Resolution of Diabetes Mellitus with Laparoscopic Sleeve Gastrectomy

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Brief Summary

The aim of our study was to evaluate sleeve gastrectomy as a potential metabolic therapy in adult patients with diabetes mellitus.

Highlights

1. Sustained weight loss and improvement in common diabetic metrics is difficult to achieve in adult patients with Type 1 and Type 2 diabetes.
2. Sleeve gastrectomy is a safe approach to significant weight loss.
3. Sleeve gastrectomy is a feasible metabolic therapy through its effects on weight loss, need for insulin regimens, and physiologic measures of diabetes in adult patients.

Abstract

Background: Laparoscopic sleeve gastrectomy (LSG) is a proven intervention to induce weight loss. Its applications as a surgical procedure may extend beyond body weight control to the realm of metabolic therapy in chronic conditions such as diabetes mellitus (DM), which results from the dysregulation of blood glucose levels.

Objective: The aim of this study is to evaluate the improvement and resolution of diabetes following sleeve gastrectomy at our facilities.

Setting: Two affiliated non-profit surgery centers, United States

Methods: Eighty-two adult diabetic patients were treated with sleeve gastrectomy. We conducted a single point analysis of our existing longitudinal data for that calendar year through a retrospective chart review. Statistical outcomes were determined for anthropometric data unique to patients with DM including prescribed medications, Hemoglobin A1C, excessive weight loss (EWL), and body mass index (BMI).

Results: Time was a significant predictor of diabetic resolution after six months post-op in patients who originally presented with Type 1 DM and change in hemoglobin A1C values held a significant association to improvement of Type 1 diabetes. BMI and EWL displayed a positive correlation to resolution at all time points of interest.

Conclusions: There are differences between the post-operative improvements in diabetic status following sleeve gastrectomy depending on the initial diagnosis of insulin-dependent or insulin-independent DM. Pathophysiological mechanism of a patient's diabetic condition, specifically auto-immune destruction of pancreatic beta cells, may contribute to the variable metabolic response following sleeve gastrectomy.

Keywords: Bariatric Surgery, Metabolic Therapy, Diabetes Mellitus, Insulin

Abbreviations: Diabetes Mellitus (DM), Excess Weight Loss (EWL), Body Mass Index (BMI),

Sleeve Gastrectomy (SG)

Diabetes mellitus (DM) is a chronic condition resulting from the dysregulation of blood glucose levels. Statistics from 2018 describe the significance of diabetes in the United States, citing prevalence as high as 10.5 percent of the population. Of the 30.3 million documented cases, 30.2 million include individuals in the adult demographic aged 18 or older [1]. Pathophysiological mechanisms of DM are usually categorized into either Type 1 or Type 2. The former describes patients with an inability to produce the hormone that regulates blood glucose, insulin, as a result of immune-mediated destruction of insulin-producing beta cells in the pancreas. The latter refers to the diabetic condition of insulin resistance in which insulin is produced, but not utilized effectively by the body to control blood glucose levels [2]. Given the systemic nature of DM, complications include retinopathy, nephropathy, neuropathy, and many more body-wide effects [3]. These complications are often linked to uncontrolled body weight, which is closely related to blood glucose regulation. Studies suggest that weight loss earlier on in the course of DM has the potential to control glycemia and significantly reduce the 8-year incidence of diabetes [4]. Additionally, comorbidity of diabetes and cardiovascular conditions results in significant mortality rates that may be reduced by intentional weight loss [5].

Many of the approaches to weight loss prescribed to diabetic patients deliver results in the short term, but prove difficult to sustain in the long term. For example, medications such as exenatide render weight loss values approaching ten pounds for 82 weeks before plateauing [6]. Another common management strategy in diabetic patients focuses on nutrition therapy, which involves an assessment of patient's current dietary habits, identification of nutritional goals, and implementation of strategically designed meal plans [7]. Intense nutritional interventions decreased plasma glucose levels by 50–100 mg/dl with an accompanied 1-2% decrease in

Hemoglobin A1C values [8]. Recently, there has been an emergence of more invasive interventions that may provide opportunity for sustained weight loss and improvement of diabetic condition beyond what is achievable through current management approaches.

A laparoscopic sleeve gastrectomy (SG) is a surgical procedure designed to remove a large portion of the stomach, commonly to induce weight loss [9]. With 30-day mortality and complication rates below one percent, the gastric sleeve has proven to be a safe weight-loss intervention [10]. The effectiveness of sleeve gastrectomy as a weight loss solution in the short and intermediate term has been demonstrated reliably with mean excessive weight loss of $55.0 \pm 6.8\%$ pounds following intervention [11]. Given the potential for significant weight loss following sleeve gastrectomy, the aim of this study is two-fold: to evaluate improvement and resolution of diabetes after sleeve gastrectomy and assess the significance of various post-operative time intervals in SG as a metabolic therapy.

