

# World Journal of *Gastroenterology*

*World J Gastroenterol* 2020 February 28; 26(8): 777-882



**REVIEW**

- 777 Therapies to modulate gut microbiota: Past, present and future  
*Gupta A, Saha S, Khanna S*

**ORIGINAL ARTICLE****Basic Study**

- 789 Promising key genes associated with tumor microenvironments and prognosis of hepatocellular carcinoma  
*Pan L, Fang J, Chen MY, Zhai ST, Zhang B, Jiang ZY, Juengpanich S, Wang YF, Cai XJ*
- 804 Downregulation of orosomucoid 2 acts as a prognostic factor associated with cancer-promoting pathways in liver cancer  
*Zhu HZ, Zhou WJ, Wan YF, Ge K, Lu J, Jia CK*

**Retrospective Study**

- 818 Neoadjuvant chemotherapy *vs* upfront surgery for gastric signet ring cell carcinoma: A retrospective, propensity score-matched study  
*Li Y, Ma FH, Xue LY, Tian YT*
- 828 Haemoglobin, albumin, lymphocyte and platelet predicts postoperative survival in pancreatic cancer  
*Xu SS, Li S, Xu HX, Li H, Wu CT, Wang WQ, Gao HL, Jiang W, Zhang WH, Li TJ, Ni QX, Liu L, Yu XJ*
- 839 Prognostic value of preoperative weight loss-adjusted body mass index on survival after esophagectomy for esophageal squamous cell carcinoma  
*Zhang HL, Yang YS, Duan JN, Shang QX, He SL, Gu YM, Hu WP, Wang WP, Hu Y, Wang Y, Yuan Y, Chen LQ*

**Observational Study**

- 850 Diverting colostomy is an effective and reversible option for severe hemorrhagic radiation proctopathy  
*Yuan ZX, Qin QY, Zhu MM, Zhong QH, Fichera A, Wang H, Wang HM, Huang XY, Cao WT, Zhao YB, Wang L, Ma TH*

**META-ANALYSIS**

- 865 Surgical outcome of laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass for resolution of type 2 diabetes mellitus: A systematic review and meta-analysis  
*Guraya SY, Strate T*

**CASE REPORT**

- 877 Diagnosis and management of a solitary colorectal juvenile polyp in an adult during follow-up for ulcerative colitis: A case report  
*Chen YW, Tu JF, Shen WJ, Chen WY, Dong J*

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The WJG is now indexed in Current Contents®/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central, and Scopus. The 2019 edition of Journal Citation Report® cites the 2018 impact factor for WJG as 3.411 (5-year impact factor: 3.579), ranking WJG as 35<sup>th</sup> among 84 journals in gastroenterology and hepatology (quartile in category Q2). CiteScore (2018): 3.43.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Responsible Electronic Editor: *Yan-Liang Zhang*

Proofing Production Department Director: *Yun-Xiaojuan Wu*

**NAME OF JOURNAL**

*World Journal of Gastroenterology*

**ISSN**

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

**LAUNCH DATE**

October 1, 1995

**FREQUENCY**

Weekly

**EDITORS-IN-CHIEF**

Subrata Ghosh, Andrzej S Tarnawski

**EDITORIAL BOARD MEMBERS**

<http://www.wjgnet.com/1007-9327/editorialboard.htm>

**EDITORIAL OFFICE**

Ze-Mao Gong, Director

**PUBLICATION DATE**

February 28, 2020

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**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjgnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

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## Surgical outcome of laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass for resolution of type 2 diabetes mellitus: A systematic review and meta-analysis

Salman Yousuf Guraya, Tim Strate

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**Author contributions:** Guraya SY designed the research, performed literature search, systematic review, meta-analysis and prepared first and final draft of the article; Strate T reviewed the initial and final results of literature search and contributed in data selection; Both authors approved the final draft.

**Conflict-of-interest statement:** The authors deny any conflicts of interest.

**PRISMA 2009 Checklist statement:** The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

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**Manuscript source:** Unsolicited manuscript

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### Abstract

#### BACKGROUND

Bariatric procedures are considered superior to medical therapies in managing type 2 diabetes mellitus (T2DM). Laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic sleeve gastrectomy (LSG) are the most commonly used procedures for weight loss and comorbidity resolution worldwide. However, it is not yet known whether the degree of T2DM is influenced by the choice of bariatric procedure.

#### AIM

To quantitatively compare T2DM resolution over 1-5 years follow-up by LRYGB and LSG in morbidly obese patients.

#### METHODS

We searched the selected databases for full-text English language clinical studies that compared the effectiveness of LRYGB and LSG for T2DM resolution. Review manager 5.3 was used for data analysis, and the overall effect summary was represented in a forest plot.

