TITLE

Weight loss outcomes in laparoscopic vertical sleeve gastrectomy (LVSG) versus laparoscopic Roux-en-Y gastric bypass (LRYGB) procedures: A meta-analysis and systematic review of randomized controlled trials

AUTHORS (EMAILS)

Emma Osland, BHSc (Nutr & Diet) MPhil[1,2] (Emma.Osland@health.qld.gov.au)

Rossita Mohamad Yunus, PhD[3] (rossita@um.edu.my)

Shahjahan Khan, PhD[4] (Shahjahan.Khan@usq.edu.au)

Breda Memon, RN, LLB, PGCEd, DipPractMan[5] (bmemon@yahoo.com)

Muhammed Ashraf Memon, MBBS, MA, DCH, FACS, FRACS, FRCSI, FRCSEd, FRCSEng[4,5,6,7,8] (mmemon@yahoo.com)

DEPARTMENTS AND INSTITUTIONS

[1]Department of Nutrition and Dietetics, Royal Brisbane and Women's Hospital, Herston, Qld, 4019 Australia.

[2]Department of Human Movements and Nutrition, University of Queensland, Brisbane, Queensland, Australia

[3]Institute of Mathematical Sciences, University of Malaya, Kuala Lumpur, Malaysia

[4]School of Agricultural, Computational and Environmental Sciences, International Centre for Applied Climate Sciences and Centre for Health Sciences Research, University of Southern Queensland, Toowoomba, Queensland, Australia

[5]Sunnybank Obesity Centre South & East Queensland Surgery (SEQS), Suite 9, McCullough Centre, 259 McCullough Street, Sunnybank, Queensland, Australia

[6]Mayne Medical School, School of Medicine, University of Queensland, Brisbane, Queensland, Australia

[7]Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Queensland, Australia

[8]Faculty of Health and Social Science, Bolton University, Bolton, Lancashire, UK

REPRINTS/CORRESPONDENCE

Professor M. A. Memon, FACS, FRACS, FRCS, Sunnybank Obesity Centre, Suite 9, McCullough Centre, 259 McCullough Street, Sunnybank, QLD 4109, Australia

Tel: +61 7 3345 6667 Fax: +61 7 3344 1752 Mobile: +61 448614170

Email: mmemon@yahoo.com

SECTION OF THE JOURNAL

Meta-analysis/Systematic Reviews

KEY WORDS

Bariatric Surgery; Laparoscopic; Sleeve Gastrectomy; Roux-en-Y Gastric Bypass; Weight Loss; Longitudinal Study; Meta-analysis; Systematic review

ABSTRACT

Purpose: Laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic vertical sleeve gastrectomy (LVSG), have been proposed as cost effective strategies to manage morbid obesity. This aim of this meta-analysis was to compared the postoperative weight loss outcomes reported in randomised control trials (RCTs) for LVSG versus LRYGB procedures.

Material and Methods: RCTs comparing the weight loss outcomes following LVSG and LRYGB in adult population between January 2000 and November 2015 were selected from PubMed, Medline, Embase, Science Citation Index, Current Contents, and the Cochrane database. The review was prepared in accordance with Preferred Reporting of Systematic Reviews and Meta-Analyses (PRISMA).

Results: Nine unique RCTs described over 10 publications involving a total of 865 patients (LVSG n=437, LRYGB n=428) were analyzed. Postoperative follow up ranged from 3 months to 5 years. Twelve-month excess weight loss for LVSG ranged from 69.7% to 83%, and for LRYGB, ranged from 60.5% to 86.4%. A number of studies reported slow weight gain between the 2nd and 3rd years of postoperative follow-up ranging from 1.4 to 4.2% EWL. This trend was seen to continue to 5 years postoperatively (8% to 10% EWL) for both procedures.

Conclusions: In conclusion, LRYGB and LVSG are comparable with regards to the weight loss outcomes in the short term, with LRYGB appearing achieving slightly greater weight loss. Slow weight recidivism is observed after the first postoperative year following both procedures. Long-

term reporting of outcomes obtained from well-designed studies using ITT analyses are identified as a major gap in the literature at present.

