Laparoscopic Sleeve Gastrectomy Versus Laparoscopic Roux-en-Y Gastric Bypass

A Systematic Review and Meta-analysis of Weight Loss, Comorbidities, and Biochemical Outcomes From Randomized Controlled Trials

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Objective: The aim of this study was to compare weight loss, obesity-related comorbidities, and biochemical outcomes of LSG versus LRYGB through a meta-analysis of randomized controlled trials (RCTs).

Summary of Background Data: LSG and LRYGB are the 2 most commonly performed bariatric surgeries for the treatment of obesity. The comparative outcomes of the 2 surgeries is a topic of ongoing debate and medium-term outcomes remain uncertain.

Methods: A search for RCTs comparing LRYGB versus LSG was conducted. Pooled outcomes between 2 procedures were compared using pairwise random-effects meta-analysis at 1, 3, and 5-year follow-up time points. Grading of recommendations, assessment, development, and evaluation was used to assess certainty of evidence.

Results: Thirty-three studies involving 2475 patients were included. LRYGB resulted in greater loss of body mass index compared to LSG at 1 year [mean difference $-1.25\,kg/m^2$, 95% confidence interval (CI) -2.01 to -0.49, $P = 0.001$; moderate certainty of evidence] which persisted at 3 years, but there was insufficient evidence at 5 years. Resolution of dyslipidemia was higher for LRYGB than LSG at 1 year (risk ratio 0.58, 95% CI 0.46–0.73, $P < 0.001$; moderate certainty of evidence) and 5 years (risk ratio 0.68, 95%CI 0.46–0.99, $P = 0.04$; low certainty of evidence). There was no difference between LRYGB and LSG for remission of type 2 diabetes, hypertension, and hemoglobin A1c, fasting insulin, homeostatic model assessment of insulin resistance, high-density lipoprotein, and the rate of 30-day major and minor complications.

Conclusions: There are insufficient data from RCTs to draw any conclusions regarding the long-term comparative effectiveness beyond 3 years between LRYGB and LSG.

Keywords: bariatric surgery, gastric bypass, meta-analysis, sleeve gastrectomy, systematic review

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Obesity has become a growing health issue worldwide and is associated with comorbidities including type 2 diabetes mellitus (T2DM), cardiovascular disease, and overall rates of cancer.[1] Bariatric surgery is the most effective and long-lasting treatment for patients with obesity, capable of resolving comorbidities, decreasing mortality, and improving quality of life.[2] Laparoscopic Roux-en-Y gastric bypass (LRYGB) has traditionally been considered the gold standard in bariatric surgery because it provides substantial, long-term weight loss and remission of comorbidities.[3] However, in recent years, laparoscopic sleeve gastrectomy (LSG) has experienced a rapid surge in popularity due to its effectiveness in achieving weight loss and remission of comorbidities, and its less technically intensive procedure and the belief that it causes fewer complications.[4] In 2016, LSG was the most commonly performed bariatric surgery in the US and worldwide, making up 53.6% of operations compared to the 30.1% of RYGB.[1–6]

Despite the recent change in trend from LRYGB to LSG, evidence comparing LRYGB to LSG has lagged behind, especially in medium- and long-term outcomes. Although short-term clinical and metabolic data were promising for LSG, only a few randomized controlled trials (RCTs) directly compared LSG to LRYGB and those that did typically had small sample sizes, or short-term follow-ups, sparking debate on the appropriateness of LSG in replacing LRYGB.[7] In response to the existing uncertainty on weight loss achieved by LSG compared to LRYGB, the American Society for Metabolic and Bariatric Surgery (ASMBS) produced an updated position statement in 2017.[3] The statement concluded that while there was no reliable conclusion regarding which bariatric operation produces the greatest weight loss early after surgery, evidence appeared to support LRYGB as producing greater percent excess weight loss (%EWL) compared to LSG after the first year.[3]

Beyond the uncertainty between LSG and LRYGB for weight loss, meta-analyses comparing LSG to LRYGB for improvements in co-morbidities have also differed in results, reporting both remission and no change in T2DM and hypertension.[8,9] To address the vigorous and ongoing debate comparing LSG and LRYGB, 2 major RCTs, The Swiss Multicenter Bypass or Sleeve Study (SM-BOSS) and Finnish Sleeve vs. Bypass (SLEEVEPASS) recently provided new evidence comparing 5-years outcomes after LSG and LRYGB.[10,11] Nonetheless, while SM-BOSS found no significant differences in percent body mass index (BMI) loss, SLEEVEPASS did find greater %EWL in the LRYGB group than the LSG group, although this difference was not clinically significant. The 2 trials also came to different conclusions on hypertension remission, and metabolic differences in LSG compared to LRYGB.

Given the considerable number of high-quality studies with medium-term follow-ups that have accumulated in recent years, and the differing conclusions proposed by RCTs, this systematic review and meta-analysis aim to compare LSG and LRYGB on weight loss, comorbidities, and complications.

METHODS

Eligibility Criteria

We included RCTs that compared LRYGB versus LSG in patients with severe obesity (BMI $>40\,kg/m^2$ or $>35\,kg/m^2$ with

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obesity-related comorbidities). Exclusion criteria were (1) non-RCTs (cohort studies, case series and reports, reviews, letters, and editorials) (2) studies which did not compare LRYGB versus LSG (3) studies with no relevant primary or secondary outcomes of interest (4) non-human studies (5) studies with less than 10 eligible patients. When the results of a single trial were reported for multiple time points across more than 1 publication, we collected the most complete data for every follow-up time point reported across all publications.

