Single Anastomosis Sleeve Ileal and One Anastomosis Gastric Bypass outcome comparison in an Obese Rat Model

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Research Article

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Abstract

Background

Complications after single anastomosis bariatric surgeries such as one anastomosis gastric bypass (OAGB) and single anastomosis sleeve ileal bypass (SASI) remain controversial. This study aimed to compare the effect, comorbidity remission, malnutrition, and most importantly, the influence of biliary reflux in rats that underwent SASI and OAGB.

Methods

Diabetic Sprague–Dawley rats received SASI (n = 8), OAGB (n = 8), esojejunostomy, (EJ) (n = 8), and SHAM (n = 8) surgeries. Changes in weight, glucose tolerance, and serum nutrient expression were analyzed. Bile acid concentration measurement and histological investigations were performed using the esogastric sections of rats. The follow-up period was 12 weeks.

Results

We did not observe statistically significant differences in weight changes between the SASI and OAGB groups. The concentration of mean bile acid was 1.5-fold higher in the OAGB group than in the SASI group. We observed esophageal hyper-papillomatosis in three groups (SASI = 37.5%, OAGB = 87.5%, EJ = 100). The OAGB group had a significantly higher level of mucosae than the SASI group, as well as lower levels of albumin and iron. No obvious dysplasia or intestinal metaplasia was observed after a 12-week follow-up.

Conclusions

The SASI procedure was proved to have a more positive anti-reflux effect than the OAGB procedure, as well as better glucose control and lower risks for hypoalbuminemia. Further clinical results are required.

Introduction

Morbid obesity has become a global health problem [1], with bariatric surgery confirmed as an effective treatment [2]. Sleeve gastrectomy with transit bipartition (SG-TB), reported by Santoro, is a relatively novel procedure [3]. SG-TB has metabolic effects similar to a Roux-en-Y gastric bypass (RYGB) or biliopancreatic diversion with duodenal switch (BPD/DS) but with fewer complications [4, 5]. Mahdy et al. proposed modifying the SG-TB into a single anastomosis sleeve ileal bypass (SASI) [6]. A SASI bypass is a valid procedural technique with excellent weight loss and comorbidity remission-inducing effects. However, patients undergoing a SASI bypass are at risk of biliary reflux [7]. An alternative, one-anastomosis gastric bypass (OAGB), is becoming an internationally recognized technique that was
acknowledged as a mainstream bariatric procedure in 2018 [8, 9]. However, OAGB still has several complications, including biliary reflux, where there can be reflux of biliopancreatic juice into the stomach or esophagus [10]. Bile acids play a significant part in developing gastric and esophageal metaplasia, which may lead to adenocarcinoma [11]. The occurrence rate of gastroesophageal reflux after the OAGB procedure varies between 0.6% and 10% [12]. There are many similarities between the two procedures, including similar anastomotic locations and gastric pouch.

This study aimed to use the diabetic rodent model to compare the results of two bariatric procedures, SASI and OAGB. We assessed and compared the two procedures for bile reflux, malnutrition, weight loss, and comorbidity remission.

**Materials And Methods**

**Animals**

Our study was approved by the ethics committee of our institution's Research Animal Center. In addition, all applicable institutional and national guidelines of the People's Republic of China for the care and use of animals were followed. All rats were single-housed.

Male Sprague–Dawley rats (age 8–10 weeks) were obtained from the Research Animal Center of our institution. Low-dose streptozotocin injections and a high-fat diet were used to induce type 2 diabetes in the rodents[13, 14]. Diabetes was diagnosed when the random blood glucose level was > 16.0 mmol/L, measured with a glucometer for 3 consecutive days.

**Surgical Procedures**

Thirty-two diabetic rats were assigned to SASI (n = 8) (Fig. 1a), OAGB (n = 8) (Fig. 1b), SHAM (n = 8), and esojejunostomy (EJ) (n = 8) (Fig. 1c) groups. In the operation, we measured the length of the small intestine of every rat. According to our data, the length of the small intestine was measured at approximately 80 cm on average, from the ligament of Treitz to the ileocolic section. We resected the greater curvature and the fundus for the SASI procedure [15]. The anastomosis was located 40 cm from the ligament of Treitz to preserve approximately half the common length. The gastric antrum was anastomosed to the small intestine, with an anastomosis width of 0.3 cm. The width of the gastrojejunostomy tube was 0.3 cm.