INTRODUCTION

Obesity is fast becoming the one of the most significant health problems facing the modern world, representing a major cause of morbidity, disability and early mortality. According to the World Obesity Federation adult obesity is now more common than under-nutrition with 670 million of the world's population now considered obese (BMI >30kg/m^2) and a further 98 million severely obese (>35kg/m^2)[1]. In countries such as the United States, Mexico, Australia and New Zealand between a quarter and a third of their population are now considered to be obese[2].

Obesity is associated with development of chronic health conditions such as Type 2 Diabetes, cardiovascular disease and some forms of cancer[1]. In addition to the health burden to the individual, there is a significant and growing economic burden associated with obesity. It is therefore essential that effective population-based prevention strategies along with sustainable individual management approaches are being urgently sought to reduce the burden of disease and economic demands caused by widespread obesity. Bariatric surgical procedures, such as laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic vertical sleeve gastrectomy (LVSG), are increasingly being utilized as cost-effective and efficacious strategies to manage obesity related chronic disease and metabolic conditions in the moderately to severely obese individuals[2-5].

This aim of this systematic review and meta-analysis is to study the peer review literature regarding postoperative *weight loss outcomes* reported from randomised control trials (RCTs) comparing LVSG and LRYGB bariatric procedures.

MATERIALS AND METHODS

Inclusion and Exclusion Criteria

RCTs comparing clinical outcomes of elective LVSG and LRYGB procedures in adult subjects (>16 years) that reported weight loss outcomes were reviewed. Qualitative review was performed on all studies that met inclusion criteria, and meta-analyses were run on outcome variables where numbers and methods of reporting were sufficient to allow statistical analysis.

Search Strategies and Data Collection

Electronic databases (Medline, Pubmed, EMBASE, CINAHL, Cochrane Register of Systematic Reviews, Science Citation Index) were cross-searched for RCTs published between 2000 and November 2015 to capture the studies since Regan et al's description of the LVSG as a stand-alone procedure[6]. Search terms were selected for each search engine to optimize identification of all published papers meeting the inclusion criteria. Limits were set to RCTs and adult patients (>16yrs) to reflect the inclusion criteria. Search strategies utilized included combinations of "laparoscopy"[MeSH Terms] OR "laparoscopy"[All Fields] OR "laparoscopic"[All Fields]), "gastric sleeve"[All Fields] OR "sleeve gastrectomy"[All Fields] AND "Roux-en-y"[All Fields] OR "*gastric bypass"[All Fields] AND "outcomes"[All Fields]. Reference lists of review articles were examined for additional citations. Authors of included papers were contacted by email for clarification or additional information where required. The review was prepared in accordance with Preferred Reporting of Systematic Reviews and Meta-Analyses (PRISMA). Two authors (EO and MAM) independently appraised identified studies to confirm compliance with agreed inclusion criteria. One author (EO) undertook the data extraction. The authors were not blinded to the source of the document or authorship for the purpose of data extraction. The data were compared and consensus was achieved through discussion or contact with corresponding authors when required. The Jadad scoring system[7] was used to assess the methodological quality of identified studies.

Statistical Analysis

Meta-analyses were performed weighted mean differences (WMDs). Random effects model (REM), developed by DerSimonian and Laird[8] using the inverse variance weighted method approach and the inverse variance heterogeneity (IVhet) model developed by Doi et al[9] were used to combine the data to estimate the common effect size of the outcome variables. Heterogeneity among the effect size measures was assessed using the Q statistic[10, 11] and I^2 index[12-14]. Funnel plots were synthesized in order to assess for the presence of publication bias in the meta-analysis. Standard error was plotted against the treatment effects (Log OR for the dichotomous and WMD for continuous variables respectively)[15] to allow 95% confidence interval limits to be displayed. Estimates were obtained using computer programs written in R package for the random effects model, while the MetaXL program was used for computations under the inverse variance heterogeneity model referred to the paper[9, 16]. All forest plots are for the estimates of the effect size obtained from the random effects model and were obtained using the ‘rmetafor’ package[16]. A significance level of 5% (α =0.05) was applied to tests of hypotheses.

