron was needed for the anemia case.\textsuperscript{13}

**DISCUSSION**

Taken together, these studies support the idea that GB and SG are effective treatment options for T2D in patients with BMI < 35. Yang et al\textsuperscript{13} found SG to have similar outcomes related to diabetes remission, as well as overall improvement, when compared to GB. Lee et al\textsuperscript{12} found an overall improvement in diabetes in both GB and SG groups; however, they found GB to be superior to SG in regards to both diabetes remission, and diabetes improvement. Lee et al\textsuperscript{12} suggests that the higher incretin effect at 5 years in the GB group may be a potential reason for the differences in glycemic outcomes. Potential reasons for the difference across the two studies include: the GB group in the Lee et al\textsuperscript{12} study had higher baseline HDL and lower fasting C-peptide, compared to the SG group, meaning the GB group may have had an improved prognosis at the start of the study.

These results suggest that although GB might be more effective at remitting T2D, SG may be a potential alternative for those who are not a candidate for GB. For example, in the Yang et al\textsuperscript{13} study, they found SG to require shorter surgical times, as well as a shorter post-operative hospital stay. Similarly, Barzin et al\textsuperscript{3} found GB to require longer surgical times, meaning longer amount of time spent under anesthesia, as well as increased cost to surgery. Additionally, SG still allows for the ability for patients to undergo endoscopy in the future, which may be a benefit as endoscopy is an important
tool to diagnose and treat diseases of the stomach.³ Another potential downfall to GB is the possibility for nutrient deficiencies. Yang et al¹³ found 1 case of anemia in GB group, which required long term treatment of B12 and iron. Similarly, Gehrer and colleagues¹⁶ found that those who underwent GB surgery had significantly more vitamin B12 and vitamin D deficiencies, as well as hyperparathyroidism when compared to those who underwent SG.

However, in the Lee et al¹² study, they found there to be more complications in the SG group compared to GB group. For example, 4 participants required conversion of SG to RYGB at varying months after surgery due to various reasons, such as esophagitis, inadequate weight loss, and aggravation of diabetes, whereas only 1 in the GB group required conversion to RYGB due to intractable bile reflux esophagitis.

A major limitation of the Yang et al¹³ study was that there was no mention of blinding of the subjects or data collectors. Additionally, both studies used a surrogate outcome, specifically A1c, and a more patient-relevant outcome, namely diabetic medication use, as markers of reduction or remission of T2D. Other limitations include a fairly homogenous sample of Chinese and Taiwanese subjects, slight differences in the type of GB procedure done (Roux-en-Y vs single anastomosis), differences in BMI inclusion criteria, differences in the definition of diabetes remission, and differences in follow-up times.

Future studies should include a longer follow-up in order to better determine safety and effectiveness. No studies were found during this review that have studied bariatric surgery as a treatment for T2D in those who are overweight for greater than 5 years. Knowing how these patients fare 10 or more years after surgery in regards to their
T2D, as well as what complications may arise would be useful information. Additionally, it would be useful to look at a more diverse population of patients, given that BMI in the Asian population does not translate as well to other races. For example, research has shown that Asians tend to have lower BMIs but higher body fat percent when compared to whites. The significance of this is that BMI is an estimation of body fat, and at a given BMI, an Asian may have greater body fat than someone who is Caucasian; which reveals some potential discrepancy when determining overweight and obese cut offs. This discrepancy may also have an influence on T2D outcomes following bariatric surgery in varying populations.

CONCLUSION
SG may be an appropriate alternative to GB surgery for the treatment of T2D in patients with a BMI < 35; however, more randomized controlled trials are needed to clarify this. Although GB tends to have higher remission rates of T2D, studies have shown SG to have a decreased cost of surgery, a shorter time in surgery (shorter time spent under anesthesia), and fewer nutrient deficiencies post-op.

As of now, the current indications for bariatric surgery do not include those with a BMI < 35; however, these results highlight certain implications in the practice of medicine, such as the inability to treat patients with T2D who have failed on current therapies, but do not yet meet bariatric surgery criteria. Overall, more studies need to be done with larger sample sizes, longer follow-ups, and the use of more patient-relevant outcomes in order to determine the differences in GB and SG for treating T2D in those with a BMI < 35.
Currently clinicians can start the conversation regarding the potential option of bariatric surgery for their patients who are no longer benefiting from medication therapy. By starting the conversation early, providers can explain the requirements needed in order to undergo bariatric surgery, as well as offer information on the different types available.
REFERENCES


### Table 1: Quality Assessment of Reviewed Articles

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Downgrade Criteria</th>
<th>Upgrade Criteria</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Limitations</td>
<td>Indirectness</td>
<td>Inconsistency</td>
</tr>
<tr>
<td>Lee et al(^{12})</td>
<td>RCT</td>
<td>Not Serious</td>
<td>Not Serious(^a)</td>
<td>Serious(^b)</td>
</tr>
<tr>
<td>Yang et al(^{13})</td>
<td>RCT</td>
<td>Serious(^c)</td>
<td>Not Serious(^a)</td>
<td>Serious(^b)</td>
</tr>
</tbody>
</table>

\(^a\) The surrogate outcome of A1c was measured; however, both studies also measure the use of anti-diabetic medication to determine diabetes reduction/remission.

\(^b\) Both studies were inconsistent in their findings.

\(^c\) Lack of blinding of participants and data collectors.