Outcomes Assessed

Primary outcome was changed in BMI at 1, 3, and 5 years after bariatric surgery. Secondary outcomes were: (1) remission of comorbidities including T2DM, hypertension, and dyslipidemia at 1, 3, and 5 years after surgery (2) changes in biochemical outcomes including hemoglobin A1c (HbA1c) (%), fasting glucose (mg/dL), fasting insulin (uIU/mL), homeostatic model assessment of insulin resistance (HOMA-IR), total cholesterol (mg/dL), high-density lipoprotein (HDL) (mg/dL), low-density lipoprotein (LDL) (mg/dL), triglycerides (mg/dL) at 1, 3, and 5 years (3) operating time (minutes) (4) 30-days minor complications (Clavien-Dindo Grade 1 and 2) and 30-days major complications (Clavien-Dindo Grade 3 and 4).[12]

Search Strategy

We searched the following databases covering the period from database inception through January 2019: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, PubMed, and the major clinical trial registries (ClinicalTrials.gov: http://clinicaltrials.gov/; International Clinical Trials Registry Platform Search Portal: http://apps.who.int/trialsearch/) were searched for ongoing trials. The search was designed and conducted by a medical librarian with input from study investigators. The search strategy included keywords such as ''gastric bypass'' and ''sleeve gastrectomy'' (complete search strategy shown in Supplementary Table 1, http://links.lww.com/SLA/B813). We did not include the term ''randomized trial'' to ensure that all randomized studies were captured manually through the screening process. We also searched the references of published studies and grey literature manually to ensure that relevant articles were not missed. We did not discriminate full texts by language. This systematic review and meta-analysis are reported in accordance with the preferred reporting items for systematic reviews and meta-analyses.[13]The protocol of this study was registered in the Prospective Register of Systematic Reviews (PROSPERO).

Data Abstraction

At least 2 reviewers independently screened the searched titles, abstracts, and full texts after the inclusion and exclusion criteria. Reviewers were not blinded to authors, institution, or the journal where the manuscript was published. Discrepancies that occurred at the title and abstract screening stages were resolved by automatic inclusion to ensure that all relevant papers were not missed. Discrepancies at the full-text or data abstraction stage were resolved by consensus between 2 reviewers and if disagreement persisted, a third reviewer was consulted. Two reviewers independently conducted data abstraction onto a standardized spreadsheet designed a priori. The following data were abstracted from included studies: study characteristics (author, country, year of publication, single or multi-center design, funding source, inclusion and exclusion criteria), patient demographics (mean age at time of surgery, % female, number of patients included, mean BMI before and after surgery), follow-up time points, type of bariatric surgery, and outcomes.

Risk of Bias Assessment and Certainty of Evidence

Risk of bias for individual RCTs was assessed using the Cochrane Collaboration's tool for assessing risk of bias in RCTs.[14] Certainty of evidence for estimates derived from each meta-analysed outcome was assessed by grading of recommendations, assessment, development, and evaluation (GRADE).[15]

Statistical Analysis

All statistical analysis and meta-analysis were performed on STATA, version 14 (StataCorp, College, TX) and Cochrane Review Manager 5.3 (London, United Kingdom) with a level of significance set at P of <0.05. We performed pairwise meta-analyses using a DerSimonian and Laird random-effects model for continuous and dichotomous outcomes. Pooled effect estimates were obtained by calculating the mean difference (MD) for continuous outcomes and risk ratio (RR) for dichotomous outcomes along with their respective 95% confidence intervals (CI) to confirm the effect estimation. In addition, mean and standard deviation were estimated for studies that only reported median and interquartile range using the estimation method proposed by Wan et al. Assessment of heterogeneity was completed using the inconsistency (I^2) statistic. Studies reporting outcomes at follow-up time points that were not exactly at 1, 3, and 5 years were pooled into time point closest to 1, 3, or 5 years. Sensitivity analysis by excluding these studies was conducted to ensure that estimate of effect is not driven by these studies. Subgroup analysis based on preoperative BMI $>40\,kg/m^2$ and BMI $\leq 40\,kg/m^2$ was conducted. We considered I^2 higher than 50% to represent considerable heterogeneity. Publication bias was assessed using a funnel plot for outcomes that contained more than 10 RCTs as having less trials than 10 RCTs can lead to bias in interpretation of the funnel plot.[16] We performed meta-analyses of outcomes based on follow-up time points of 1, 3, and 5 years after surgery. These time points were selected after data extraction as these were the most common time points reported across all trials.

RESULTS

Study Characteristics

From 5783 potentially relevant citations from the search, 33 studies met the inclusion criteria.[10,11,17–47] Fig. 1 depicts a preferred reporting items for systematic reviews and meta-analyses flow diagram of study selection process. Studies were conducted between 2006 and 2018 in 13 countries including Brazil, China, Finland, France, Greece, Israel, Netherlands, New Zealand, Poland, Spain, Sweden, Switzerland, and United States. All studies were RCTs comparing LRYGB versus LSG in patients with class 2 obesity or greater (BMI $\geq 35\,kg/m^2$). Peterli et al published 5 studies of the same trial at follow-up time points of 3 months, and 1, 2, 3, and 5 years. Salminen et al published 3 studies of the same trial at follow-up time points of 1 and 6 months, and 1, 3, and 5 years. Vix et al published 2 studies of the same trial at follow-up time points of 6 months and 1 year. In total, 2475 patients were included, with 1223 randomized to LRYGB and 1252 randomized to LSG. Of these patients, 70% were female with a weighted mean age of 43.4 (range, 29.3–51.5) years, and a weighted mean preoperative BMI of 43.47 (4.29) kg/m^2. The detailed characteristics of included trials are reported in Supplementary Table 2, http://links.lww.com/SLA/B813. Raw values for all outcomes are reported in Supplementary Tables 3 and 4, http://links.lww.com/SLA/B813.