RESULTS

Included Studies

Search outcomes identified 478 citations through literature searches (k=473) and hand searches of bibliographical information (k=5). After removal of duplicates and screening of abstracts, 57 full text articles were retrieved and assessed against eligibility criteria. Of the 48 studies excluded, 39 were found not to be in conformity with RCT study design, 11 were reviews (including existing systematic reviews or meta-analyses), three studies reported different outcomes or follow up time frames of otherwise eligible studies, one did not report on clinical outcomes, one described outcomes of bariatric procedures in an adolescent population, one reported clinical outcomes of LVSG versus open LRYGB, while another reported LVSG versus mini gastric bypass. In addition, two protocols describing studies eligible for inclusion in this meta-analysis that currently in progress were also located[17, 18]. Nine unique RCTs described over 10 publications involving a total of 865 patients (LVSG n=437, LRYGB n=428) reported postoperative weight loss in sufficient detail for inclusion in the systematic review and meta-analysis, as reported data allowed (Figure 1).

Included studies represented a range of countries internationally including China[19, 20], Finland[21, 22], Switzerland[23], Greece[24, 25], Israel(26), France[27] and Brazil[28]. All included studies were published within the last five years reporting on studies conducted between 2005 and 2015. Postoperative follow up ranged from 3 months to 5 years postoperatively, reporting in intervals ranging from 1 month to 1 year. Included studies were of a moderate methodological quality, with an average Jadad score of 3 (range 2 to 5). All studies reported randomization methods and accounted for all patients throughout the follow up period, while blinding was reported to have occurred in only one study[26]. No study described preoperative weight loss dietary interventions (i.e. very low energy/calorie diets), however three studies stated that full multidisciplinary assessments and preoperative workups (including nutritional, psychological, endocrine, cardiology) were undertaken[21, 27, 28]. Table 1 outlines the characteristics of included studies.

Loss to follow up

Considering loss to follow up rates across all studies, a median of 93% (range 32% to 100%) of participants continued to be followed up for the full study duration. Four studies[19, 20, 24, 25] retained patients throughout their reported follow up periods either through use of intention to treat (ITT) statistics and/or no loss of patients to follow up. Though retaining 100% of patients at one year follow up, Peterli et al[23] reported the highest rate of loss to follow-up with only 112 (51.6%) at 2 years and 70 (32%) at three years of the original 217 patients who commenced the SM-BOSS study continuing: Reported weight outcomes were limited to one year postoperative follow up.

BMI and Weight at baseline

All studies reported baseline BMI. These ranged from around 32 to 39 kg/m^2 in studies conducted in China[19, 20] to 42 to 45 kg/m^2 in the other countries represented by the included studies [21-28]: this reflects the anthropometric differences and definitions of obesity in different cultural groups.

Seven studies[19, 23-28] also reported weight in kilograms at baseline. Again, the Chinese study[19] reporting this outcome disclosed a lower baseline weight (88-94 kg) than the papers from other countries which revealed consistent preoperative weights of ~120-130kg.

Percent Excess Weight Loss (%EWL)

Systematic Review

%EWL was the most commonly reported weight loss outcome, being reported in seven studies[19-22, 24, 25, 27, 28]. The computation of this, however, was defined in only one study[19] but was assumed to be consistent to all studies. All studies reported %EWL in means, and SD was not consistently provided.

Reported follow up intervals on %EWL ranged from one month (k=3) to four years (k=1) postoperatively, with three (k=6), six (k=4) and twelve (k=5) month intervals, and annual follow up thereafter (2 yrs k=2; 3 yrs k=3).

Considerable variation in %EWL achieved and trends in %EWL reported during the follow up periods were noted between studies reporting this outcome. All studies reported trends of consistent and increasing losses of percent excess weight to 12 months follow-up irrespective of procedure performed. Weight loss achieved in LVSG at 12 months ranged from 69.7%EWL[24] to 83%EWL[27] (median 73.9 %EWL), with similar outcomes seen with LRYGB over the same time period (median 80.4 %EWL, ranging from 60.5%EWL[24] to 86.4%EWL[19]).