According to M'Harzi et al. [16], for the OAGB procedure, the forestomach was carefully resected, with a resection site between the esophagus and left gastric artery. A gastric pouch was then created parallel to the transaction line of the forestomach. The jejunum was located 25 cm distally from the pylorus. A 0.3 cm jejunostomy was created, and the jejunum was then anastomosed horizontally to the anterior of the stomach. The width of the gastrojejunostomy tube was 0.3 cm.
In the EJ procedure, the esophagus was minimally resected, a 0.3 cm jejunostomy created, and an anastomosis made between the jejunum and esophagus. The small intestine anastomosis was located approximately 40 cm from the ligament of Treitz.

The study lasted 12 weeks. Body weight changes, food intake, and fasting blood glucose (FBG) levels were measured every 2 weeks preoperatively and postoperatively. Every month, FBG levels were measured postoperatively after a 12 h fast. In addition, the oral glucose tolerance test (OGTT, 50% glucose solution, 3 mg/kg) and insulin tolerance test (ITT, insulin, 0.5 IU/kg) were performed after a 12 h fast preoperatively and at 4 and 12 weeks postoperatively [14].

Retroorbital blood samples were collected after a 12 h fast preoperatively and at 4 and 12 weeks postoperatively to investigate serum hormones such as glucagon-like peptide-1 (GLP-1) and insulin. Nutrients such as albumin (Alb), iron (Fe), calcium (Ca), and hemoglobin (Hb) were also monitored using enzyme-linked immunosorbent assay kits [13].

**Histology And Bile Acid Measurement**

The rats were sacrificed after a 12 h fast, 12 weeks postoperatively. Half of the gastroesophageal junctions, identified as 1 cm from both the esophagus and stomach of the rats, were removed. They were flushed with phosphate-buffered saline and stored at -80 °C until bile acids analysis. The bile acids were measured using high-performance liquid chromatography-tandem mass spectrometry [16, 17]. The gastroesophageal junctions were formalin-fixed, routinely embedded in paraffin for histological analysis, and hematoxylin-eosin-Safran staining was performed on each slide [18]. We investigated the incidences of esophageal hyperpapillomatosis (EHP), dysplasia, metaplasia, and cancer. We also measured the total esophageal mucosal height in every group. EHP lesions were identified by the presence of epithelial crests with a sinuous aspect of the esophageal mucosa.

**Statistical Analyses**

Quantitative values are expressed as mean ± standard deviation. The area under the curve (AUC) was calculated using GraphPad Prism 8 software. The groups and differences between the means were evaluated using one-way analysis of variance. A p-value < 0.05 was considered statistically significant.

**Results**

**Mortality and Morbidity**

No mortality occurred in the SHAM and EJ groups. The mortality rate in the SASI and OAGB groups was 25% and 12.5%, i.e., two cases of hemoperitoneum in the SASI group and one case of peritonitis (anastomotic fistula). We added two rats in the SASI group and one rat in the OAGB group. No mortality occurred afterward. No rats were euthanatized postoperatively.
Weight Loss, Food Intake, And Fasting Blood Glucose

No significant differences in body weight change or food intake were observed between groups preoperatively (Fig. 2a, b). Postoperatively, in the SASI and OAGB groups, body weight was significantly lower than that in the SHAM group (p < 0.05). Additionally, in the SASI and OAGB groups, food intake was significantly less than that in the SHAM group postoperatively (p < 0.05). There were no significant differences in percentage total weight loss between the SASI and OAGB groups.

The SASI and OAGB groups showed significantly lower FBG postoperatively (p < 0.05) (Fig. 2c). The SASI group presented lower levels of FBG postoperatively than the OAGB group (6.1 ± 0.4 vs. 6.4 ± 1.4), but with no significant difference.

