



Relationship Between Bariatric Surgery and Gastroesophageal Reflux Disease: a Systematic Review and Meta-analysis

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Abstract

The purpose of this study was to investigate the relationship between bariatric surgery (laparoscopic sleeve gastrectomy [LSG] and laparoscopic Roux-en-Y gastric bypass [LRYGB]) and gastroesophageal reflux disease (GERD). The number of obese patients with newly onset, worsened, or improved GERD after bariatric surgery in each article were extracted. In the pooled analysis, LSG was associated with a higher risk of GERD than LRYGB (odds ratio [OR] = 5.10, 95% confidence interval [CI] 3.60–7.23, $p < 0.001$). Compared with LSG, LRYGB had a better effect on GERD (OR = 0.19, 95% CI 0.12–0.30, $p < 0.001$). LRYGB was more effective for treating GERD in obese patients than LSG and the incidence of newly onset GERD after LRYGB was lower.

Keywords Bariatric surgery · Sleeve gastrectomy · Roux-en-Y gastric bypass · Gastroesophageal reflux disease · Meta-analysis

Introduction

Obesity has become one of the most severe global public health problems. Over 2.1 billion adults worldwide are considered overweight or obese; 640 million of these are

classified as obese. Moreover, the number and percentage of people who are overweight or obese are soaring [1]. Presently, bariatric surgery (metabolic surgery) is very useful and safe for treating obesity. Metabolic surgery reduces weight and improves obesity-related complications [2, 3]. However,

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surgical treatment of obesity can result in complications, including gastroesophageal reflux disease (GERD), nutrition malabsorption, and dumping syndrome [4, 5].

Interestingly, GERD is also, potentially, an obesity-related complication and a complication of bariatric surgery. Laparoscopic sleeve gastrectomy (LSG) could lead to the development of GERD after weight loss in obese patients. In most patients, the symptoms of GERD can be improved through medical treatments; a few patients require reoperation, which is usually conversion to laparoscopic Roux-en-Y gastric bypass (LRYGB) surgery. This shows that patients having LSG appear to have a higher risk of GERD [6]. However, no significant difference was observed in the risk of GERD between LSG and LRYGB in a recent randomized clinical trial [3]. Another randomized clinical trial suggested that the high incidence of GERD after LSG might be because a specific patient subpopulation undergoes LSG due to surgeon bias rather than an inherent property of LSG itself [7].

LSG and LRYGB have become the most widely used procedures of metabolic surgery. GERD could reduce the quality of life of patients. Therefore, it is of great clinical significance to investigate the difference between the two surgical methods (LSG vs. LRYGB) in the treatment of GERD and the risk of GERD after surgery. To date, however, there is no consensus in this regard. Therefore, this study aimed to compare the efficacy of LSG and LRYGB in the treatment of GERD for obese patients, as well as the risk of GERD after surgery.

Materials and Methods

Database Search

According to recommendations from the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement [8], we systematically searched all clinical studies that evaluated GERD and compared LSG with LRYGB. The databases we searched included Web of Science, PubMed, EBSCO, Medline, and Cochrane Library. The databases were searched for articles published before June 2019. The search keywords used were “laparoscopic sleeve gastrectomy” OR “sleeve gastrectomy” OR “SG” OR “LSG” AND “laparoscopic Roux-en-Y gastric bypass” OR “gastric bypass” OR “GB” OR “LRYGB.” GERD was used as the observation index, including the improvement of GERD after bariatric surgery, and the number of cases of newly onset or worsened GERD after bariatric surgery. At the same time, in order not to omit potential studies, especially those with negative results, the search terms related to GERD were not restricted. Two authors independently reviewed the full text of all clinical studies comparing LSG and LRYGB for GERD information. Additionally, the reference lists of the selected

articles were individually examined to obtain other, potentially relevant, studies.

Study Selection

The inclusion criteria for this meta-analysis were as follows: (1) the efficacy of LSG and LRYGB on GERD for obese patients was compared or (2) newly onset or worsened GERD after LSG and LRYGB were compared. The exclusion criteria were as follows: (1) there was no comparison between the two types of surgery; (2) results for GERD did not show available data; (3) the study reported non-clinical original research or was not written in English. Only the most recent, relevant, or comprehensive publications were included in the analysis to avoid duplicates, ambiguity, or papers reporting data from the same study population.