In the three studies[19, 20, 25] that reported %EWL outcomes between 1 and 2 years postoperatively, excess weight loss was reported to continue (LVSG 79.6% to 84.9%EWL, LRYGB 86.4% to 95.1%EWL[19]), stabilize (LVSG 72.9% to 73.2%EWL, LRYGB 65.6% to 65.3%EWL[25]) or be slowly regained (LVSG 73.9% to 69.4%EWL, LRYGB 84.5% to 81.2%EWL[20]). These same three studies[19, 20, 25] reported slow weight gain between the second and third years of postoperative follow up (ranging from 1.4 to 4.2%EWL regain). This trend was seen to continue to 5 years postoperatively where 8% to 10% of EWL was put on during the follow-up period[20]. Rates of weight regain appear to be similar within intervention groups within studies irrespective of surgical procedure.

Helmio et al[22], Yang et al[19] and Zhang et al[20] reported superior %EWL achieved with LRYGB procedure i.e. 52.9%EWL vs 49.4%EWL at 6 months[22], 92.3%EWL vs 81.9%EWL at 3 years[19] and 76.2%EWL vs 63.2%EWL at 5 years[20] for LRYGB and LVSG respectively. Conversely Karamankos et al[24], Kehagias et al[25] and Vix et al[27] report higher %EWL at the completion of study follow-up was achieved with LVSG i.e. 69.7 vs 60.5%EWL[24] and 83 vs 80.4%EWL[27] at 12 months, and 68.5 vs 62.1%EWL at 3 years[25] for LVSG vs LRYGB respectively (Figures 2a and 2b).

Meta-analysis

Three studies[24, 27, 28] provided sufficient data to allow meta-analysis to be performed on %EWL at 1 month, representing 170 patients (LVSG n=89; LRYGB n=81). A non-statistically significant reduction in WMD was observed in favor of LRYGB (WMD 0.71; 95% CI -2.69, 4.11; p=0.7) using the REM, while the IVhet model provided a similar but more conservative estimate (WMD= 0.84; 95% CI -2.58, 4.25; p=0.6). Moderate heterogeneity was observed (Q=3.81 p=0.1; I^2 =47.4%).

Four studies(22, 24, 27, 28) representing 403 patients (LVSG n=211; LRYGB n=192) provided sufficient data to allow meta-analysis to be performed on %EWL at 3 month. %EWL favored LRYGB (WMD 1.15; 95% CI -3.26, 5.56; p=0.6) using the REM, while the IVhet model provided a considerably different effect estimate though 95% CI remained similar to that of the REM (WMD= 0.43; 95% CI -3.98, 4.85, p=0.8). Moderate and statistically significant heterogeneity was observed (Q=10.96 p=0.01; I^2 =73.9%).

Three studies[22, 24, 27] provided sufficient data to allow meta-analysis to be performed on %EWL at 6 month, representing 351 patients (LVSG n=186; LRYGB n=165). A non-statistically significant reduction in WMD was observed in favor of LRYGB (WMD 0.51; 95% CI -4.97, 6.0; p=0.8) using the REM, while the IVhet model provided a considerably different effect estimate though 95% CI remained similar to that of the REM (WMD= 0.18; 95% CI -5.77, 6.12, p=0.9). A significant degree of heterogeneity was observed (Q=7.15 p=0.03; I^2 =69.26%).

Only two studies[24, 27] provided sufficient data to allow meta-analysis to be performed on %EWL at 12 months, representing 111 patients (LVSG n=57; LRYGB n=54). A statistically significant reduction in WMD was observed in favor of LRYGB (WMD 7.61; 95% CI -0.12, 15.3; p=0.05) using the REM. The estimates obtained using the IVhet model provided identical results as the REM. No heterogeneity was identified (Q=0.51 p=0.5; I^2 0% not computable) (Figure 3).

Total Weight loss

Systematic Review

Total weight loss was reported by three studies[19, 23, 26]: Keider et al[26] reported this as their only primary weight loss outcome, and was the only study to report this outcome on more than one time point post baseline. They observed an average total weight loss of ~24 kg and ~21 kg at

3 months and total of ~34 kg and ~30 kg weight loss at 12 months in the LVSG and LRYGB groups respectively[26]. Peterli et al[23] reported total weight loss between baseline and 12 months to be ~36-37 kg post LVSG and ~40 kg post LRYGB, and state no further weight loss in those continuing follow up to the second and third year postoperatively. Finally Yang et al[19] reported total weight loss of ~25 kg post LVSG and ~30 kg post LRYGB at 3 years.