Ogtt And Itt

All groups showed a significant improvement in glucose control postoperatively, except for the SHAM group (p < 0.05) (Fig. 3a-c). Furthermore, a comparison of the SASI and OAGB groups showed that OGTT levels were significantly lower in the SASI group 12 weeks postoperatively (p < 0.05) (Fig. 4c).

Postoperatively, the ITT results of the SASI and OAGB groups showed significant improvements in insulin response (p < 0.05) (Fig. 3d-f). Compared with the OAGB group, the SASI group showed no significant differences in insulin response.

Hormonal Analysis

No significant differences in GLP-1 and insulin levels were observed among the groups preoperatively (Fig. 5a, b). However, 12 weeks postoperatively, the SASI and OAGB groups had significantly higher GLP-1 and lower insulin levels (p < 0.05). The GLP-1 levels in the OAGB group were lower than those in the SASI group (54.4 ± 5.9 vs. 56.8 ± 4.6), but no significant difference was observed. As for the insulin level, no significant differences were observed between the SASI and OAGB groups postoperatively (160.5 ± 6.8 vs. 157.4 ± 83).

Nutritional Status

No significant differences in Alb, Hb, iron, and calcium levels were observed in the SASI, OAGB, and SHAM groups preoperatively (Fig. 5c-f). Twelve weeks postoperatively, the SASI and OAGB groups showed significantly lower Alb levels than the SHAM group (p < 0.05) (Fig. 5c). In addition, significantly lower iron levels were observed in the OAGB group than in the other two groups at 12 weeks (p < 0.05) (Fig. 5d). No significant differences in the levels of Hb and calcium were observed among the groups.

Histology
After sacrifice, esophageal hyperpapillomatosis (EHP) was observed in 87.5% (7/8) of the OAGB group, 37.5% (3/8) of the SASI group, 100% (8/8) of the EJ group, and none of the SHAM group (Fig. 6c-f). Mean mucosal height was 154.29 ± 4.06 µm for the SASI group, 174.58 ± 8.3 µm for the OAGB group, 100.55 ± 2.82 µm for the SHAM group, and 534.7 ± 29.76 µm for the EJ group. The SHAM group had a significantly lower mucosal height than the SASI and OAGB groups (p < 0.05). The mucosal height was significantly higher in the OAGB group than in the SASI group (p < 0.05) but was the highest in the EJ group. No dysplasia, intestinal metaplasia, or cancer were observed after 12 weeks of follow-up.

**Total Bile Acid Concentration**

At 12 weeks postoperatively, the SHAM group had significantly lower mean total bile acid concentration than the SASI and OAGB groups (p < 0.05) (Fig. 6a, b). The OAGB group had 10.3 times higher mean total bile acid concentration levels in the esogastric segment than the SHAM group (97347 ng/g vs. 9437 ng/g; p < 0.05). The esogastric segment mean total bile acid concentration in the OAGB group was 1.5 times higher than that in the SASI group (97347 ng/g vs. 64983 ng/g; p < 0.05).

**Discussion**

This study reports the metabolic, nutritional, and biliary reflux outcomes of SASI and OAGB procedures. We found that the OAGB procedure had a higher risk of biliary reflux than the SASI procedure, with a higher incidence of malnutrition post-surgery. Both the SASI and OAGB procedures had excellent effects on weight loss and blood glucose control.

OAGB is considered an effective, IFSO-approved bariatric procedure [9], but it is associated with a risk of malnutrition due to its hypo-absorptive outcome [19]. Furthermore, the procedure cannot be performed endoscopically. SG-TB was proposed as a way to reduce the incidence of malnutrition while providing similar bariatric and metabolic results [3]. SASI is an adapted surgical procedure for SG-TB that is shown to improve weight loss, comorbidity remission, and lower complication rates [20–23]. However, all single anastomosis procedures, such as OAGB and SASI, are associated with bile reflux, anastomotic, and nutritional deficiencies [7, 21, 24, 25].