#### RESULTS

From 1,650 titles retrieved by an initial search, we selected nine studies for this research. We found insignificant differences for T2DM resolution by LRYGB and LSG, with an odds ratio of 0.93 (95%CI: 0.64-1.35, Z statistics = 0.38,  $P = 0.71$ ). Additionally, subset analyses for T2DM resolution showed insignificant differences after 24 mo ( $\chi^2 = 1.24$ ,  $df = 4$ ,  $P = 0.87$ , overall Z effect = 0.23), 36 mo ( $\chi^2 = 0.41$ ,  $df = 2$ ,  $P = 0.81$ , overall Z effect = 0.51), and 60 mo ( $\chi^2 = 4.75$ ,  $df = 3$ ,  $P = 0.19$ , overall Z effect = 1.20) by LRYGB and LSG. This study reports a T2DM remission rate of 82.3% by LRYGB and 80.7% by LSG.

**Received:** September 24, 2019  
**Peer-review started:** September 24, 2019  
**First decision:** November 27, 2019  
**Revised:** December 23, 2019  
**Accepted:** January 19, 2020  
**Article in press:** January 19, 2020  
**Published online:** February 28, 2020

**P-Reviewer:** Das U, Emile S, Saligram S  
**S-Editor:** Zhou JJ  
**L-Editor:** Filipodia  
**E-Editor:** Zhang YL



## CONCLUSION

This study reports similar T2DM resolution rates by both LRYGB and LSG during 1-5 years of follow-up. However, long-term follow-up of 10 years is needed to further substantiate these findings.

**Key words:** Morbid obesity; Type 2 diabetes mellitus; Laparoscopic sleeve gastrectomy; Laparoscopic Roux-en-Y gastric bypass

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**Core tip:** Based on our research findings, both laparoscopic Roux-en-Y gastric bypass and laparoscopic sleeve gastrectomy can be used for type 2 diabetes mellitus resolution in morbidly obese patients.

**Citation:** Guraya SY, Strate T. Surgical outcome of laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass for resolution of type 2 diabetes mellitus: A systematic review and meta-analysis. *World J Gastroenterol* 2020; 26(8): 865-876  
**URL:** <https://www.wjgnet.com/1007-9327/full/v26/i8/865.htm>  
**DOI:** <https://dx.doi.org/10.3748/wjg.v26.i8.865>

## INTRODUCTION

Bariatric surgery is effective in treating morbid obesity, and in the resolution of its associated co-morbidities including metabolic syndrome, hyperlipidemia, type 2 diabetes mellitus (T2DM), sleep apnea, osteoarthritis, and psychological disorders<sup>[1]</sup>. Out of a host of surgical remedies for morbid obesity, laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic sleeve gastrectomy (LSG) remain the most commonly performed bariatric surgery procedures worldwide<sup>[2]</sup>. Both LRYGB and LSG have been shown to be safe, feasible and effective in accomplishing excess weight loss and resolution of co-morbidities<sup>[3,4]</sup>. Literature has shown a rapid escalation in the prevalence of T2DM and its associate complications, particularly cardiovascular<sup>[5]</sup>, gallstones<sup>[6]</sup>, peripheral arterial system and foot ulcers<sup>[7,8]</sup>, stroke<sup>[9]</sup>, and colorectal cancer<sup>[10]</sup>. In this perspective, bariatric procedures such as LRYGB and LSG have been successfully used for the resolution of T2DM and its comorbidities<sup>[11]</sup>.

The mechanisms of T2DM resolution by LRYGB and LSG are largely unknown. It has been postulated that changes in gastrointestinal hormone secretions following LRYGB account for the resolution of T2DM, as the duodenum and upper jejunum are bypassed for direct delivery of nutrients to the midgut<sup>[12]</sup>. In contrast, weight loss induced by LSG is mediated by a primarily restrictive mechanism that leads to the simultaneous resolution of T2DM.

Literature has reported a T2DM resolution rate of 81.2% by LRYGB and 80.9% by LSG<sup>[13]</sup>. However, the selection of weight loss procedure is influenced by a wealth of factors. Praveenrai *et al*<sup>[14]</sup> proposed that the choice of bariatric surgery procedure is primarily driven by therapy goals (weight loss or glycemic control), associated gastro-esophageal reflux or nutritional deficiencies, patient preferences and expertise of the surgeon. Generally, LRYGB is recommended for patients with long-standing, refractory T2DM with low serum C peptides, and LSG for other patients with morbid obesity. Interestingly, the majority of patients prefer LSG over LRYGB for the weight loss and resolution of associated metabolic disorders. In a double blind randomized clinical trial by Lee *et al*<sup>[15]</sup>, the authors investigated T2DM resolution by LRYGB and LSG (fasting glucose 126 mg/dL and HbA1c 6.5% without anti-glycemic treatment)<sup>[15]</sup>. The study concluded that the patients in the LRYGB group had greater weight loss, a lower waist circumference, and had rapid T2DM regression and lipid control compared to LSG. On the other hand, Vidal *et al*<sup>[16]</sup> showed that LSG was as effective as LRYGB in securing the resolution of T2DM and metabolic syndrome at a 12-mo follow-up after surgery. Similarly, in a systematic review of randomized clinical trials by Osland *et al*<sup>[17]</sup>, the authors reported significant remission of T2DM by both LRYGB as well as by LSG across all stages of follow-up.