Data Extraction and Quality Assessment

Data from each included study was extracted by two investigators and reviewed independently by a third investigator following fundamental indicators from each article into Table 1. These indicators included study country and year, sample size, follow-up time, indications for bariatric surgery, and definition of GERD. The quality of randomized controlled trials (RCTs) and observational studies was assessed by the Cochrane risk of bias tool and the Newcastle-Ottawa Quality Assessment Scale (NOS) checklist, respectively [9, 10]. Any discrepancies between reviewers were resolved by the consensus of two authors and the third reviewer.

Statistical Analyses

Odds ratios (OR) including 95% confidence intervals (CI) were used to analyze the relationship between bariatric surgery and the risk of GERD. Heterogeneity was checked by Cochrane collaboration's risk of tool, chi-squared test, and I^2 statistics, and identified when $p < 0.1$ and $I^2 > 50\%$. Begg's test evaluated publication bias. All statistical analyses were two-tailed, and $p < 0.05$ was considered statistically significant. The Stata 12.0 Software (Stata, College Station) was used to perform the meta-analysis.

Results

Overall, 9523 studies were pooled from all databases; 4730 were excluded due to duplication. After browsing the full text, 25 were excluded because they were non-clinical original studies, while 12 were excluded because they did not compare LSG and LRYGB. Furthermore, 227 studies did not include GERD-related results and were excluded. Nine articles were excluded because they did not provide available GERD data.

Table 1 Characteristics of included studies in the meta-analysis

Author, year	Country	LSG	LRYGB	Follow-up (year)	Patient inclusion criteria	GERD	Study
Lakdawala, 2010	India	50	50	1	NA	Symptoms	Retrospective
Mohos, 2011	Austria	47	47	1	BMI ≥ 40 kg/m ² ; ≥ 35 kg/m ² with comorbidities	PPI; symptoms	Prospective
Kehagias, 2011	Greece	30	30	3	BMI 40–50 kg/m ²	PPI; endoscopy	RCT
Yaghoubian, 2012	USA	192	345	1	NA	NA	Retrospective
Moon, 2013	USA	13	41	2	Conversion of failed of LAGB	NA	Retrospective
Zhang, 2013	USA	200	358	1	BMI ≥ 40 kg/m ² ; ≥ 35 kg/m ² with comorbidities	PPI; endoscopy	Prospective
Leyba, 2014	Venezuela	42	75	5	BMI 35–50 kg/m ²	NA	Prospective
Jammu, 2015	India	339	295	5	NA	NA	Prospective
Ignat, 2016	France	55	45	5	BMI 40–60 kg/m ²	NA	RCT
Lee, 2016	Korea	116	73	1	BMI ≥ 30 kg/m ²	NA	Retrospective
Vitello, 2016	USA	51	34	2	NA	NA	Retrospective
Schauer, 2017	USA	49	50	5	BMI 27–43 kg/m ² with HbA1c > 7.0%	NA	RCT
Garg, 2017	India	40	40	2	BMI > 40 kg/m ² ; ≥ 35 kg/m ² with comorbidities	NA	Retrospective
Arapis, 2018	France	91	119	6	BMI ≥ 60 kg/m ²	PPI; symptoms; endoscopy	Retrospective
Avsar, 2018	Turkey	20	29	1	Conversion of failed of LAGB BMI ≥ 40 kg/m ² ; 30–40 kg/m ² with comorbidities	NA	Retrospective
Du, 2018	China	97	79	1	BMI ≥ 32.5 kg/m ² ; ≥ 27.5 kg/m ² with comorbidities	NA	Retrospective
Salminen, 2018	Finland	121	119	5	BMI ≥ 40 kg/m ² ; ≥ 35 kg/m ² with comorbidities	NA	RCT
Peterli, 2018	Switzerland	107	110	5	BMI ≥ 40 kg/m ² ; ≥ 35 kg/m ² with comorbidities	NA	RCT
Catheline, 2019	France	163	84	3	BMI ≥ 40 kg/m ² ; ≥ 35 kg/m ² with comorbidities	PPI; symptoms + endoscopy	RCT
Dewberry, 2019	USA	67	161	5	Adolescents with BMI ≥ 35 kg/m ²	Symptoms + antacid medication	Prospective
Lin, 2019	China	82	79	1	BMI ≥ 35 kg/m ²	NA	Retrospective
Seip, 2019	USA	461	258	2	NA	NA	Retrospective
Raj, 2019	India	30	16	1	NA	DeMeester score < 14.7	Prospective

