Sleeve gastrectomy and type 2 diabetes mellitus: a systematic review

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Abstract

Background: Existing evidence has suggested that bariatric surgery produces sustainable weight loss and remission or cure of type 2 diabetes mellitus (DM). Laparoscopic sleeve gastrectomy (LSG) has garnered considerable interest as a low morbidity bariatric surgical procedure that leads to effective weight loss and control of co-morbid disease. The objective of the present study was to systematically review the effect of LSG on type 2 DM.

Methods: An electronic data search of MEDLINE, PubMed, Embase, Scopus, Dare, Clinical Evidence, TRIP, Health Technology Database, Conference abstracts, clinical trials, and the Cochrane Library database was completed. The search terms used included LSG, vertical gastrectomy, bariatric surgery, metabolic surgery, and diabetes (DM), type 2 DM, or co-morbidities. All human studies, not limited to those in the English language, that had been reported from 2000 to April 2010 were included.

Results: After an initial screen of 3621 titles, 289 abstracts were reviewed, and 28 studies met the inclusion criteria and the full report was assessed. One study was excluded after a careful assessment because the investigators had combined LSG with ileal interposition. A total of 27 studies and 673 patients were analyzed. The baseline mean body mass index for the 673 patients was 47.4 kg/m² (range 31.0–53.5). The mean percentage of excess weight loss was 47.3% (range 6.3–74.6%), with a mean follow-up of 13.1 months (range 3–36). DM had resolved in 66.2% of the patients, improved in 26.9%, and remained stable in 13.1%. The mean decrease in blood glucose and hemoglobin A1c after sleeve gastrectomy was −88.2 mg/dL and −1.7%, respectively.

Conclusion: Most patients with type 2 DM experienced resolution or improvement in DM markers after LSG. LSG might play an important role as a metabolic therapy for patients with type 2 DM.

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Keywords: Sleeve gastrectomy; Type 2 diabetes mellitus; Obesity; Bariatric surgery

Description of obesity

Worldwide, >1.7 billion adults are considered overweight, with ≥300 million considered clinically obese [1]. Obesity is generally defined as a body mass index (BMI) ≥30 kg/m². Co-morbid diseases related to obesity include hypertension, sleep apnea syndrome, and type 2 diabetes mellitus (DM). It has been proposed that in obese patients, a failure might occur of β-cells to secrete adequate levels of insulin to compensate for the insulin resistance in peripheral tissues, which ultimately leads to type 2 DM [2]. People with both obesity and type 2 DM have an increased risk of cardiac events and early death.

Description of intervention

During the past decade, bariatric surgical procedures such as Roux-en-Y gastric bypass and biliopancreatic diversion have demonstrated long-term control of obesity and...
type 2 DM [3,4]. In a recent systematic review, Buchwald et al. [5] demonstrated that 76% of people had resolution of type 2 DM after bariatric surgery. The bariatric surgical procedures included in their review were gastric banding, gastric bypass, gastroplasty, and biliopancreatic diversion with duodenal switch (BPDDS) [5].

Laparoscopic sleeve gastrectomy (LSG) was initially proposed as a staged approach to BPDDS for high-risk, severely obese, surgical candidates [6]. It has been increasingly considered as a definitive surgical procedure for obesity because of early data [7]. LSG involves removing most of the fundus of the stomach, creating a gastric “tube” 60–100 mL in capacity, which in turn limits the capacity for food intake.

How the intervention might work

LSG-associated weight loss is believed to be secondary to restriction of food intake by the small gastric reservoir. However, the mechanism behind LSG and the resolution of type 2 DM has not been clearly defined. Currently, both hormonal changes and a hindgut theory have been postulated to be involved. Karamanakos et al. [8] found a marked reduction of fasting ghrelin levels after LSG surgery. Ghrelin is a hormone produced primarily by the gastric fundus, which inhibits insulin secretion and blocks hepatic insulin signaling [8]. Abbatini et al. [9] stated that by reducing ghrelin levels and its “insulinostatic effect,” the islet cells will be able to secrete additional insulin by increasing the maximal capacity of glucose-induced insulin release. The hindgut theory postulates that rapid delivery of undigested nutrients to the distal bowel upregulates the production of L-cell derivates such as glucagon-like peptide 1 (GLP-1) and peptide-YY [10,11]. GLP-1 is secreted by the ileal “L-cells” in response to eating and was shown to be increased in the LSG group in an animal model [12]. GLP-1 acts to stimulate insulin release and might increase the β-cell mass [13]. Peptide-YY is also secreted from L-cells and might ameliorate insulin resistance in mice [14]. The hindgut theory has been supported by Melissas et al. [15], who found that despite preservation of the pylorus in LSG, gastric emptying was accelerated.