Methods

Participants

Eighty-five diabetic adult patients were treated with sleeve gastrectomy at Banner Gateway Medical Center (BGMC) and Banner Estrella Medical Center (BEMC) in Arizona over the course of 2015. IRB Approval received from Banner Health (Project ID: 0004299) prior to retrospective review. Patients were previously classified as having Type 1 or 2 diabetes based on meeting a single diagnostic criterion of a documented A1C greater than 6.5%, elevated fasting plasma glucose greater than 126 mg/dl, or symptoms of diabetes with a random blood sugar greater than 200 mg/dl. Initial indications for SG included BMI greater than 40 or in the range of 35 to 39.9 with weight-related health issues including elevated blood pressure or obstructive sleep apnea.

Metrics

Patients were monitored preoperatively using a variety of metrics including prescribed medications, Hemoglobin A1C, excess weight loss (EWL), body mass index (BMI), and post-operatively with the same variables at various time intervals including 1-week, 1-month, 3-month, 6-month, and 1-year. Hemoglobin A1C values were obtained through standard procedures involving the collection of hemoglobin A1C cells from patients' sample of red blood cells. Percentage of glycated cells was calculated and recorded. EWL was determined using actual weight loss values compared against ideal weight goals according to Metropolitan Life Tables. Lastly, BMI was calculated using the accepted metric formula: weight (kg) ÷ $height^2$ (m^2). We employed a retrospective chart review to identify metabolic outcomes of the SG with exclusion criteria limited to patients with loss-to-follow up at all of the intervals outlined above, resulting in the exclusion of twenty patients. The experimental protocol was approved by the Institutional Review Board of Banner Hospital.

Data Collection and Analysis

Patient data including name, date of operation, principal operative procedure, and diabetes diagnosis was collected from the MBSAQIP database and Exemplo EMR. Preliminary patient data was used to compile a Master Log consisting of additional categories relevant to the specific goals of this investigation including (pre-operative, 2-week, 1-month, 3-month, 6-month, and 1-

year follow-up) medications, Hemoglobin A1C percentage, EWL at follow-up, and BMI at the time of the procedure. Data was collected and analyzed for consistencies and patterns. Different groups of patients were formed based on follow up and those groups were compared with a Kaplan Meier plot and paired t-test. The outcome of interest was the resolution or improvement of diabetes, which was determined by the criteria measured in the study including a trending in A1C to physiologically normal levels less than 5.7% and freedom from insulin medications.

Results

Study Population

The individuals included in the study covered a wide range of physiological stats as they relate to diabetic condition. 29 of the patients were diagnosed with insulin-dependent diabetes with the remaining 53 included in analysis being diagnosed with non-insulin dependent diabetes. At baseline, mean BMI was 35.8 +/- 5.8 and over the course of the study mean EWL was 44% +/- 15%. 51 of the analyzed patients are female and baseline mean A1C for the entire study population was 6.8% +/- 1.6%.

Post-Op Therapeutic Timeline

Time was a significant predictor of diabetic improvement after six months post-op in patients who originally presented with Type 1 DM extended out to at least 1 year after SG ($P < 0.005$ and 0.001, Table 1). Earlier points of interest in the presented study of 2 weeks and 1 month did not show a significant time effect in terms of improvement in Type 1 diabetes. At 3 months post-sleeve gastrectomy, the results approached statistical significance ($P = 0.055$).

Post-Op Insulin Regimen

Changes in various diabetic metrics were observed over the longitudinal course of therapy associated with the actual SG procedure and the ensuing post-operative period. The percentage of patients with improvement of diabetes based on freedom from insulin medications post-op was significant at each time point when stratified by pathophysiologic mechanism of diabetes (2 weeks, $P < 0.05$; 1 month, $P < 0.01$; 3 Months, $P < 0.001$, 6 months, $P < 0.005$, 1 year, $P <0.05$, Table 2).

Hemoglobin A1C

A significant effect was observed in A1C reduction when Type 1 and 2 diabetic patients were analyzed together ($P < 0.001$) in the post-op period extended out to one year. Probability of normal A1C values following SG held a significant association to improvement in Type 1 diabetes (Figure 1) when analyzed over the course of one calendar year. A more pronounced normalization in A1C values was observed in the subset of patients included in the study diagnosed with insulin dependent DM.

BMI and EWL

BMI and EWL were also stratified according to initial diagnosis of either insulin dependent or independent DM. Percentage of excessive body weight lost was reported as a percentage from pre-op to last documented visit post-op within the year. Alterations in BMI and EWL demonstrated a positive correlation over the time course, but failed to reach statistical significance ($P = 0.56$ and $P = 0.82$).