LG laparoscopic sleeve gastrectomy, LRYGB laparoscopic Roux-en-Y gastric bypass, LAGB laparoscopic adjustable gastric band, GERD gastroesophageal reflux disease, BMI body mass index, NA no available, HbA1c glycosylated hemoglobin, PPI proton pump inhibitors, RCT randomized clinical trial

Finally, 23 studies were included, including 6 RCTs, 6 prospective observational studies, and 11 retrospective observational studies [3, 4, 11–31]. Figure 1 shows the details of the retrieval process and filtering. All included studies met the inclusion criteria and showed available results. The quality assessment of the included studies is shown in Supplementary Table 1.

Study Characteristics

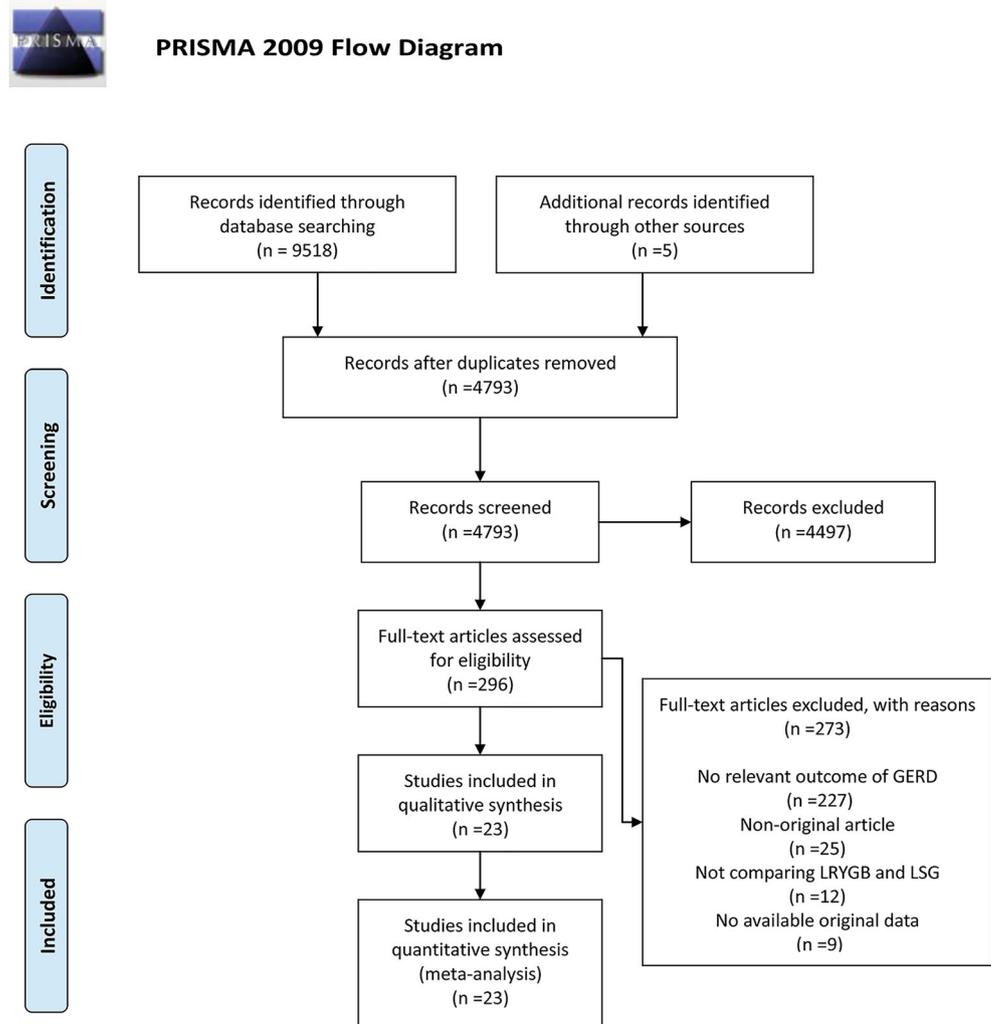
From 2010 to 2019, a total of 23 studies including 5000 patients (2463 in LSG and 2537 in LRYGB) from the USA, India, China, Korea, Austria, France, Greece, Venezuela, Turkey, Finland, and Switzerland, and clinical follow-up ranging from 1 to 6 years were selected. Nine studies, four studies