Body Mass Index

Supplementary Table 5, http://links.lww.com/SLA/B813 presents the meta-analysis of all outcomes with its certainty of evidence according to GRADE. In total, 16 RCTs (n = 1673)

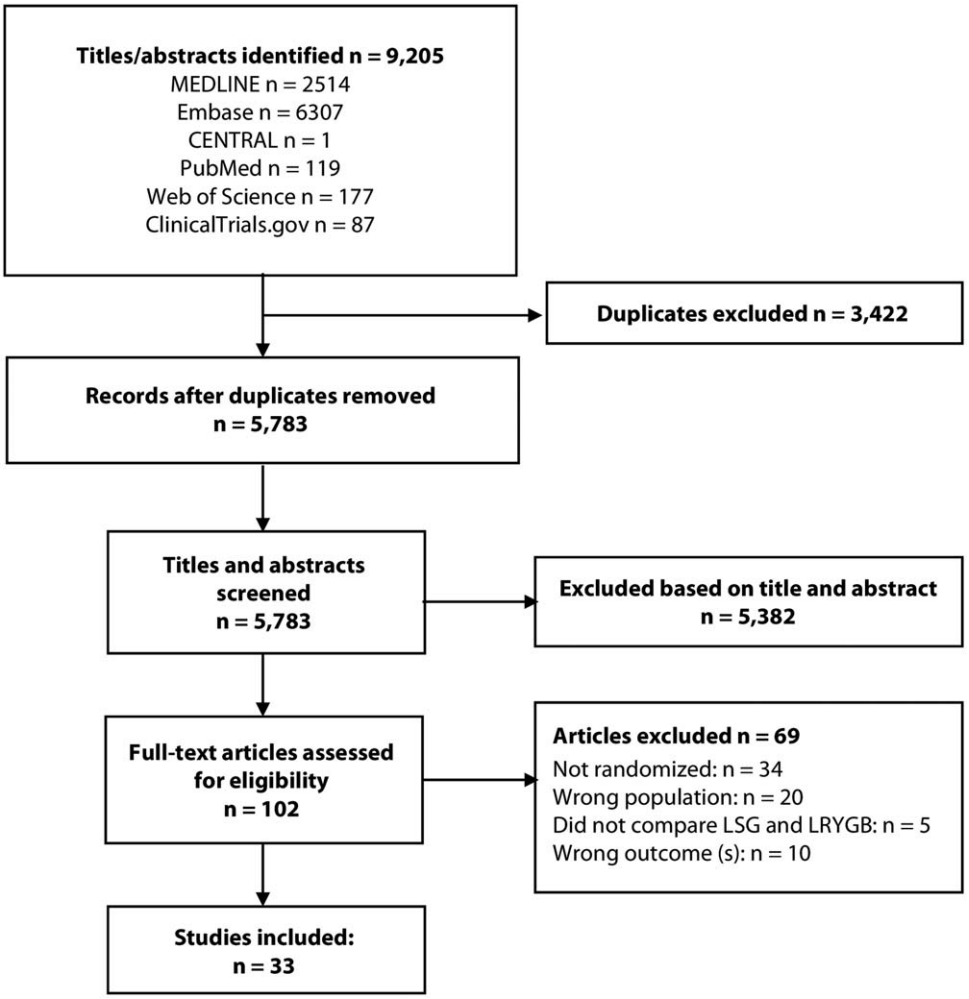

FIGURE 1. PRISMA diagram – transparent reporting of systematic reviews and meta-analysis flow diagram outlining the search strategy results from initial search to included studies. PRISMA indicates preferred reporting items for systematic reviews and meta-analyses.

reported changes in BMI at 1 year after bariatric surgery. Patients who received LRYGB had significantly greater decrease in BMI than LSG by 1.25 kg/m^2 at 1 year (95% CI −2.01 to −0.49, $P = 0.001$; $I^2 = 88\%$; 1673 patients; 16 trials; moderate certainty of evidence) (Fig. 2A). At 3 years after surgery, the LRYGB group had significantly greater decrease in BMI by 1.71 kg/m^2 than the LSG group (95% CI −2.68 to −0.74, $P < 0.001$; $I^2 = 47\%$; 595 patients; 5 trials; moderate certainty of evidence) (Fig. 2B). However, at 5 years after surgery, the data were insufficient to estimate the difference in BMI change between 2 procedures with precision (MD −1.46, 95% CI −3.15 to 0.23, $P = 0.09$; $I^2 = 91\%$, 719 patients; 4 trials; low certainty of evidence) (Fig. 2C). However, much of the heterogeneity at 5 years was introduced by a trial by Ruiz-Tovar et al[40] and after performing a sensitivity analysis excluding this study, weight loss favored LRYGB at 5 years with no heterogeneity (MD −2.20, 95% CI −2.36 to −2.04, $P < 0.001$; $I^2 = 0\%$, 353 patients; 3 trials). There were 2 studies with preoperative BMI less than 40.[37,46] Subgroup analysis of patients with preoperative BMI greater than 40 did not change the effect estimate that is present at 1 and 3 years after surgery.

Type 2 Diabetes

The rate of remission for T2DM was reported by 9 trials (n = 508) at 1 year, 4 trials (n = 208) at 3 years, and 4 trials (n = 351) at 5 years. There was no significant difference in the rate of remission for T2DM between LRYGB and LSG at 1 year (RR 0.86, 95% CI 0.71–1.04, $P = 0.12$; $I^2 = 40\%$; 508 patients; 9 trials; high certainty of evidence) (Fig. 3A), 3 years (RR 0.88, 95% CI 0.72–1.07, $P = 0.19$; $I^2 = 0\%$; 208 patients; 4 trials; moderate certainty of evidence) (Fig. 3B), or 5 years after surgery (RR 0.79, 95% CI 0.57–1.10, $P = 0.17$; $I^2 = 57\%$; 351 patients; 4 trials; low certainty of evidence) (Fig. 3C).