Bile reflux is a common problem associated with one-anastomosis type bariatric surgery [7, 25]. Patient symptoms should be monitored after bariatric surgery to reduce the risk of esophageal transformations such as Barrett esophagus and esophageal cancer [11]. Bile reflux can lead to esophageal or gastric cancer if it is not diagnosed and treated promptly. Several studies have reported that bile reflux could contribute to the progress of gastric cancer after gastrectomy [26–28].

Overwhelming evidence suggests a relationship between bile reflux and Barrett’s mucosa (BE) [29]. According to a study by Rhonda et al., bile acid can induce the secretion of cytokines, which could induce T lymphocytes and cause basal cell proliferation. The epithelial injury eventually results in BE: a pathological esophageal mucosa that could evolve into adenocarcinoma [30]. Owing to this
complication, many surgeons choose not to use OAGB as a routine technique. According to a recent cohort study by Szymański et al. [31], 2 years after OAGB, 48% (24/50) of patients had either grade A or B esophagitis and 8% (4/50) had suspected esophageal metaplasia. Approximately 68% (34/50) of patients had various esophageal histopathological changes, including four patients with Barrett's esophagus.

A cohort study by Shenouda et al. enrolled 20 patients who underwent OAGB, with 30% reporting bile reflux post-procedure [32]. Studies on bile reflux post-SASI are rare, but the study by Kehalaf et al. reported bile reflux with bilious vomiting in 17 patients (5.3%) [21].

Twelve weeks of bile exposure in rats equals 9–12 years in humans [32]. In this study, bile reflux was measured by bile acid concentration in the esophagogastric blocks of the rats. According to our study, bile acid concentrations were ten times higher in the OAGB group and seven times higher in the SASI group than in the SHAM group. The total bile concentration was significantly higher in the OAGB group than in the SASI group. Furthermore, we identified a significant difference in mucosal height between the OAGB and SASI groups.

In the present study, we found that the SASI group had a lower bile acid concentration and mucosal height than the OAGB group. We hypothesized that SASI preserves the pylorus so that it has two food outlets, ensuring bile acid can be mixed with gastric contents. Therefore, when bile acid arrives at the gastro-ileal anastomosis, the acid will be more dilute in rats that have undergone SASI than OAGB. In addition, the gastric tube in SASI is longer and larger than that in OAGB. However, the amount of food that goes to the duodenum or ileum remains unclear. Future studies should investigate the relationship between the amount of food passing through the two outlets with the bariatric and metabolic effects of the transit bipartition.

Malnutrition is an important issue when choosing bariatric procedures. Both SASI and OAGB are associated with various types of malnutrition. The OAGB procedure was associated with a significantly higher incidence of hypoalbuminemia along with iron deficiency. The SASI group showed a decrease in calcium levels, but we did not observe statistically significant differences. We deduce that compared with the OAGB procedure, the SASI procedure has a lower incidence of malnutrition. Nevertheless, further advanced clinical research is required to confirm these results.

The SASI and OAGB procedures showed significant weight loss effects throughout the study. The SASI resulted in lower body weights than the OAGB procedure postoperatively, but we did not observe any significant differences. While SASI and OAGB procedures both resulted in excellent postoperative glucose control, the 12-week OGTT results were lower in the SASI group. The GLP-1 levels were significantly higher in the SASI and OAGB groups than that of the SHAM group. This suggests that the SASI procedure might have a better effect on glucose remission, as it excludes a greater percentage of the small intestine. Evidence collected from the literature and during this study is unclear on whether bypassing the duodenum is necessary [33].
The main limitations of the present study are (i) the small sample size and (ii) insufficient follow-up. In addition, animal experiments cannot fully represent clinical results. Therefore, further clinical studies and advanced detection techniques are needed to evaluate the severity and long-term outcomes of bile reflux post-bariatric surgery.

**Conclusion**

We suggested that SASI was superior to OAGB for limiting bile reflux, as it preserves two gastric outlets. Moreover, SASI was associated with better glucose control and a much lower risk of malnutrition than OAGB. However, there was no significant difference in weight loss between the SASI and OAGB groups. Therefore, further clinical studies are required.