and two studies showed the results of 1, 2, and 3 years of follow-up, respectively. Eight studies provided data from a follow-up of ≥ 5 years after surgery. Ten studies compared the efficacy of LSG and LRYGB for GERD in obese patients. Conversely, seventeen studies reported the results of newly onset GERD after LSG and LRYGB, and two reports reported worsened GERD after surgery. Study characteristics are shown in Table 1.

Bariatric Surgery Led to Newly Onset or Worsened GERD

In terms of the adverse effects of bariatric surgery on GERD, 3534 obese patients were analyzed; 1918 patients received LSG and 1616 patients received LRYGB, and the occurrence

Fig. 1 Flow chart of study selection



of de novo GERD was 9.3% after LSG and 2.3% after LRYGB (179 in LSG group and 37 in LRYGB group). In addition, 25 patients had worsened GERD (22 in LSG and 3 in LRYGB). In the pooled analysis, LSG was associated with a higher risk of GERD than LRYGB (OR = 5.10, 95% CI 3.60–7.23, $p < 0.001$) (Fig. 2). Subgroup analysis showed that the analysis results were consistent according to the study type (RCT vs. observational study) and the follow-up time (within 3 years vs. > 3 years), with low heterogeneity, and the risk of postoperative GERD associated with LSG was higher than that of LRYGB (Table 2).

Bariatric Surgery Improves GERD

Conversely, bariatric surgery also improved obesity-related GERD. LSG and LRYGB were performed in 166 and 244 patients with GERD, respectively. Two hundred and forty-eight patients eventually showed improvement or remission for GERD (40.4% in LSG, 74.2% in LRYGB). The pooled analysis showed that compared with LSG, LRYGB had a

better effect on GERD (OR = 0.19, 95% CI 0.12–0.30, $p < 0.001$) (Fig. 3). According to subgroup analysis, in the observational study and in the follow-up results within 3 years and > 3 years, LRYGB had a better effect on GERD improvement than LSG (Table 3).