Objectives of present review

The primary goal of bariatric surgery is to produce long-term, sustainable weight loss, with improvement of comorbid disease such as type 2 DM. Despite the efficacy of both gastric bypass and BPDDS, these remain complex surgical procedures with significant postoperative morbidity. LSG is a technically less-complex surgical procedure that has been reported to improve weight loss and type 2 DM remission rates. However, existing studies have consisted of small heterogeneous patient populations. The published data on LSG has not yet been systematically reviewed or subjected to a meta-analysis.

In the present study, we systematically reviewed the published data regarding the efficacy of LSG for weight loss and the resolution of type 2 DM in obese patients.

Methods

The criteria for considering studies for the present review included the study type, participants, interventions, and outcome measures used.

The types of studies we considered included human retrospective and prospective case series (both with >5 patients), nonrandomized controlled trials, and randomized controlled trials.

We considered studies with a target population of adult (>18 years old) male or female patients with type 2 DM who had undergone LSG. Patients considered clinically obese with a BMI >30 kg/m² were included.

The intervention under study was LSG as a solitary procedure or as a first-stage procedure in a staged bariatric procedure.

The types of outcome measures included primary and secondary outcomes. The primary outcome was resolution of type 2 DM. The resolution of type 2 DM was defined as discontinuation of all hypoglycemic medications and/or insulin and a normal fasting plasma glucose level, normal postprandial glucose excursions, and normal hemoglobin A1c (HbA1c).

The secondary outcomes included the percentage of excess weight loss, change in BMI, and change in glucose levels, HbA1c levels, mortality, and postoperative complications.

The search method for the identification of studies was primarily electronic. We considered unpublished and/or non-English language studies for review inclusion. A comprehensive search of electronic databases (i.e., MEDLINE, PubMed, Embase, Scopus, Dare, Clinical Evidence, BIOSIS Previews, TRIP, Health Technology Database, Conference abstracts, clinical trials, and the Cochrane Library database) using broad search terms was completed. All human studies reported from 2000 to April 2010 were considered.

In addition, we used other resources to search for studies. The reference lists of all included studies were examined to identify additional potentially relevant publications. “Gray literature,” including conference abstracts, registered clinical trials, and Web sites were searched. These included the conference papers Index and OCLC Papers First. Ongoing trials were identified using controlled trial registration Web sites, including the International Clinical Trials Registry Platform Search Portal for the World Health Organization. The Google search engine was also used to search for clinical practice guidelines and government documents.
Data collection and analysis

Studies of any design that involved LSG for adult obese patients with type 2 DM from 2000 to 2010 were considered. A trained librarian conducted the electronic searches, and one of us conducted a prescreen to identify the clearly irrelevant reports by title, abstract, and Keywords of the publication. Two independent reviewers then assessed the studies for relevance; inclusion; and methodologic quality. The studies were classified as relevant (meeting all specified inclusion criteria); possibly relevant (meeting some; but not all; inclusion criteria); and rejected (not relevant to our review).

Two reviewers independently reviewed the full-text versions of all studies classified as relevant or possibly relevant. Any disagreements were resolved by repeat extraction.

Data extraction and management

Two reviewers independently extracted the data from the full versions of the reports. The extracted information included details of the methods (e.g., retrospective case series, clinically controlled trial), demographics (e.g., age, gender), clinical characteristics, study inclusion and exclusion criteria, number of patients excluded and lost to follow-up, details of the intervention (e.g., solitary LSG, staged bariatric procedure), baseline and postintervention outcomes (e.g., glucose levels, HbA1c, BMI), and methods of analysis.

Measures of treatment effect

Weight loss is reported as a mean percentage of excess weight loss, currently considered standard in bariatric surgery. It is calculated as follows: percentage of excess weight loss = (weight loss/excess weight) × 100, where excess weight is the total preoperative weight minus the ideal weight [5]. We have also reported the BMI when appropriate.

The resolution of type 2 DM was calculated as the percentage with DM resolution according to the number of patients in whom type 2 DM had disappeared or no longer required therapy. We extracted the number of patients evaluated as the denominator.

Assessment of risk of bias in included studies

All included trials were assessed independently by 2 reviewers for methodologic quality using the Cochrane (concealment of allocation) and risk of bias tools [16].