There seems to be no standard consensus about the superiority of LRYGB or LSG in achieving the resolution of T2DM. The available data are scarce, and very few studies have rigorously compared the outcome of LRYGB and LSG for attaining remission of



T2DM in obese patients. This systematic review and meta-analysis provides quantitative comparison of the effectiveness of LRYGB and LSG for the resolution of T2DM in morbidly obese patients.

## MATERIALS AND METHODS

### Literature search

In January 2019, this systematic review and meta-analysis was performed using the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)<sup>[18]</sup>. The Medical Subject Headings (MeSH) terms used for systematic review included: Morbid obesity, type 2 diabetes mellitus, laparoscopic sleeve gastrectomy, laparoscopic Roux-en-Y gastric bypass, and fasting blood glucose. The databases of PubMed, Ovid, Wiley online library, Cochrane library, CINAHL, ISI Web of knowledge, ScienceDirect, and EBSCO were searched for full-text English original clinical studies published from Jan 2013 to Jan 2018. The original studies that compared the effectiveness of LSG and LRYG for the resolution of T2DM in morbidly obese patients during 1-5 years of follow-up were included in this search. The remission of T2DM was considered when HbA1c < 6.0% without anti-diabetic therapy was achieved by bariatric procedures<sup>[19]</sup>. As defined by review articles, editorials, expert opinions, commentaries, and short communications were excluded. The original studies with incomplete data as mean  $\pm$  SD (for continuous outcome), number, percentage (for dichotomous outcome) or an average follow-up of less than one year were excluded. In addition, research articles that attempted to determine surgical outcomes of LSG and LRYGB in patients with a body BMI < 27 kg/m<sup>2</sup> or < 18- or > 65-years-old were excluded. The indicators of glycemic control were HbA1C and fasting blood glucose levels. Finally, research showing combined data of revision or conversion bariatric procedures was not included in this study.

### Data extraction and synthesis

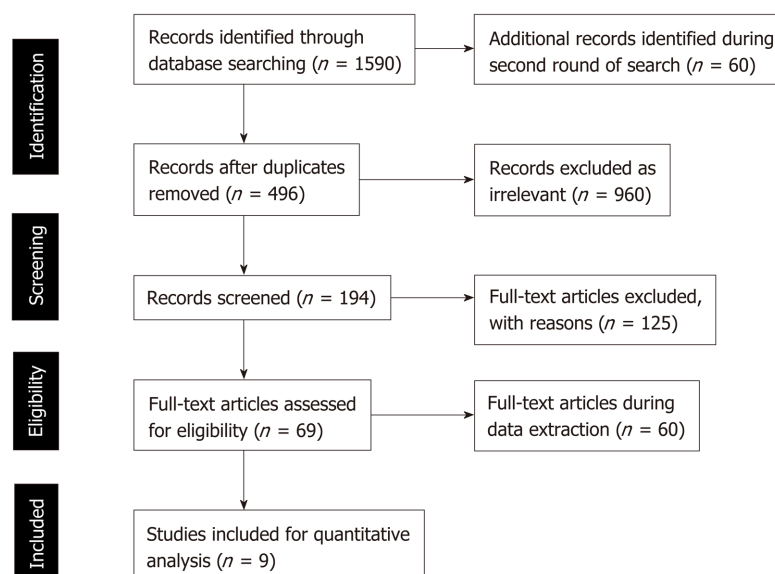
During two rounds of searches in the selected databases, 1650 studies were retrieved. Review of the searched titles showed 496 duplicate and 960 irrelevant titles that were excluded from further literature review. At the next stage of analysis of the 194 titles, another 125 articles were excluded, as the contents and study outcomes did not match our systematic review primary outcomes. As many as 69 articles were found to be relevant, as they compared the effectiveness of LSG and LRYGB for T2DM resolution. However, during full text review of these 69 articles, 60 studies were further excluded, as they contained incomplete data and inconsistent findings. Finally, a total of nine relevant studies were selected in this meta-analysis (Figure 1).

### Quality assurance

Two independent researchers (Salman Yousuf Guraya and Tim Strate) searched, analyzed, reviewed the retrieved titles and full-text articles for suitability and study representativeness. Using the Cochrane Collaboration tool, we found some element of selection bias that was reflected by the blinding of participants and personnel preferences (performance bias)<sup>[10,20]</sup>. The risk of bias and conflict of interest were eliminated by discussions and by reaching a general consensus.

### Quantitative analysis of data

Review Manager 5.3 software, developed by Cochrane Library, was used for the quantitative analysis of data from the selected studies in this meta-analysis<sup>[21]</sup>. The findings of the meta-analysis were graphed on a forest plot, which quantitatively demonstrates the consistency and reliability of results. In a forest plot, the effect size of each study is computed as an outcome measure, and pooled effect summary is calculated to determine heterogeneity across selected studies. Statistically, Q tests reflect heterogeneity in the selected studies using the null hypothesis that all studies are identical. In this meta-analysis, the I squared ( $I^2$ ) statistical analysis was used to validate heterogeneity in percentage terms<sup>[20]</sup>. In the case of low heterogeneity ( $P > 0.10$ ,  $I^2 < 50\%$ ), a fixed effects model is recommended. On the other hand, a random effects model is employed in the case of higher heterogeneity ( $P < 0.10$  or  $I^2 > 50\%$ ). The Tau squared ( $Tau^2$ ) test is applied to estimate variance in the calculated data using the random effects model. We estimated publication bias by visual inspection of the funnel plot, and the level of significance in this study was considered as 5% ( $P < 0.05$ ).