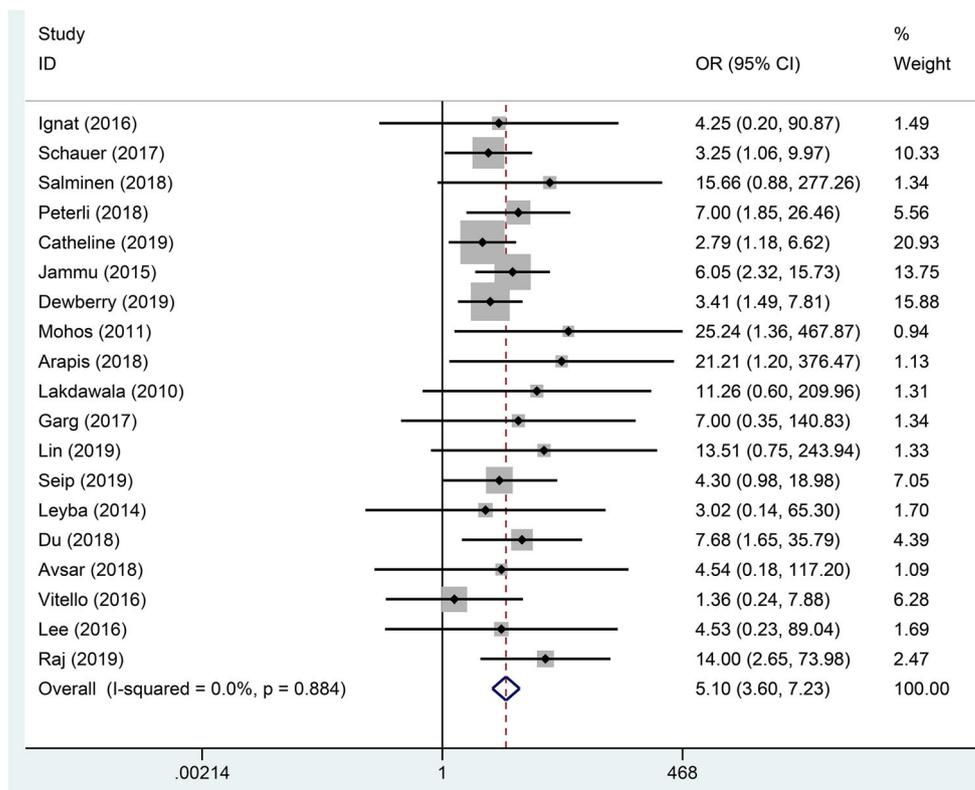
LSG was Converted to LRYGB Due to GERD

Since some patients suffered from severe GERD after LSG surgery, LRYGB was a common treatment method. This study analyzed relevant results and showed that 4 studies reported relevant outcomes. Of the 290 patients who underwent LSG, 18 were converted to LRYGB for severe reflux. The proportion of conversion was approximately 1.82–8.91%.

Sensitivity Analysis and Publication Bias

The Begg test revealed no publication bias and that LSG was associated with a higher risk of GERD after surgery than LRYGB ($p < 0.05$). Moreover, in the analysis of newly onset

Fig. 2 Forest plots showing newly onset or worsened GERD between LSG and LRYGB. GERD, gastroesophageal reflux disease; LSG, laparoscopic sleeve gastrectomy; LRYGB, laparoscopic Roux-en-Y gastric bypass



or worsened GERD after bariatric surgery, each study was excluded and the overall effect was consistent (Supplementary Figure 1).

Discussion

Obesity is one of the most important risk factors for GERD. With the sharp increase in the number of obese patients worldwide, the incidence of GERD has significantly increased [32]. Obesity has been reported to increase the incidence of GERD with an OR of 1.73 and Barrett’s esophagus with an OR of 1.24; esophageal adenocarcinoma is the most serious complication of GERD (OR, 2.45) [33, 34]. Laparoscopic anti-reflux surgery alone was considered not suitable for the treatment of GERD in obese patients. If the weight was not lost through this procedure, the efficacy of the treatment would be reduced; in other words, the recurrence rate of GERD after surgery was high [35]. Bariatric surgery is considered an effective treatment for obesity and related complications, but there is currently a lack of standard surgical procedures, especially for GERD.

Recently, LSG and LRYGB have been established as the most common methods of metabolic surgery that can improve GERD. However, surgery might lead to newly onset or worsened GERD. Therefore, for obese patients with GERD, it is necessary to carefully choose the surgical method. Yeung et al.

comprehensively analyzed 46 studies that included > 10,000 obese patients who underwent LSG. The results showed that the incidence of newly onset GERD after LSG was 23%, and 4% patients were converted to LRYGB due to the occurrence of GERD after LSG. However, that meta-analysis lacked a control group and had high heterogeneity; therefore, the results needed to be further confirmed. Some researchers believe that GERD can occur after LSG, but to a degree that is not serious [36, 37]. Furthermore, ambulatory 24-h pH monitoring was used to diagnose GERD, and its conclusions seemed more reliable.

In this study, 23 studies were included, and the results showed that LRYGB had a better effect on the treatment of GERD compared with LSG, regardless of the short-term or long-term results, although both surgeries had good effects. The mechanism of bariatric surgery for GERD is unclear. The hypothesis was mainly related to factors such as weight loss, reduction of intra-abdominal pressure, improvement of type-2 diabetes and peripheral nerve function, and repair of combined esophageal hiatus hernia [38–40]. Petersen et al. believed that lower esophageal sphincter pressure (LESP) could be increased independently in addition to weight reduction after LSG [41]. Gastric fundectomy, accelerated gastric emptying, and reduced gastric acid were also thought to improve GERD. The symptoms of GERD could reportedly be significantly improved after LSG, and the occurrence of newly onset GERD after surgery was very low. In addition, most cases of