**Declarations**

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**Conflicts of Interest**

Author 1 declares that he has no conflict of interest.

Author 2 declares that he has no conflict of interest.

Author 3 declares that he has no conflict of interest.

Author 4 declares that he has no conflict of interest.

Author 5 declares that he has no conflict of interest.

Author 6 declares that he has no conflict of interest.

Author 7 declares that he has no conflict of interest.

**Author contributions** Author 1, Author 2, and Author 5 contributed to the conception and design of the study. Author 3 performed the statistical analysis. Author 4 wrote the first draft of the manuscript. Author 2 and Author 3 wrote sections of the manuscript. Author 6 and Author 7 contributed to the assistance and funding and revision of the manuscript. All authors have reviewed and agreed to submit the manuscript.

Yuxiao Chu, Jason Widjaja, and Jian Wang contributed equally to this study.

**Ethical Approval Statement**

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration
and its later amendments or comparable ethical standards.

References


Figures

**Figure 1**

Graphical demonstration of the three surgical models. **a** Single Anastomosis Ileal Bypass (SASI), **b** One Anastomosis Gastric Bypass (OAGB), and **c** Esojejunostomy (EJ)

**Figure 2**
Changes in **a** body weight, **b** food intake, and **c** fasting blood glucose level between all groups. All data are presented as mean± SD. *Significant SASI, OAGB compared with SHAM (p<0.05). SASI, Single Anastomosis Ileal Bypass; OAGB, One Anastomosis Gastric Bypass.

![Graphs showing changes in body weight, food intake, and fasting blood glucose level between groups.](image)

**Figure 3**

Preoperative (Preop) and postoperative (Postop) oral glucose tolerance test (OGTT) and insulin tolerance test (ITT). All data are presented as mean ± SD. **a, d** (SASI OGTT and ITT, respectively); **b, e** (OAGB OGTT and ITT, respectively); **c, f** (SHAM OGTT and ITT, respectively). *Significant difference compared with preoperative level (p<0.05). SASI, Single Anastomosis Ileal Bypass; OAGB, One Anastomosis Gastric Bypass.
Figure 4

Between-group comparison before and after surgery, a, b, c Oral glucose tolerance test (OGTT) and d, e, f insulin tolerance test (ITT). All data are presented as mean±SD. *Significant SASI, OAGB compared with SHAM (p<0.05). &Significant SASI compared with OAGB (p<0.05). SASI, Single Anastomosis Ileal Bypass; OAGB, One Anastomosis Gastric Bypass.
Figure 5

Area under the curve (AUC) of glucagon-like peptide-1 (GLP-1) and insulin levels and nutritional status comparison between-groups. a GLP-1 AUC; b insulin AUC; c ALB, albumin; d Fe, iron; e Ca, calcium; f HB, hemoglobin. All data are presented as mean±SD. *Significant compared with SHAM at that particular period (p<0.05). #Significant compared with OAGB at that particular period (p<0.05). SASI, Single Anastomosis Ileal Bypass; OAGB, One Anastomosis Gastric Bypass.
Figure 6

Between-group comparison after surgery, **a** the quantitative mucosal height was observed through the histology; **b** postoperatively concentration of bile acid in a liquid lavage from esogastric regions if rats had undergone a SASI, OAGB or EJ surgery. Bile acids were obtained using solid-phase extraction and measured (as previously described) by a HPLC MS/MS system. All data are presented as mean±SD. *Significant compared with the SASI, EJ, and SHAM groups (p<0.05). #Significant compared with the OAGB, SHAM, and EJ groups (p<0.05). &Significant compared with the SASI, OAGB, and SHAM groups (p<0.05).

Hematoxylin and eosin (H&E) histology (×100) in **c** SASI, **d** OAGB, **e** SHAM, and **f** EJ. The black line (close to the arrow) shows the mucosal length being measured. Single Anastomosis Ileal Bypass; OAGB, One Anastomosis Gastric Bypass; EJ Esojejunostomy.