Loss to Follow Up

Minimum criteria for inclusion in the statistical analysis included one post-operative visit at the 2-week time point. Of the participants, two were excluded for failing to meet the aforementioned criterion. Three patients of the remaining eighty-three were documented as loss-to-follow-up at the 1-month time point. Seven were lost to follow up at the 3-month time point, sixteen at 6 months, and twenty-two at one year. Loss-to-follow-up was factored for in statistical analyses to reflect the changes in sample size.

Discussion

In the present study, we explored the application of SG as a potential metabolic therapy in the treatment of insulin dependent and independent diabetes. After 6 months post-op in patients who originally presented with Type 1 DM, time was a significant predictor of resolution as measured by insulin regimen and return to physiologically normal levels of hemoglobin A1C. The changes seen in hemoglobin A1C observed over the course of the study held a significant association to improvement in Type 1 diabetes while BMI and EWL displayed a positive correlation that failed to reach statistical significance.

The conclusions that can be drawn from this study are highly dependent on the universal applicability of variables being used as measures of diabetes. Monitoring and controlling the course of DM requires daily blood glucose measurements in addition to adherence to a well-designed insulin regimen. Other metrics exist to assess the condition of diabetes in a diagnosed patient including, but not limited to, prescribed medications, Hemoglobin A1C, excessive weight loss (EWL), and pre-operative body mass index (BMI). Each of the aforementioned provides insight into the progression or lack thereof of a patient's condition. Hemoglobin A1C values are commonly referenced in the analysis of diabetes using a hematological profile as they represent mean glycemia over a two- to three-month period of time. There are some limitations to consider when relying solely on Hemoglobin A1C levels including the effects of hemolysis, certain drugs, and hemoglobin variants on accuracy of obtained values [12]. Therefore, another common metric used when assessing diabetes is the list of medications prescribed to the patient throughout the course of the disease. Ideally, as the patient's dependence on medications to achieve normal blood glucose values decreases, so too will the list of pharmaceutical therapies necessary for health maintenance. Similarly, BMI values are important to consider in the management of diabetes as studies have demonstrated a significant relationship between the two. Narayan et al. determined the lifetime risk of diabetes in underweight 18-year-old males was 7.6% compared to 70.3% in extremely obese men, corresponding to 12.2% and 74.4%, respectively, in women [13]. Overall, there are many metrics to consider beyond daily blood glucose to better understand the progression of DM in patients. Given the proven reliability of the discussed metrics in evaluation of diabetic condition, the results from this study indicate that the improvements seen in A1C and elimination of the need for a post-operative insulin regimen identify a potential for SG to succeed as a metabolic therapy. Additionally, the positive correlations observed when trending BMI and EWL suggest that the post-surgical outcomes of routine sleeve gastrectomy can lead to significant changes in body habitus.

The timeline of therapy is another important outcome to consider when evaluating the metabolic effects of SG. From the data presented in this study, significant resolution was seen in patients greater than or equal to 6 months removed from the sleeve gastrectomy procedure. The reassuring outcomes observed at the time intervals farther out from day of surgery may be the result of the pathophysiologic mechanism of diabetes, specifically in Type 1 diabetes. One possibility is that islet autoantibodies developed over years in insulin-dependent diabetes continue to circulate in the body in the short term post-operatively. There have been other studies aiming to identify the effects of SG as a metabolic therapy in Type 2 diabetic patients. A retrospective review of 166 patients who underwent sleeve gastrectomy at an academic institution in Canada revealed that resolution of diabetic condition occurred in 78% of patients [14]. Additionally, recent investigations have supported the therapeutic effects of sleeve gastrectomy in diabetic patients using a quantitative approach known as the ABCD score, which factors in a patient's age, BMI, C-peptide level, and duration of Type-2 diabetes [15]. Patients with higher scores displayed higher remission rates, indicating that the ABCD score can help predict the effectiveness of sleeve gastrectomy in the resolution of Type-2 diabetes.

It is important to recognize the scale of SG's effectiveness as a metabolic therapy. Sleeve gastrectomy outcomes go beyond treatment and persistence of DM; there is a range of improvement preceding absolute resolution that must be considered when assessing this surgical procedure's role in the management of diabetes. There is considerable debate about the appropriate terminology for describing the outcomes of bariatric surgery as it relates to diabetes as well [16]. In order to fully understand the application of SG as a metabolic therapy, it is imperative to compare it to other standards in the field including gastric bypass. A prospective, randomized controlled study has the potential to delineate differences between long term outcomes post-op SG and gastric bypass, which have both been shown to significantly reduce weight-related burden in obese patients. Additionally, it is beneficial to extend follow-up well beyond one year to determine rates of long-term remission in these patients.