Statistical analysis

We performed an analysis of the data from the included studies. Descriptive statistics (simple counts and mean values) were used to report the study-, patient-, and treatment-level data. The number of patients enrolled was used in the calculation of the study and patient demographics. Efficacy outcomes of interest were synthesized by pooling the data from the LSG patients. Because of the high heterogeneity among the studies and the lack of randomized controlled trials, a meta-analysis was not deemed appropriate. All calculations were performed using Stata, version 10 (StataCorp, College Station, TX), statistical software.

Results

Search results

A total of 3621 studies were identified using our search criteria for screening (Fig. 1). After an assessment according to our exclusion criteria, 3332 were rejected and 289 studies remained for abstract review. Of the 289 studies, 28 were identified; 1 was excluded because they had combined LSG with ileal interposition [17]. Thus, a total of 27 primary studies meeting the inclusion criteria were identified after a careful screening. These included 3 nonrandomized prospective controlled trials [18–20], 3 retrospective controlled trials [21–23], 15 prospective case series [7,24–37], and 6 retrospective case series [38–43].

Included studies

All 27 studies reported LSG-associated outcomes data on BMI, excess weight loss, and type 2 DM-related measurements. The baseline patient characteristics in the included studies are listed in Table 1. A total of 673 patients were assessed in the 27 studies, and numbers of patients ranged from 7 to 75. The average patient age was 46.6 ± 3.8 years (range 42–51); approximately 66% of the patients were women. The mean preoperative BMI was 47.4 ± 7.9 kg/m² (range 31–53.5) based on 13 included studies. The patients had a mean follow-up of 13.1 ± 8.1 months (range 3–36).

The primary outcome of type 2 DM resolution was assessed by 26 of the included studies. LSG resulted in a DM resolution rate of 66.2% (Table 2). Within the studies,
16 reported both resolution and improvement of type 2 DM, and 97.1% of the patients had experienced DM resolution or improvement. Four studies reported DM resolution, improvement, or stable disease in 94.8% of their patients. The secondary outcomes included the percentage of excess weight loss, postoperative BMI, and changes in glucose and HbA1c levels. A substantial percentage of excess weight loss of 47.3%/H11006 19.1% (range 6.3–74.5%) was seen in patients included in 11 studies with a mean follow-up of 13/H11006 8.1 months (range 3–36). The postoperative BMI had decreased to 35.9/H11006 6.6 kg/m² (range 24.6 – 44.7) based on 8 included studies. Within the 7 studies that reported the plasma glucose levels, the levels had decreased from a baseline of 181.2 mg/dL to 119.2 mg/dL. The HbA1c levels had also decreased from a baseline of 7.9% to a postoperative level 6.2%, based on 11 studies.

The operative mortality at ≥30 days was .36% for all LSG (not only DM patients) procedures (4 deaths of 1117 patients) based on 16 studies [7,20,21,23,25,26,28,29,32,33,35–37,39,42,43]. Postoperative complications such as bleeding occurred in a 1.79% (20 of 1117) patients. Postoperative abscess or infection occurred in .27% (3 of 1117 patients). Postoperative leaks occurred in 22 of 1117 patients (1.97%).

Discussion

A systematic review of the existing evidence has suggested that LSG for morbid obesity results in resolution or improvement of type 2DM in most patients. Although approximately two thirds of the patients experienced complete DM resolution, the remaining 30% of patients had significant improvement.

A systematic review by Buchwald et al. [5] demonstrated similar improvement in type 2 DM resolution after other bariatric surgical procedures. Gastric banding, gastric bypass, and BPDDS resulted in resolution of type 2 DM in 48%, 84%, and 98% of patients, respectively [5]. In our analysis of LSG, the overall DM resolution and improvement rate was 97.1%. Similarly, the Swedish Obesity Subjects study demonstrated that the 2-year recovery rate from DM in the group treated with bariatric surgery was significantly greater [44]. Furthermore they demonstrated an 80% reduction in annual mortality in the surgically treated group compared with the control group [44]. Similarly, MacDonald et al. [45] found that gastric bypass reduced the progression of type 2 DM within the surgically treated patients. The mortality rate in the bypass group was 9% compared with 28% in the medically treated controls. The reduction was
attributed to a decrease in cardiovascular-related death [45]. It remains to be seen whether the LSG-related resolution or improvement in type 2 DM will translate into a long-term decrease in patient mortality.

In 705 morbidly obese patients, LSG reduced excess weight by 47.3%. Buchwald et al. [5] found gastric banding, gastric bypass, and BPDDS to reduce excess weight in patients by 47%, 62%, and 70%, respectively. A prospective observation study by Williamson et al. [46] found intentional weight loss by overweight women with obesity-related health conditions was associated with a 20% reduction in total mortality. Bariatric surgery, other than LSG, has previously been shown to result in substantially greater weight loss than with medical treatment [47].