**Figure 1** Schematic algorithm for selection of studies in the meta-analysis for comparison of effectiveness of type 2 diabetes mellitus resolution by laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass.

## RESULTS

A close comparative analysis of the resolution of T2DM by LSG and LRYGB is illustrated in [Figure 2](#). We found that the Cochrane  $Q$  ( $\chi^2 = 154.43$ ) test was significant at 5% ( $P < 0.05$ ). This rejected the null hypothesis that all studies were identical. Due to substantial heterogeneity ( $I^2 = 88\%$ ), a random effect model was deemed necessary. In our meta-analysis, the forest plot generated by Review Manager 5.3 for the comparison of resolution of T2DM by LSG and LRYGB showed insignificant differences for T2DM resolution by LSG and LRYGB, with an odds ratio of 0.93 (95%CI: 0.64-1.35, Z statistics = 0.38,  $P = 0.71$ ), as shown in [Figure 3](#). [Figure 4](#) includes a forest plot that compares the resolution of T2DM by LSG and LRYGB after 24, 36 and 60 mo. Insignificant differences are reported between the two weight loss surgical procedures. The scientific evidence of symmetry and homogeneity of the selected articles for effectiveness of LSG and LRYGB in resolution of T2DM is demonstrated in the funnel plot in [Figure 5](#). The remission rate of T2DM by LRYGB and LSG is estimated to be 82.3% and 80.7%, respectively. Characteristics of the selected studies, including the complete citation of articles, study design, number of patients at the time of surgery, and key outcomes by both LSG and LRYGB are shown in [Table 1](#).

## DISCUSSION

Our systematic review and meta-analysis showed insignificant differences in T2DM resolution by LSG and LRYGB. Additionally, a deeper analysis of subgroups also demonstrated insignificant differences after 24 mo ( $\chi^2 = 1.24$ ,  $df = 4$ ,  $P = 0.87$ , overall Z effect = 0.23), 36 mo ( $\chi^2 = 0.41$ ,  $df = 2$ ,  $P = 0.81$ , overall Z effect = 0.51), and 60 mo ( $\chi^2 = 4.75$ ,  $df = 3$ ,  $P = 0.19$ , overall Z effect = 1.20) in T2DM resolution by LSG and LRYGB. In the absence of a clear consensus about the superiority of LRYGB over LSG for T2DM resolution, the findings of our study provide landmark evidence for the management of morbid obesity and its comorbidities.

In the clinical trial by Yang *et al*<sup>[22]</sup>, the researchers followed up with patients after LRYGB and LSG for 3 years, and have reported similar T2DM remission rates. Similar results have been reported elsewhere<sup>[23,24]</sup>. In the same study, complete T2DM resolution rates, as defined by HbA1c  $< 6.0\%$  without anti-diabetic therapy, were 78.6% in the LSG group and 85.2% in the LRYGB group. These findings are in agreement with the previously published prospective clinical studies on patients with a BMI  $> 35$  kg/m<sup>2</sup><sup>[25,26]</sup>. However, in the randomized controlled trial by Lee *et al*<sup>[15]</sup>, the investigators argued that LRYGB was superior in achieving better blood glucose control than LSG at 1 and 5 years after surgery on patients with a BMI of 25-35 kg/m<sup>2</sup>. Nonetheless, our systematic review and meta-analysis could not find superiority of LRYGB or LSG in T2DM throughout 1-5 years of follow-up.

In the study by Perrone *et al*<sup>[27]</sup>, the authors compared long-term results on weight

**Table 1 Characteristics of the nine selected studies comparing type 2 diabetes mellitus resolution by laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass in this study**