Limitations

We identify the following limitations to our study: (1) the retrospective review was restricted to a single institution limiting generalizability of our data. (2) The sample size after application of exclusion criteria and consideration of patients who meet the inclusion criteria such as confirmed diabetes diagnosis and long-term follow up was relatively small compared to larger scale reviews in the field.

Conclusion

The present study showed that SG in adult diabetic patients results in significant improvement in Type 1 diabetes greater than six months post-operatively and improvement in A1C with positive correlations in change in BMI and EWL. These findings suggest that SG has a potential role as a metabolic therapy in addition to its well-demonstrated positive effects on weight control.

Conflicts of Interest

The authors declare that there is no conflict of interest.

Table 1. Odds ratio (95% CI) calculated using the Generalized Estimating Equation to ascertain the likelihood of resolution over time

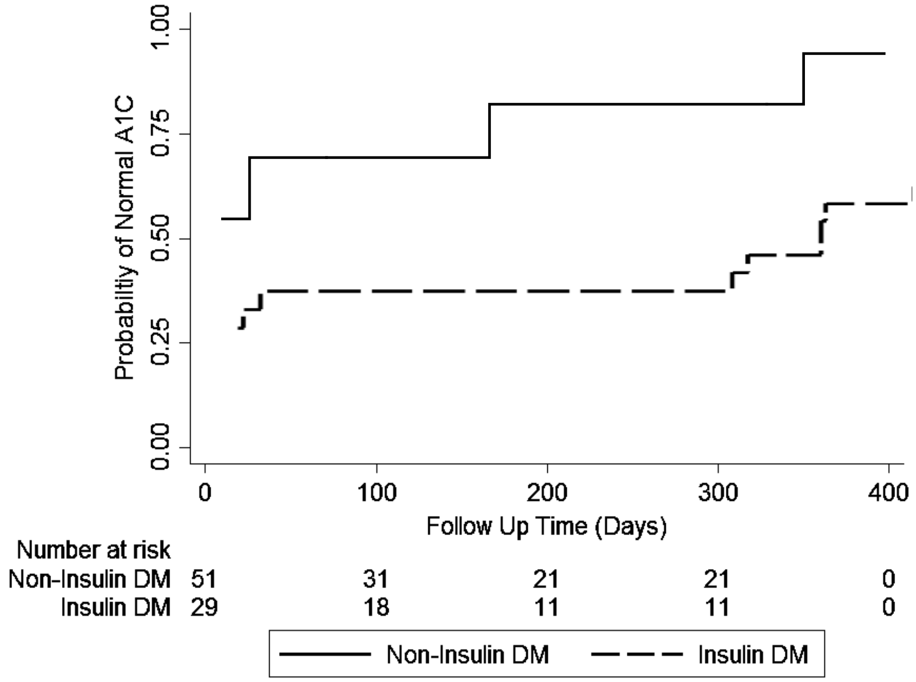
Predictors	OR (95% CI)	P-Value
Diabetes		
Non-Insulin	**REF**	
Insulin	**0.19 (0.08, 0.48)**	**<0.001**
Time		
2 Weeks	**REF**	
1 Month	**1.11 (0.79, 1.56)**	**0.53**
3 Months	**1.58 (0.99, 2.52)**	**0.055**
6 Months	**2.47 (1.36, 4.47)**	**0.003**
1 Year	**6.97 (2.78, 17.5)**	**<0.001**

Table 2. Resolution at each time point and associated values in physiological measures.

	Overall N=82	Non-Insulin N=53	Insulin N=29	P-value
Diabetic Resolution (%)				
2 Weeks (N=78)	**38 (48.7)**	**29 (58.0)**	**9 (32.1)**	**0.02**
1 Month (n=76)	**38 (50.0)**	**30 (61.2)**	**8 (29.6)**	**0.008**
3 Months (N=70)	**38 (54.3)**	**31 (70.5)**	**7 (26.6)**	**<0.001**
6 Months (n=53)	**35 (66.0)**	**29 (80.6)**	**6 (35.3)**	**0.001**
1 Year (N=30)	**26 (86.7)**	**22 (95.6)**	**4 (57.1)**	**0.03**
A1C, % (mean, SD)	**6.29 (0.86)**	**5.95 (0.35)**	**6.88 (1.14)**	**<0.001**
BMI at Time of Resolution, kg/m^2 (mean, SD)	**35.8 (5.82)**	**36.1 (6.24)**	**35.1 (5.09)**	**0.56**
EWL, % (mean, SD)	**43.7 (15.1)**	**44.3 (16.1)**	**42.7 (13.6)**	**0.82**

BMI = Body Mass Index, EWL = Excess Weight Loss

Figure 1. Associating time post-op with return to physiologically normal A1C values.



DM = Diabetes Mellitus

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