Table 2 Subgroup analysis of newly onset or worsened GERD between LSG and LRYGB

	No. of studies	OR	95% CI	<i>p</i>	<i>I</i> ²	Effect-model
RCTs	5	3.99	2.24–7.12	< 0.001	0	Fixed
Observational studies	14	5.83	3.76–9.05	< 0.001	0	Fixed
Follow-up ≤ 3 years	11	5.00	2.98–8.38	< 0.001	0	Fixed
Follow-up > 3 years	8	5.20	3.25–8.34	< 0.001	0	Fixed

newly onset GERD were asymptomatic; therefore, the diagnosis of GERD needs to be standardized [42, 43]. Careful intraoperative procedures could reduce the incidence of GERD after LSG [44]. Conversely, some studies suggested that LSG might lead to inadequate treatment of GERD [45]. Burgerhart et al. reported that LESP decreased, the pH remained < 4, and the reflux time after LSG was prolonged [46].

Conversely, because LRYGB can divert the gastrointestinal tract and divert bile with a Roux loop of 100–150 cm, it reduces body weight and is beneficial for reflux. In theory, LRYGB has a better therapeutic effect on GERD. Symptoms of GERD reportedly improved by 90% with LRYGB, and reflux esophagitis decreased from 45 to 19% after surgery [47, 48]. However, there are still a few patients who develop GERD after LRYGB; the reason is unclear but could be related to the disruption of esophageal sphincter integrity. Disrupting the integrity of the esophageal sphincter due to dissection of the phrenoesophageal membrane for stapler placement close to the angle of His might play a role in GERD development [49]. Our study showed that the

improvement of GERD by LRYGB was significantly better than that by LSG, consistent with the results of most current studies. LRYGB can not only improve reflux but is more suitable for patients with Barrett's esophagus because it can prevent or reverse the progression of the disease. However, it must be emphasized that reflux contains both acidic and non-acidic components. The incidence of non-acid reflux might reportedly increase after LRYGB [41]. In clinical practice, GERD might not be adequately controlled by LRYGB in all patients. Besides, non-acid reflux is associated with Barrett's esophagus and esophageal adenocarcinoma [47, 50].

More importantly, this study also analyzed the incidence of newly onset or worsened GERD in patients who underwent LSG or LRYGB. We found that the rate of newly onset GERD after LSG was significantly higher than that after LRYGB. This result had low heterogeneity and high reliability. LSG could lead to newly onset GERD after surgery, thereby reducing patients' quality of life. Patients with LRYGB reportedly had a higher quality of life after surgery but did not indicate that the surgery was directly related to GERD [51, 52]. Oor et al. found that the hazard ratio of newly onset GERD after

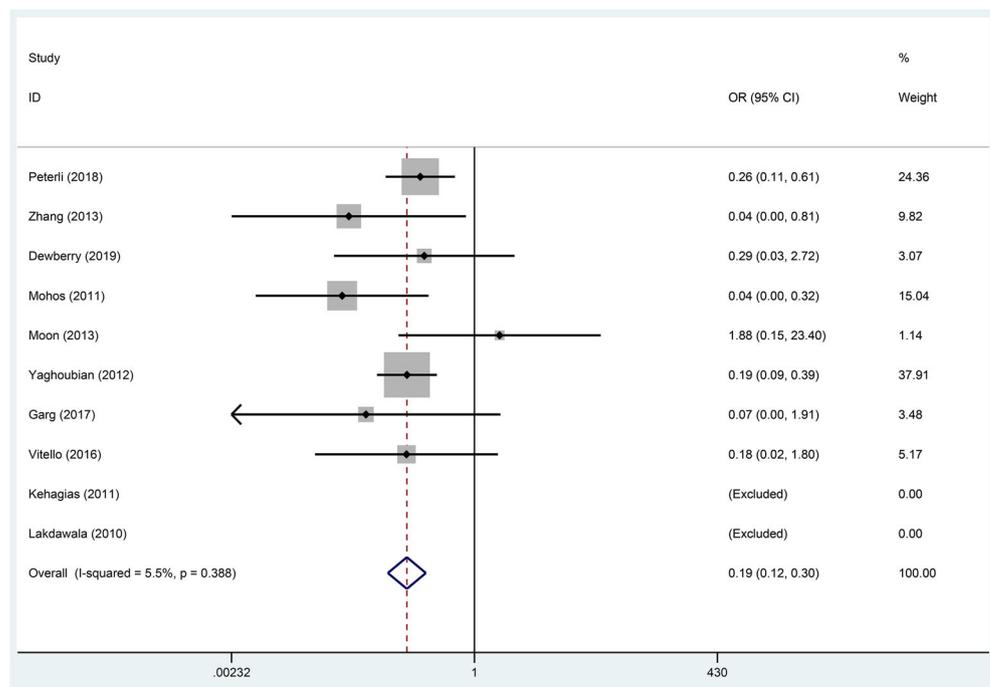
Fig. 3 Forest plots showing improvement of GERD between LSG and LRYGB. GERD, gastroesophageal reflux disease; LSG, laparoscopic sleeve gastrectomy; LRYGB, laparoscopic Roux-en-Y gastric bypass