Ref.	Country	Study type	Sample size		Key findings
			LSG	LRYGB	
Du <i>et al</i> <sup>[11]</sup> , 2017	China	Randomized clinical trial	19	74	Overall remission rate achieved with LRYGB and LSG was 75.9% at 1 yr and 56.4% at 3 yr  Safety profile, T2DM resolution and other morbid obesity-related comorbidities by both procedures are comparable
Garg <i>et al</i> <sup>[42]</sup> , 2017	India	Retrospective clinical	40	40	The median duration of T2DM was higher in LRYGB than LSG (2.2 <i>vs</i> 1.8), respectively  Both LRYGB and LSG showed significant but similar improvement in T2DM remission
Park and Kim <sup>[43]</sup> , 2015	South Korea	Retrospective Cohort Study	104	236	The study found comparable results with insignificant differences between LRYGB and LSG
Perrone <i>et al</i> <sup>[27]</sup> , 2016	Italy	Prospective clinical trials	162	142	LSG is more effective in obese men than in women for excess weight loss. However, there is no difference in terms of the remission of comorbidities  LRYGB showed similar findings in both genders for excess weight loss and comorbidity resolution, including T2DM
Perrone <i>et al</i> <sup>[44]</sup> , 2017	Italy	Prospective clinical trial	162	142	LRYGB showed better T2DM resolution rate in the short-term  Neither LRYGB nor LSG showed a significant difference in T2DM remission in the long-term
Praveenraj <i>et al</i> <sup>[14]</sup> , 2016	India	Retrospective clinical trial	54	32	LRYGB showed better surgical outcomes than LSG in patients > 50 yr  LSG had shorter operative times and shorter hospital stays
Peterli <i>et al</i> <sup>[45]</sup> , 2018	Finland	The SLEEVEPASS multicenter, randomized clinical trial	120	120	Complete or partial remission of T2DM was reported in 37% after LSG and in 45% LRYGB. No significant difference in terms of T2DM resolution is reported between LRYGB and LSG
Wallenius <i>et al</i> <sup>[29]</sup> , 2018	Sweden	Prospective clinical trial	15	18	There was a similar decrease in post-op fasting blood glucose in both the LRYGB and LSG groups



Yang <i>et al</i> <sup>[22]</sup> , 2015	China	Randomized clinical study	22	23	LYRYGB and LSG showed similar outcomes in glycemic control, with insignificant differences in short- and mid-term follow-up
					LSG and LRYGB had comparable effects on T2DM remission in the Chinese study cohort with a BMI of 28-35 kg/m <sup>2</sup>

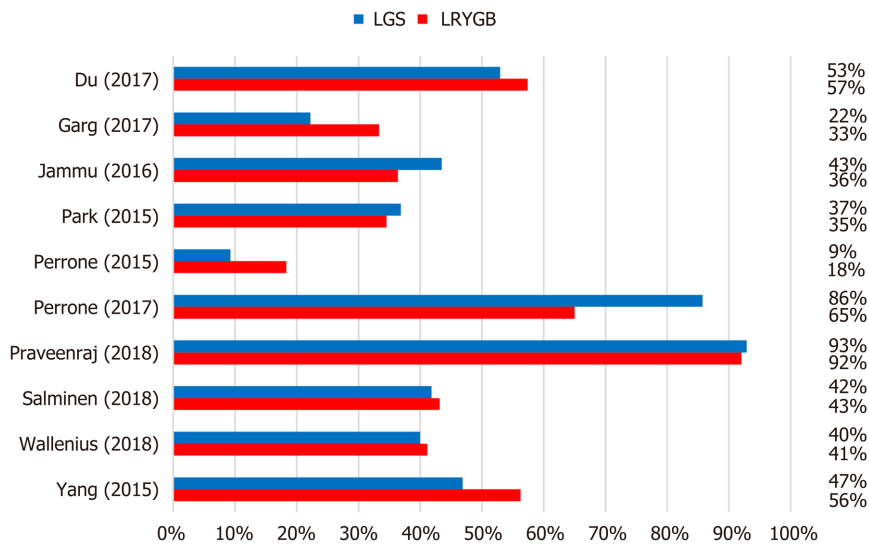
LSG: Laparoscopic sleeve gastric bypass; LRYGB: Laparoscopic Roux-en-Y gastric bypass; T2DM: Type 2 diabetes mellitus.

loss and comorbidity resolution for LRYGB and LSG on a cohort of 304 consecutive patients. Though LSG was more effective in the percentage of excess weight loss at 180 d and at 1 year of follow-up, however, LRYGB and LSG showed similar results at 5 years of follow-up; 72.34 *vs* 70.26, respectively. Generally, LRYGB was shown to be more effective in T2DM remission than LSG. These findings reflect the lack of a gold standard bariatric procedure that can help achieve excess weight loss and comorbidity resolution<sup>[28]</sup>. The study by Wallenius *et al*<sup>[29]</sup> compared early weight-independent and later weight-dependent influence by LRYGB and LSG on glycemic control. Initially, there was a similar drop in fasting blood glucose levels in both the LRYGB and LSG groups;  $8.1 \pm 0.6$  mmol/L *vs*  $8.2 \pm 0.4$  mmol/L, 2 d;  $7.8 \pm 0.5$  mmol/L *vs*  $7.4 \pm 0.3$  mmol/L, 21 d;  $6.6 \pm 0.4$  mmol/L *vs*  $6.6 \pm 0.3$  mmol/L, respectively. This study reported similar effects on glycemic controls by both surgical procedures. On the other hand, the study by Gray *et al*<sup>[30]</sup> reported a greater improvement in T2DM, hypertension, hyperlipidemia, and gastroesophageal reflux disease by LRYGB over LSG during a median follow-up of 39 mo. From a different perspective, some investigators have recommended LRYGB as a gold standard for effective weight loss and resolution of comorbidities, and to keep LSG as an attractive substitute<sup>[31,32]</sup>. Unfortunately, as of today, the literature is divided on this argument, and we need more concrete evidence to validate these observations.