The average weight of subjects at the end of the 12 month follow up period was around 85-90 kg irrespective of which procedure was performed, and no procedure demonstrated superior weight loss outcomes to the other. The final weights at 3 years follow up reported by Yang et al[19] are lower at ~60-65 kg, however this cannot be directly compared to the 12 months results due to the ethnic differences between subjects, and should rather be interpreted in view of the lower baseline body weights in the Chinese subjects.

Meta-analysis

Only two studies[23, 26] provided sufficient information to allow meta-analysis to be performed on total weight loss at 12 months postoperatively: this represents 254 patients (LVSG n=125; LRYGB n=129). The WMD demonstrates no significant difference in total weight loss outcome (WMD 0.26; 95% CI -5.16, 5.69; p=0.9). While also not statistically significant, the IVhet model provides a WMD of 0.70, CI -4.80, 6.19 (p=0.8). Minimal heterogeneity was observed (Q=1.42 p=0.2; I^2 29.8%).

<u>BMI changes throughout follow up</u>

Systematic Review

BMI was reported in seven[19-26, 28] of the eight eligible studies at a range of time points between 1 month and 5 years postoperatively. Most studies reported results as means (±SD), while one reported median and range[21, 22] and another reported means with a range[28].

A review of the trends in BMI change throughout the follow up period indicates consistent weight loss in the order of 9.7 to 16.2 kg/m^2 (average 12.7 kg/m^2) post LVSG and 10.6 to 15.1 kg/m^2 (average 13.0 kg/m^2) post LRYGB in the 12 month postoperative period by the studies reporting this outcome[20, 23, 24, 26]. In the studies[19, 20, 23, 25] that report BMI outcomes at3 year follow up, reduction in BMI from baseline range from 9 to 15.3 kg/m^2 (average 11.2 kg/m^2) post LVSG and from 10.3 to 14.5 kg/m^2 (average 12.3 kg/m^2) post LRYGB. Between the 1 and 3 year time periods BMI is seen to stabilize and a slow upward trend in the weight gain in the order of 0.5 to 1.5 kg/m^2 and 0.5 to 1.3 kg/m^2 in LVSG and LRYGB respectively is noticed[20, 23]. This trend is seen to continue in to five years in the one study[20] that continue to follow up their patients with a gain of 3.4 kg/m^2 post LVSG and 2.7 kg/m^2 post LRYGB when considered from the lowest point at 12 months. Overall weight change represented by BMI appears reasonably comparable between procedures, with perhaps a slightly slower regain and marginally greater weight loss achieved with LRYGB on direct comparison. (Figures 4a and 4b).

<u>*Percent BMI loss (%BMIL)*</u>

Systematic Review

Three studies[23, 25, 27] reported %BMIL, reporting on varying time points from one months to three years postoperatively. Vix et al[27], the only study to report on multiple time points within the first postoperative year, described consistent and ongoing %BMIL at 1, 3, 6 and 12 month intervals in both LVSG and LRYGB. Peterli et al[23] reported outcomes between 1 and 3 years postoperatively and demonstrate what appears to be a stabilisation of %BMIL at ~ 70%BMIL following the first postoperative year.

Those that reported data at the same time points reported reasonably consistent outcomes at 12 months with ~70%BMIL for LVSG and ~70-75%BMIL for LRYGB[23, 27]. Greater variation in %BMIL between procedures was reported at 3 years between studies in the LRYGB groups with 61.4%BMIL reported by Kehagias et al[25], and 74.1%BMIL reported by Peterli et al[23]. %BMIL results at 3 years were consistently reported at ~70% for LVSG between the same studies[23, 25]. (Figures 5a and 5b).

Publication Bias

Funnel plots do not suggest the presence of publication bias as all points remain within the 95% CI limits in plots of Log OR against standard error. (Figure 6).

DISCUSSION

The results of this systematic review of RCTs reporting weight loss outcomes of up to 5 years postoperatively suggest that LRYGB and LVSG achieve comparable weight loss within the first postoperative year, and thereafter stabilize before transforming into slow trend towards slow weight recidivism. LRYGB may provide a greater degree of weight loss moving from 2 to 5 years postoperatively compared to LVSG, however due to the low number of RCTs studies reporting long term weight outcomes these results require further confirmation. Where meta-analysis was able to be performed, with the exception of %EWL at 12 months, no statistically significant differences were seen in weight loss outcomes. In the case of %EWL at 12 months, the meta-analysis favored LRYGB for superior weight loss outcomes compared to LVSG, however this should be viewed with caution due to the low number of studies for this time point (k=2) and the subsequently low number of study participants compared to other meta-analyses in this study (n=111).