Cardiovascular Risk Profile

The remission of dyslipidemia was reported by 4 trials (n = 364) at 1 year, and 6 for hypertension (n = 630) at 1 year. Compared to LSG, LRYGB had significantly greater remission of dyslipidemia at 1 year (RR 0.58, 95% CI 0.46–0.73, $P < 0.001$; $I^2 = 0\%$; 364 patients; 4 trials; moderate certainty of evidence) and 5 years (RR 0.68, 95% CI 0.46–0.99, $P = 0.04$, $I^2 = 77\%$; 351 patients; 4 trials; low certainty of evidence) (Supplementary Fig. 1, http://links.lww.com/SLA/B813). However, there was no difference in the remission of hypertension between the 2 surgeries at 1 year (RR 0.91, 95% CI 0.81–1.01, $P = 0.08$; $I^2 = 0\%$; 478 patients; 5 trials; high certainty of evidence) or 5 years post-surgery (RR 0.86, 95% CI 0.68–1.10, $P = 0.24$; $I^2 = 47\%$; 446 patients; 4 trials; high certainty of evidence) (Supplementary Fig. 2, http://links.lww.com/SLA/B813).

Lipid Biochemical Outcomes

Ten trials reported levels of triglycerides (n = 753) at 12 (range, 3–60) months, 6 for total cholesterol (n = 429) at 1 year, 6 for

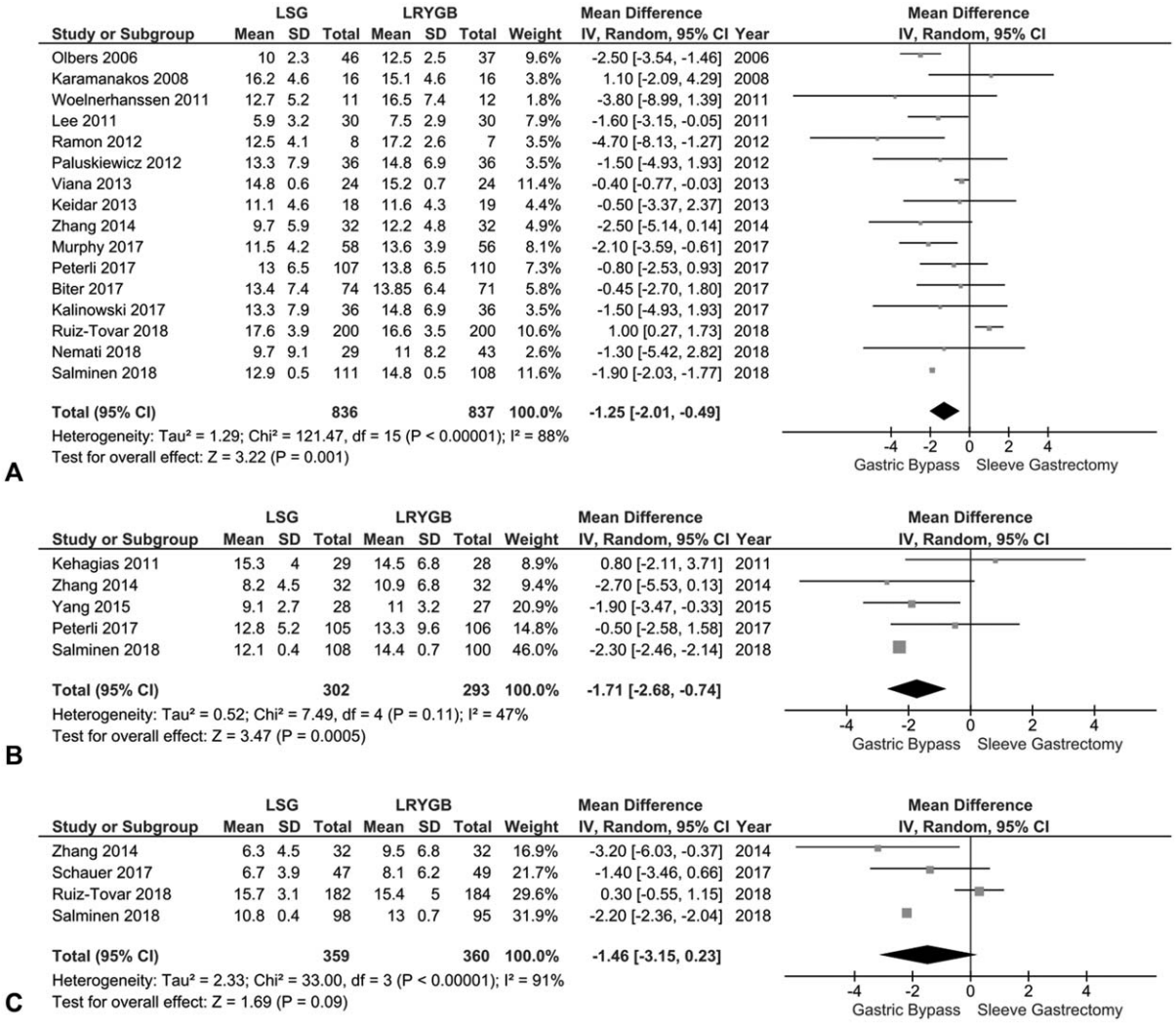

FIGURE 2. Pairwise random-effects meta-analysis forest plot comparing laparoscopic sleeve gastrectomy versus laparoscopic Roux-en-Y gastric bypass on (A) Change in BMI 1 yr after surgery. (B) Change in BMI 3 yr after surgery. (C) Change in BMI 5 yr after surgery. BMI indicates body mass index.