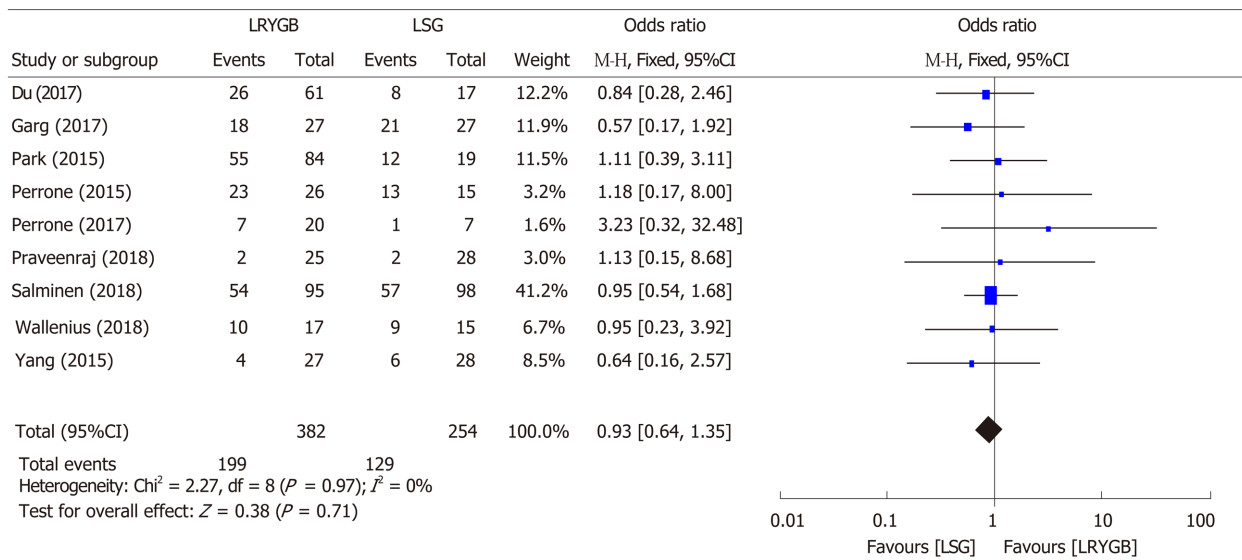
By and large, the mechanisms of T2DM remission by LRYGB and LSG are unclear, although several hypotheses exist. The literature has shown a greater inclination toward LSG as an anti-diabetic surgical remedy, which induces early glucose homeostasis similar to that of LRYGB<sup>[33]</sup>. In an interesting study by Nannipier *et al*<sup>[34]</sup>, the authors investigated the mechanism for T2DM remission by GI hormones, and found similar results from LRYGB and LSG. The study concluded that glucagon-like peptide (GLP-1) and polypeptide YY (PYY) were the key predators of glucose homeostasis in the post-operative follow-up. Though the exact mechanisms underlying better glucose homeostasis following LSG is uncertain, a fall in ghrelin levels and unexpected changes in serum levels of distal intestinal hormones (GLP-1, GLP-2 and PYY) are considered to play some role. Furthermore, insulin resistance is decreased and incretin hormones levels are substantially elevated. On the other hand, since LRYGB bypasses the proximal intestine, a host of neurohormonal changes ensue, particularly low insulin resistance, as well as changes in ghrelin, GLP-1, GLP-2 and PYY level<sup>[35]</sup>. On a similar note, Peterli *et al*<sup>[36]</sup> found that 1 year after operation, post-prandial serum cholecystokinin levels increased less in the LRYGB than in the LSG group. The authors have argued that bypassing the foregut is not the sole underlying reason for improved glucose homeostasis.

LSG has several advantages over LRYGB: Easier to perform, preserves pylorus and antrum with less chance of dumping syndrome, no risk of internal herniation, and decreased risk of nutritional deficiencies<sup>[37,38]</sup>. In terms of its shorter learning curve, LSG is gaining popularity over LRYGB among bariatric surgeons. The results of our meta-analysis would further strengthen the value of LSG in achieving weight loss and remission of comorbidities, particularly T2DM due to its comparable profile with LRYGB. Additionally, improving surgeons skills<sup>[39]</sup> and adhering to professional codes tend to lead to better surgical outcomes<sup>[40]</sup>.

In conclusion, this study reports similar T2DM resolution rates by both LRYGB and LSG during 1 to 5 years of follow-up. However, long-term follow-up of 10 years is needed to further endorse these findings.