Compared with the review by Buchwald et al. [5], our findings have demonstrated that patients undergoing LSG had a greater degree of excess weight loss and resolution of type 2 DM than with gastric banding. Abbatini et al. [9] reached a similar conclusion when comparing LSG and gastric banding in 60 morbidly obese patients. They reported a type 2 DM resolution rate of 80.9% for LSG compared with 60.8% after gastric banding, as well as greater improvements in insulin resistance in the LSG-treated group. Additional benefits for the patients undergoing LSG included the lack of a need for adjustments to a gastric band and the avoidance of needles. LSG restricts the size of the stomach by removing the gastric fundus. Furthermore, the pylorus functions as a natural band, facilitating additional restriction. The removal of the gastric fundus reduces ghrelin levels [8], a stimulator of food intake in humans [48]. Karamanakos et al. [8] found significantly decreased levels of ghrelin in 16 patients after LSG surgery, which might be associated with greater appetite suppression. A hormonal mechanism has also been suggested by Abbitini et al. [9], who found a similar type 2 DM resolution rate with LSG and laparoscopic gastric bypass surgery.

LSG was initially proposed as a staged approach to BPDDS for superobese patients [6]. The finding by Melissas et al. [15] that LSG results in increased transit of stomach contents and absent or very mild vomiting after eating is uncharacteristic of a restrictive procedure. However, it might have added benefits similar to that of gastric bypass or BPDDS according to the hindgut theory. With the rapid transit of undigested nutrients, the distal bowel upregulates the production of GLP-1 and peptide YY. Both derivatives of L-cells, GLP-1 stimulate insulin secretion and has an

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HbA1c = hemoglobin A1c; EWL = excess weight loss; Pre = preoperatively; Post = postoperatively; DM = diabetes mellitus.
antiapoptotic effect on β-cells in the pancreas [49]. Peptide YY might ameliorate insulin resistance in mice [14]. If the hindgut theory holds true, it could explain the additive improvement of type 2 DM after LSG compared with other restrictive procedures. Although the excess weight loss and type 2 DM resolution has been lower after LSG compared with after both gastric bypass and BPDDS, benefits exist. LSG remains a less technically complex procedure and might have wider applicability to general surgeons. The risks of surgery such as malabsorption and internal hernias postoperatively are minimal. Dumping syndrome has not been reported as a postoperative issue.

Buchwald et al. [5] reported a mortality rate of .1% for purely restrictive procedures (3000 patients), .5% for gastric bypass (5644 patients), and 1.1% for BPDDS (3030 patients). From 16 studies, the estimated mortality rate for LSG is .35% (4 deaths in 1117 patients). Postoperative complications such as bleeding (1.79%) and staple line leak (1.97%) compared favorably with the rates reported for gastric bypass and BPDDS [40].

**Study limitations**

To our knowledge, no randomized controlled studies comparing LSG and medical therapy or other bariatric surgical procedures assessing the resolution of type 2 DM in obese patients have been published. The primary studies included in the present review, therefore, consisted largely of nonrandomized controlled trials or case series, which are inherently biased. Thus, in most available studies, a single bariatric surgical procedure was assessed without comparison with a control group. Furthermore, because of the considerable heterogeneity among the studies, a meta-analysis was not feasible. In addition, a potential source of heterogeneity (e.g., age, gender) could not be addressed in our review because of the lack of consistent outcome reporting. Other possible sources of heterogeneity (e.g., study design, population, and interventions) were sufficiently similar to support the decision to pool the data.

Given the potential sources of bias inherent in nonrandomized studies, the results of our systematic review should be interpreted with caution. Missing demographic data and limited outcome data could have produced misleading results. This situation, however, appears inherent to a vast proportion of bariatric surgical data and has led to calls for standardized reporting in future studies. Despite these limitations, our review supports the idea that LSG is associated with the resolution and improvement of type 2 DM and could thus serve as a basis for the development of high-level randomized clinical trial evidence on this important issue.

**Conclusion**

Our findings have shown that LSG has a substantial effect on type 2 DM, producing resolution or improvement in most cases. With the potential to be revised to a gastric bypass or BPDDS procedure, LSG is a promising surgical procedure for the treatment of morbid obesity and type 2 DM.

**Disclosures**

The authors have no commercial associations that might be a conflict of interest in relation to this article.

**References**