LDL (n = 429) at 1 year, and 9 for HDL (n = 549) at 12 (range, 3–60) months. The LRYGB group had significantly greater reduction in triglycerides levels than the LSG group (MD −12.60 mg/dL, 95% CI −24.78 to −0.42, $P = 0.04$; $I^2 = 91\%$; 753 patients, 10 trials; moderate certainty of evidence) (Supplementary Fig. 3, http://links.lww.com/SLA/B813). Moreover, LRYGB had significantly lower total cholesterol levels compared to LSG at 1 year after surgery (MD −15.55 mg/dL, 95% CI −21.98 to −9.11, $P < 0.001$; $I^2 = 73\%$; 429 patients; 6 trials; moderate certainty of evidence) but no difference was found at 3 years ($P = 0.22$) (Supplementary Fig. 4, http://links.lww.com/SLA/B813). Similarly, patients with LRYGB had significantly lower LDL levels compared to patients with LSG at 1 year (MD −19.04 mg/dL, 95% CI −28.66 to −9.42, $P = < 0.001$; $I^2 = 93\%$; 429 patients; 6 trials; moderate certainty of evidence), 3 years (MD −14.50 mg/dL, 95% CI −16.56 to −12.45, $P < 0.001$; $I^2 = 71\%$; 407 patients; 3 trials; low certainty of evidence), but not 5 years ($P = 0.65$) (Supplementary Fig. 5, http://links.lww.com/SLA/B813). There was no significant difference between HDL levels between the 2 surgeries ($P = 0.06$) (Supplementary Fig. 6, http://links.lww.com/SLA/B813).

Diabetes Related Biochemical Outcomes

Overall, 10 trials reported outcomes for fasting glucose (n = 563) at 1 year, 11 for %HbA1c (n = 761) at 12 (range, 3–60) months, 7 for fasting insulin (n = 340) at 12 (range, 3–12) months, and 7 for HOMA-IR (n = 340) at 12 (range, 3–60) months. Although LRYGB did not significantly reduce fasting glucose compared to LSG at 1 year, LRYGB did reduce fasting glucose compared to LSG at 5 years (MD −21.04 mg/dL, 95% CI −33.94 to −8.14, $P = 0.001$; $I^2 = 87\%$; 231 patients; 3 trials; low certainty of evidence) (Supplementary Fig. 7, http://links.lww.com/SLA/B813). Conversely, there was no difference between LRYGB and LSG for changes in % HbA1c ($P = 0.45$), fasting insulin ($P = 0.41$), and HOMA-IR ($P = 0.44$) (Supplementary Fig. 8, http://links.lww.com/SLA/B813).

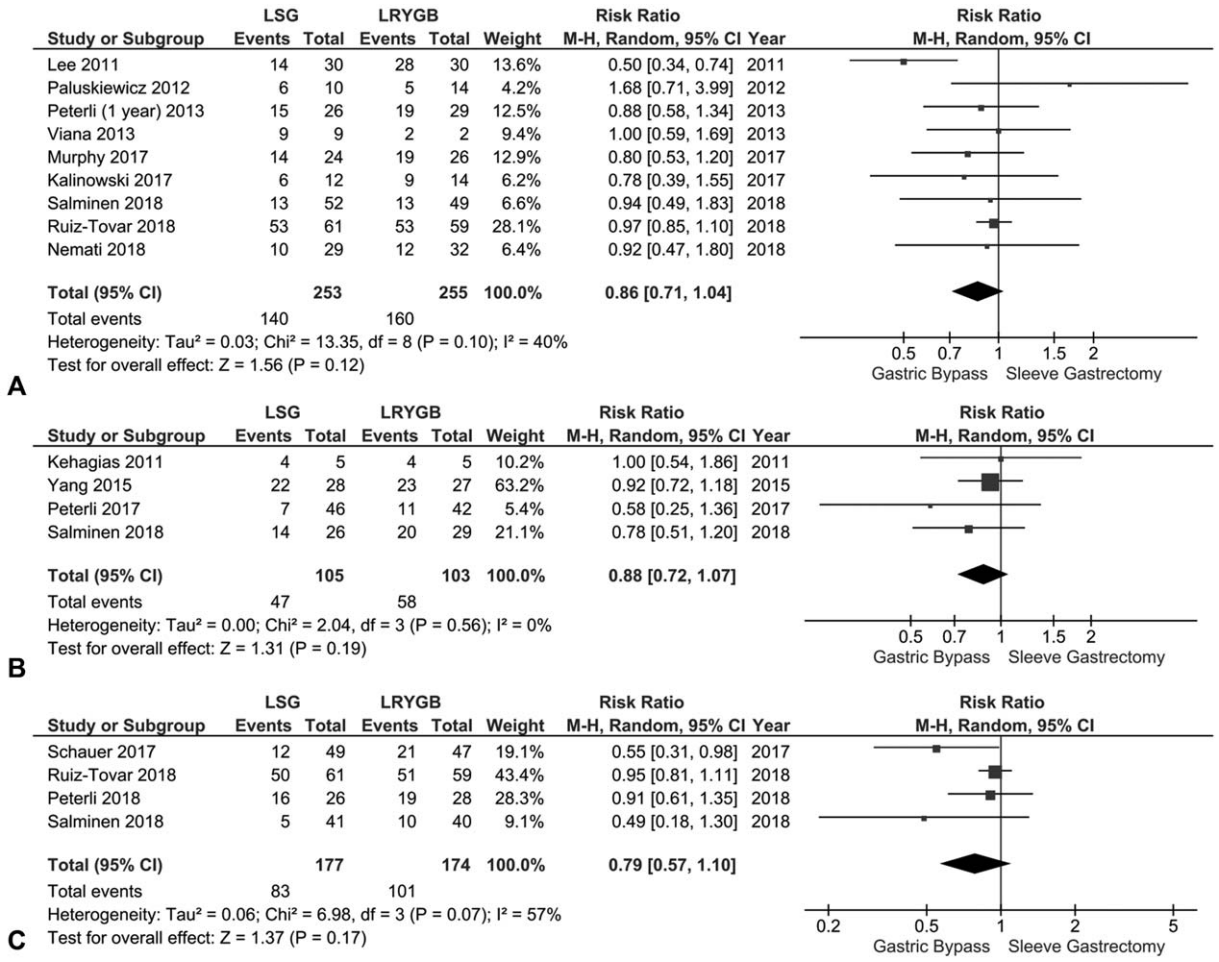

FIGURE 3. Pairwise random-effects meta-analysis forest plot comparing laparoscopic sleeve gastrectomy versus laparoscopic Roux-en-Y gastric bypass on (A) Remission of type 2 diabetes 1 yr after surgery. (B) Remission of type 2 diabetes 3 yr after surgery. (C) Remission of type 2 diabetes 5 yr after surgery.