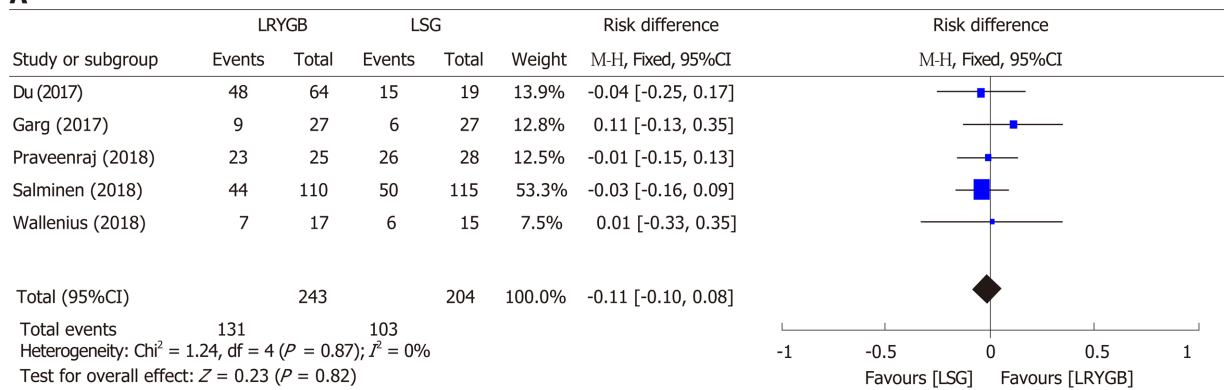


**Figure 2** Comparison of the resolution of type 2 diabetes mellitus between laparoscopic sleeve gastrectomy and laparoscopic Roux-en-Y gastric bypass. LSG: Laparoscopic sleeve gastrectomy; LRYGB: Laparoscopic Roux-en-Y gastric bypass; T2DM: Type 2 diabetes mellitus.

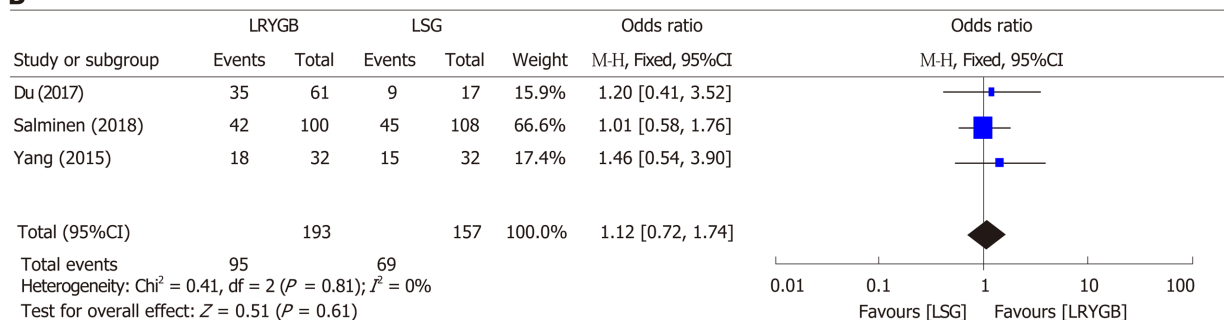


**Figure 3** Forest plot comparing the resolution of type 2 diabetes mellitus by laparoscopic sleeve gastrectomy and laparoscopic Roux-en-Y gastric bypass. LSG: Laparoscopic sleeve gastrectomy; LRYGB: Laparoscopic Roux-en-Y gastric bypass; T2DM: Type 2 diabetes mellitus.

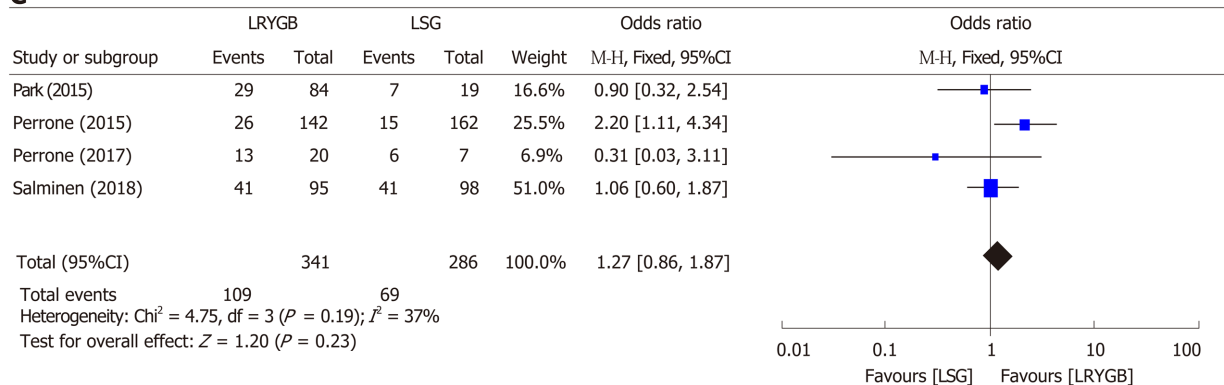
**A**



**B**



**C**



**Figure 4 Forest plots comparing the resolution of type 2 diabetes mellitus by laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass after 24 mo (A), 36 mo (B), and 60 mo (C). LSG: Laparoscopic sleeve gastrectomy; LRYGB: Laparoscopic Roux-en-Y gastric bypass; T2DM: Type 2 diabetes mellitus.**