Table 3 Subgroup analysis of improvement of GERD between LSG and LRYGB

	No. of studies	OR	95% CI	<i>p</i>	<i>I</i> ²	Effect-model
Observational studies	8	0.16	0.09–0.29	< 0.001	13%	Fixed
Follow-up ≤ 3 years	8	0.16	0.09–0.28	< 0.001	25%	Fixed
Follow-up > 3 years	2	0.26	0.12–0.59	0.001	0	Fixed

LSG was 4.3% compared with that before surgery, and the incidence was approximately 20% [53]. However, this result has high heterogeneity. Braghetto et al. thought the LESP drop was an important cause of GERD after LSG [54]. The destruction of the angle of His and the movement of the proximal sleeve at the level of the hiatus were the main causes of GERD [54, 55]. In addition, decreased postoperative gastric compliance and increased intragastric pressure were also involved in the occurrence of GERD. According to Himpens's study, the incidence of GERD decreased with a longer postoperative follow-up [56]. However, our subgroup analysis showed that this pooled effect remains unchanged in both RCTs and observational studies. It was noteworthy that, with a longer follow-up time, the differences in the incidence of GERD between the two surgical methods also persisted.

In addition, this study summarized 18 patients who were converted to LRYGB after LSG due to severe gastroesophageal reflux. Although the rate was low, it should still be considered. Studies by Yeung et al. showed that the proportion of reoperations after LSG was 4%, which was mainly due to severe reflux and weight loss failure [6, 57, 58]. Therefore, they believed that LRYGB was preferred for patients with extreme obesity or those with GERD. Presently, the diagnosis of GERD mostly depends on typical symptoms and drug efficacy; hence, there is a certain error. GERD was reportedly diagnosed based on symptoms and responses to drug therapy, with a sensitivity of 53.4% and specificity of 68.4% [43]. Therefore, there are limitations in the diagnosis of GERD. Moreover, the severity of symptoms was not necessarily related to the severity of reflux.

There were some limitations in this study. For the diagnosis of GERD, most studies included in this meta-analysis relied on symptoms and drug efficacy without an objective evaluation, which inevitably lead to inaccurate diagnosis of GERD. Follow-up times varied among studies, leading to differences in the incidence of GERD. Furthermore, this study included retrospective studies, which led to the existence of selection bias, recall bias, and other risks. It must be emphasized that GERD is a complex disease with multiple pathogenic factors and is not unique to obese patients. Again, obesity does not necessarily cause GERD. Bariatric surgery is not a 100% cure for GERD. Therefore, for obese GERD patients, the selection of surgery should still be cautious.

Despite these risks, this study was the first to comprehensively analyze the relationship between bariatric surgery and

GERD, providing clinical insights on surgical treatments for obese patients with GERD. This study adopts scientific and rigorous analytical methods to detect publication bias and sensitivity of the results. To avoid omitting negative results, the relevant literature should be searched as comprehensively as possible. Fortunately, the heterogeneity of the final analysis results was very low, and the results of this study were highly reliable. The results of this study need to be further validated by large multicenter randomized clinical trials.

Conclusion

Our study showed that LSG and LRYGB were effective in treating GERD for obese patients, with LRYGB showing a better effect. Compared with LSG, obese patients receiving LRYGB had a lower risk of newly onset or worsened GERD. A few patients were converted to LRYGB treatment due to severe reflux after LSG. Therefore, we recommend LRYGB as the preferred treatment for obese patients with GERD.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Statement This article does not contain any studies with human participants or animals performed by any of the authors.

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