Perioperative Outcomes

Operating time for bariatric surgery was reported by 4 trials (n = 462). LSG had a significantly shorter operating time compared to LRYGB (MD −50.58, 95% CI −76.29 to −24.86, $P = 0.0001$; $I^2 =$ 95%; 4 trials; 462 patients) (Supplementary Fig. 9, http://links.lww.com/SLA/B813). Due to the inadequate reporting of late (greater than 30 days) complications across majority of the trials, meta-analysis was only possible for early (within 30 days) minor and major complications. There was no difference in minor early complications between LRYGB and LSG (RR 0.82, 95% CI 0.52–1.27, $P = 0.37$; $I^2 = 25\%$; 1128 patients; 10 trials; moderate certainty of evidence) (Fig. 4A). Similarly, from 10 RCTs (n = 1518), there was no difference in major early complications between LRYGB and LSG (RR 0.82, 95% CI 0.58–1.16, $P = 0.25$; $I^2 = 0\%$; moderate certainty of evidence) (Fig. 4B). Specific complications reported by each trial is presented in Supplementary Table 6, http://links.lww.com/SLA/B813.

Quality Assessment of Studies

A summary of the risk of bias across all studies is provided in Fig. 5. In brief, all included trials had appropriate random sequence generation. Allocation concealment was present in 97% (32/33) of studies, and 88% of studies (29/33) adequately explained incomplete outcome data or loss to follow-up. However, blinding of participants occurred in only 9% (3/33) of studies, blinding of healthcare providers in 9% (3/33) of studies, and blinding of outcome assessment in 15% (5/33) of studies. No study had selective reporting of outcomes or other biases. Therefore, following the Cochrane Risk of Bias tool, the majority of the studies had low selection bias, high-performance bias, high detection bias, and low reporting bias.

GRADE certainty of evidence is summarized in Supplementary Table 5, http://links.lww.com/SLA/B813. No outcomes were rated down for risk of bias because most studies had adequate randomization, allocation concealment, low attrition bias, and low reporting bias. However, the majority of studies did not blind participants, healthcare providers, and outcome assessors due to the nature of the comparison including surgery. Nonetheless, blinding has less impact on the objective outcomes analyzed in the present meta-analysis such as BMI, comorbidities, and biochemistry profiles of patients. Several outcomes including BMI, biochemical outcomes, and dyslipidemia, and T2DM at 5 years were rated down for inconsistency because of either high heterogeneity ($I^2 > 50\%$), or

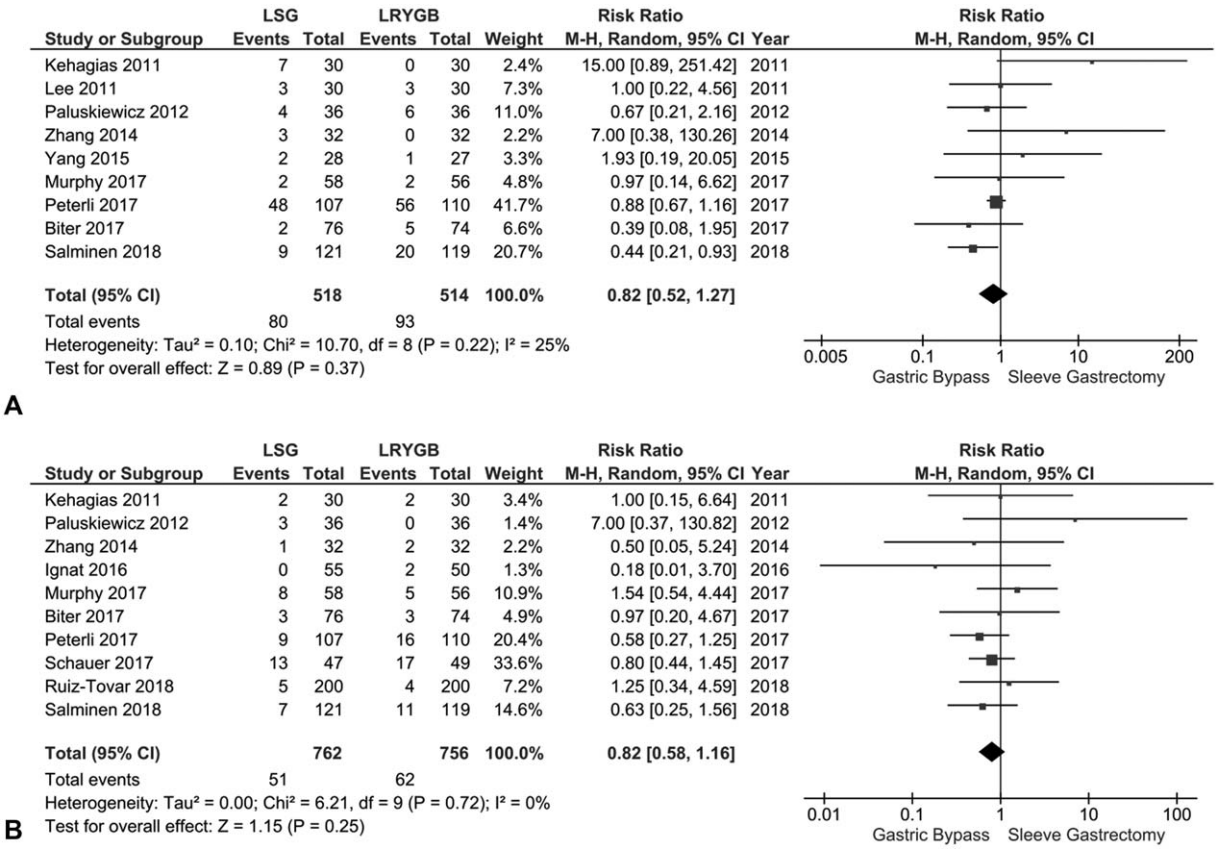

FIGURE 4. Pairwise random-effects meta-analysis forest plot comparing laparoscopic sleeve gastrectomy versus laparoscopic Roux-en-Y gastric bypass on (A) minor early (less than 30 d) complications. (B) Major early (less than 30 d) complications.