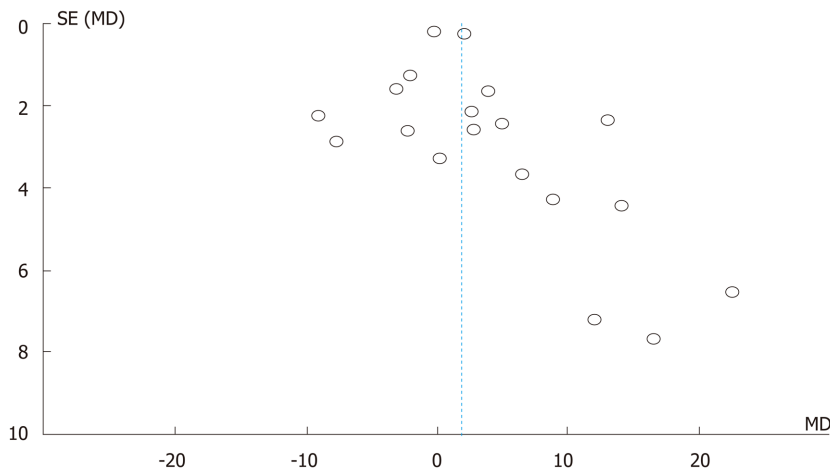


Figure 5 Funnel plot illustrating the symmetry of selected studies for type 2 diabetes mellitus resolution by laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass. LSG: Laparoscopic sleeve gastrectomy; LRYGB: Laparoscopic Roux-en-Y gastric bypass; T2DM: Type 2 diabetes mellitus.

## ARTICLE HIGHLIGHTS

### Research background

There is a staggering rise in the incidence of obesity worldwide. A sedentary lifestyle, unhealthy food, and multiple comorbidities such as Type 2 diabetes mellitus (T2DM), hypertension and hyperlipidemia are major risk factors for obesity. In order to curtail the epidemic of obesity, a host of treatment strategies are offered, including lifestyle change, dietary consultations, medications, as well as surgical therapies. Of these, surgical remedies carry great promise in achieving effective weight loss and the resolution of comorbidities. Generally, bariatric procedures are considered superior to medical therapies in treating obesity-related T2DM. Though Laparoscopic Roux-en-Y gastric bypass (LRYGB) and Laparoscopic sleeve gastric bypass (LSG) are the most popular bariatric surgical procedures worldwide, there is no consensus about the superiority of one procedure over the other in terms of the resolution of obesity-related T2DM.

### Research motivation

This study determines the effectiveness of LSG and LRYGB for treating obesity-related T2DM. Short-, mid- and long-term follow-up results after bariatric surgery were analyzed. The literature is divided about the estimated outcomes by various bariatric surgical procedures in achieving excess percentage weight loss and T2DM. This study quantitatively compares the resolution of T2DM by LSG and LRYGB.

### Research objectives

We conducted the current study to quantitatively compare the impact of LSG and LRYGB in T2DM resolution over 1 to 5 years post-surgery follow-up.

### Research methods

We conducted a literature search by using selected keywords in pre-defined databases for full-text English language clinical studies. This study compared short-, mid- and long-term outcomes of T2DM resolution by LRYGB and LSG. The data from all selected studies were analyzed by Review Manager® 5.3. Forest plots were generated for overall effect summaries. The homogeneity of the selected studies was determined by funnel plots and, finally, the findings were interpreted and compared with published reports.

### Research results

A total of 1650 titles were retrieved from the selected databases. Using PRISMA guidelines, both investigators shortlisted and then finally selected nine studies for further analysis. We report a T2DM remission rate of 82.3% by LRYGB and 80.7% by LSG. This study shows insignificant differences for T2DM resolution by LRYGB and LSG, with an odds ratio of 0.93 (95%CI: 0.64-1.35, Z statistics = 0.38,  $P = 0.71$ ). Deeper analysis of subsets for T2DM resolution for short-, mid- and long-term follow-up showed similar results at 24 mo ( $\chi^2 = 1.24$ ,  $df = 4$ ,  $P = 0.87$ , overall Z effect = 0.23), 36 mo ( $\chi^2 = 0.41$ ,  $df = 2$ ,  $P = 0.81$ , overall Z effect = 0.51), and 60 mo ( $\chi^2 = 4.75$ ,  $df = 3$ ,  $P = 0.19$ , overall Z effect = 1.20).

### Research conclusions

This study provides comparative quantitative evidence regarding the role of LSG and LRYGB in treating obesity-related T2DM. Technically, compared to LRYGB, LSG is much easier to perform, and takes significantly shorter operative time. Being a relatively easier bariatric surgical procedure, LSG may be favored in achieving T2DM resolution. However, before we can reach a

consensus, the results of long-term follow-up over 10 years should be quantitatively analyzed. By and large, this study implies a comparable achievement in T2DM resolution by both procedures up to 5 years follow-up.

### Research perspectives

LSG and LRYGB, although quite different bariatric surgical procedures, achieve similar T2DM resolution up to 5 years post-surgery. Future research should investigate different neurohormonal mechanisms that lead to a common goal of T2DM resolution by both surgical procedures.

## ACKNOWLEDGEMENTS

We acknowledge the support in literature review and meta-analysis provided by Mr B Bilal, Associate Professor Hubei Centre for Accounting Development Research School of Accountancy Hubei University of Economics, Wuhan, China.

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