varied point estimates with little overlap of CIs. Outcomes with large CIs overlapping no effect, or fewer than 400 patients were also downgraded for imprecision. Other outcomes with 10 or more RCTs had low publication bias as their funnel plots were symmetrical (Supplementary Fig. 10, http://links.lww.com/SLA/B813). Overall, there was low certainty of evidence for change in BMI at 5 years, remission of T2DM at 5 years, dyslipidemia, and biochemical outcomes at 5 years after surgery. There was a high certainty of evidence for remission of T2DM at 1 year after surgery, and remission of hypertension at all time points. There was a moderate certainty of evidence for change in BMI at 1 and 3 years, minor and major complications, and all other outcomes.

DISCUSSION

This is the most comprehensive systematic review and meta-analysis to date comparing LRYGB with LSG. In this review with 2475 patients, LRYGB results in a significantly greater decrease in BMI than LSG at 1 and 3 years after surgery. However, certainty of evidence was low for BMI loss at 5 years because of wide CIs that include a large effect favoring LRYGB. Therefore, additional studies are needed to improve the precision of the point estimate. Comparing the impact of the 2 surgeries on comorbidities, LRYGB results in a greater remission of dyslipidemia than LSG at both 1- and 5-years post-surgery. LRYGB also provides greater improvements in biochemical outcomes than LSG, including greater reductions in total cholesterol at 1 year, LDL at 1 and 3 years, and fasting glucose at 5 years. In addition, though not significant, diabetes remission rates at every interval favored LRYGB. LSG has long been thought to result in fewer complications than LRYGB; however, no differences in major or minor early complications were found in this systematic review. Despite the inclusion of only RCTs, the overall certainty of evidence ranged from low to high across all outcomes according to GRADE.

Previous reviews have explored the effects of LRYGB compared to LSG. A meta-analysis by Yang et al included 15 RCTs and 1381 patients.[48] The study concluded that LRYGB results in greater weight loss than LSG at 3 and 5 years but not at time points less than 3 years. In contrast, the present study included 1094 more patients by conducting a comprehensive search of the literature and concluded that LRYGB results in a greater reduction in BMI at 1 and 3 years, but results were inconclusive at 5 years. Furthermore, although Yang et al concluded that LSG results in fewer complications than LRYGB, the definition of a complication was unclear.[48]Our review stratified complications by severity as major or minor and by time point as early and late to reduce ambiguity in accordance with ASMBS reporting standards, concluding that there were no differences in either major or minor early complications.[49] The findings of the current study also agree with 2 previous meta-analyses by Shoar et al and Li et al that found statistically improved long-term weight loss for LRYGB compared to LSG.[50,51] However, Shoar et al and Li et al provided conflicting reports on the remission of comorbidities and

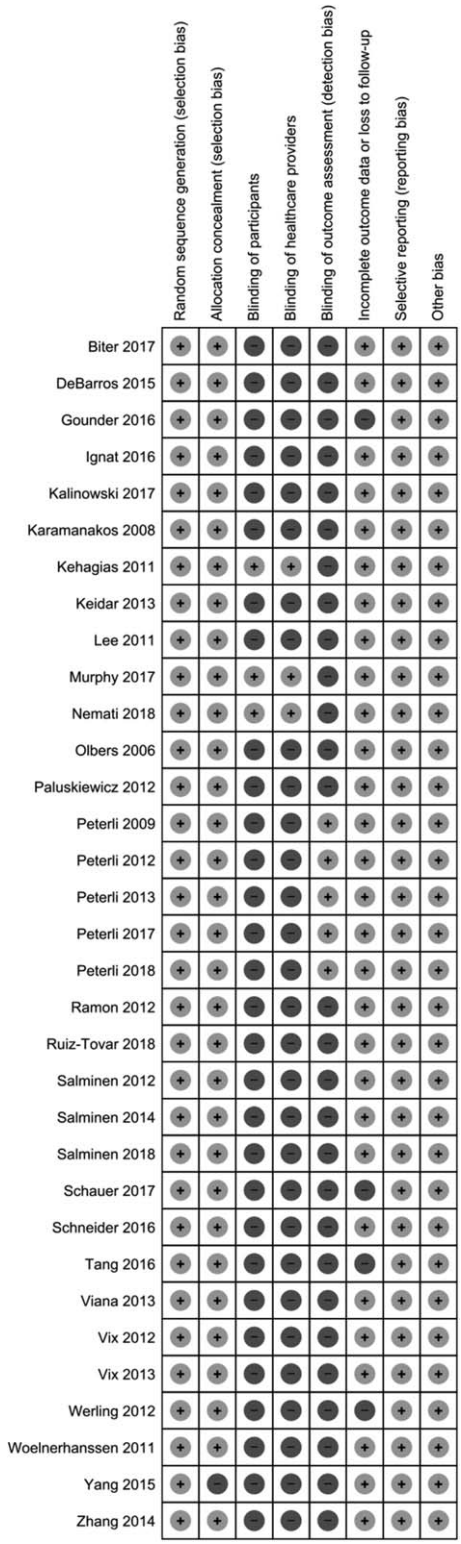

FIGURE 5. Cochrane risk of bias assessment of included randomized controlled trials.

included 3 and 11 RCTs respectively, with both reviews lacking several recently published high-quality trials.[10,11,41] The present review also examines important biochemical outcomes including HbA1c, fasting glucose, total cholesterol, LDL, HDL, and triglycerides. Finally, our study differs from previous reviews in its rigorous assessment of included studies, both on the individual study level for risk of bias using the Cochrane Risk of Bias Tool, and on the body of evidence level using GRADE.

The outcomes of the present review are supported by previous high-quality studies. Although this meta-analysis reports that LRYGB results in a significantly greater reduction in BMI compared to LSG at 1 year, a 1.25 kg/m^2 reduction in BMI is unlikely to be clinically significant. Typically, a 5%–10% reduction in weight is considered to be clinically important with some studies calling for even greater weight reductions.[52]Two recent high-quality RCTs have also reported a marginal difference in weight loss between LRYGB and LSG. The SLEEVEPASS trial found a trend towards higher %EWL at 5 years for LRYGB compared to LSG (57% vs 49%); however, this difference did not meet prespecified equivalence margins for clinical significance.[11] The SM-BOSS trial also found a trend towards improved excess BMI loss at 5 years for LRYGB compared to LSG (68% vs 61%); however, this difference was not significant after adjustment for multiple comparisons.[10] Conversely, a retrospective cohort study of 46,510 patients using the National Patient-Centered Clinical Research Network did find a significantly greater percentage total weight loss at 5 years with RYGB compared to LSG (25.5% vs 18.8%), albeit with a higher rate of complications for RYGB.[53] However, the study's retrospective, nonrandomized design limits its conclusions and outcomes for comorbidities were not reported. In contrast, both the SLEEVEPASS and SM-BOSS trials found similar outcomes for comorbidities to the present study, concluding that there were no differences between LRYGB and LSG for the remission of type 2 diabetes.[10,11] Additionally, in the SLEEVEPASS trial, a higher percentage of patients receiving LRYGB achieved remission in dyslipidemia and in the SM-BOSS trial, a trend towards remission of dyslipidemia favoring the LRYGB group was seen ($P = 0.03$ unadjusted, $P = 0.09$ adjusted for multiple comparisons).[10,11] These results support the benefit for dyslipidemia in the LRYGB group found in the present meta-analysis. In the analyses of BMI change at 5 years after surgery, the trial by Ruiz-Tovar et al appeared to be an outlier, with a much larger sample size than other trials but with a mean that favored greater BMI loss after LSG.[40] However, Ruiz-Tovar et al's trial presented methodological issues, including limited data regarding patient selection, baseline characteristics, and biological outcomes, and did not report missing data including for their primary outcome of excess BMI loss.[40] Importantly, the sensitivity analysis excluding this trial demonstrated a significantly greater loss of BMI in the LRYGB group compared to LSG at 5 years with no heterogeneity (MD −2.20, 95% CI −2.36 to −2.04, $P < 0.0001$; $I^2 = 0\%$, 353 patients; 3 trials). It is difficult to assess potential biases without knowing precisely how the trial by Ruiz-Tovar was conducted, but it is likely that these biases are a major source of heterogeneity and imprecision in this review. However, another source of heterogeneity could be the lack of generalizability of results from the remaining 3 studies due to a strict inclusion criterion. Although the sensitivity analysis likely represents a true signal for the 3 remaining trials, it is overall difficult to conclude that the results are completely representative of the true difference without future trials in other cohorts with long-term (≥5 years) follow-ups.

The findings of the present study at 1-year and 3-year follow-up support the 2017 ASMBS guidelines for LSG, suggesting that RYGB may provide greater weight loss compared to LSG.[3] For context, using the average height, BMI difference of 1.25 kg/m^2

represents about 10 pounds for average female patients and 11.5 pounds for average male patients, which could represent up to 15% of weight loss. Nonetheless, no current trials have compared LSG and LRYGB with long-term (>10 years) follow-up. An obesity-related comorbidity that often plays a significant role in decision-making is GERD. Unfortunately, limited number of trials have so far compared GERD status after LRYGB and LSG.[10,27] Given the growing body of evidence demonstrating that LSG may lead to the development of GERD or worsen existing GERD, future trials should aim to compare the long-term GERD outcome difference between LRYGB and LSG.

This study has several limitations. First, only a small number of studies reported outcomes at a follow-up time of 5 years, limiting the certainty of evidence on medium-term outcomes comparing LRYGB versus LSG. Nonetheless, RCTs that reported outcomes at 5 years were typically higher quality than trials that reported only short-term outcomes.[10,11] Second, low numbers of patients were studied for some outcomes including fasting glucose at 5 years and HOMA-IR, and results were inconclusive for BMI loss at 5 years, supporting a need for future studies. Third, substantial heterogeneity existed across outcomes. This may be because of differences in postoperative management, surgeons' skill level, and patient populations across the 13 countries studied. Nevertheless, the effects of key outcomes including BMI and comorbidities including dyslipidemia were similar across different time points, making it less likely for heterogeneity to explain the results found in the present review. Fourth, the present review analyzed changes in BMI rather than %EWL, which is now a more common outcome.[11] This was because many included trials did not report %EWL, precluding a uniform weight loss outcome data collection. Nonetheless, change in BMI is still a commonly used outcome for weight loss and is a recommended outcome according to the ASMBS reporting standards.[49] Fifth, patients and surgeons were unblinded to the type of surgery performed. In particular, both LRYGB and LSG possess unique complications, such as internal hernia being exclusive to LRYGB. Therefore, blinding would make the management of complications challenging, and would be difficult to justify ethically.[10] Only Kehagias et al reported the blinding of patients and medical staff.[27]

In conclusion, LRYGB resulted in greater BMI loss at 1 and 3 years; however, there was insufficient randomized evidence to draw any conclusions regarding weight loss between the 2 procedures at 5 years. No differences between the 2 procedures were found in remission of type 2 diabetes, despite a trend at every time interval favoring LRYGB, hypertension, and rates of major and minor complications. Compared to LSG, LRYGB provides a higher remission of dyslipidemia and lower LDL and total cholesterol levels. Large RCTs with low risk of bias and long-term (>5 year) follow up are necessary to provide valid data on the relative effectiveness of LRYGB and LSG for long-term weight loss.

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