Yip et al[29] in their systematic review and meta-analysis of RYGB versus (V)SG in obese patients with type 2 diabetes found comparable weight loss outcomes (%EWL and %EBMIL) between the procedures at 3 and 12 month follow-up, however longer term weight loss was not addressed as included studies did not report beyond three years postoperative follow up. Zhang et al [30] reviewed weight loss outcomes over a variety of follow-up intervals in a similar fashion to the present work but with different inclusion criteria, and likewise reported a trend for comparable weight loss outcomes between LRYGB and LVSG within the first year, with the separation in greater sustained weight loss becoming more apparent with LRGYB beyond this time point to 4 years follow up. Other systematic reviews and meta-analyses reporting weight loss outcomes at 2 year follow-up post-surgery[31] and for non-specified follow up time periods[32, 33] also report that greater weight loss outcomes were achieved with LRYGB compared to LVSG. However, it should be noted that these analyses included a variety study methodologies - including observational, cohort, case control studies as well as RCTs (level I to level IV evidence) and therefore the overall conclusions are unreliable and invalid from these analyses. The one meta-analysis currently in the literature using data solely from RCTs investigating this topic in patients exclusively in patients type 2 diabetes also found that %EWL was greater in LRYGB compared with LVSG[34].

While the results of this review suggest LRYGB and LVSG appear to be efficacious in bringing about desired weight loss in the short term, the trends described suggest that weight recidivism over time is a common feature to both procedures. Indeed Cooper et al[35] have recently described between 21% and 29% regain after the first year in patients who have undergone RYGB, with excessive weight gain reported in around one third of the 300 patients they followed for a mean of 7 years. Similarly weight gain following LVSG has also been reported between 15 to 75% at 5 year follow-up[36].

The aetiology driving weight recidivism for both procedures is considered to be multifactorial. Anatomical changes, such as an enlargement of the gastric pouch/gastrojejunostomy diameter may occur, in both procedures that reduce the restriction[37, 38]. Additionally the development of gastro-gastric fistulae have also been described to occur after RYGB which may further negate the effect of volume restriction[37]. Roux-en-Y gastric bypass has been associated with changes to gastric hormones such as increased Peptide YY (PYY), and animal studies have suggested that over time the reversal of early postoperative modifications to the PYY:leptin ratio may account for weight regain through a variety of mechanisms that promote energy conservation[39, 40]. Similarly gherlin levels, which stimulate appetite and have been shown to decrease initially post RYGB, are observed to slowly increase in the follow up period and may also contribute to weight regain as appetite suppression declines[37]. Similar mechanisms are hypothesized to occur post LVSG, however conflicting research presently exists and further studies are required[38, 41-43]. A further physiological mechanism currently being investigated is the role bile acid signalling that occurs following LVSG and its potential role in facilitating weight loss and metabolic improvements, particularly around fatty liver[43-45]. Failure to adhere to appropriate dietary behaviours post-surgery is also a significant contributor to weight regain in both procedures. Dietetic follow up has been observed to wane after two years postoperative follow up, with only 3% remaining in regular dietetic follow up at 5 years after RYGB[46]. Similarly, ongoing postoperative psychological support to facilitate lifetime behaviour change along with the management of concurrent psychological issues such as depression have been identified as important factors in sustained weight loss post bariatric surgery[37]. This is particularly the case for those patients identified as having binge eating or other maladapted eating behaviours preoperatively[47]. Structured postoperative programs providing psychological and combined pharmacological and lifestyle change interventions have been shown to be effective at reducing postoperative weight regain following a range of bariatric procedures[48-50]. These findings also highlight need for thorough preoperative dietetic and psychological assessment to identify behaviours and underlying conditions that may represent risks for weight recidivism postoperatively.

Our review, along with much of the literature in this area, suggests LRYGB may provide a comparatively greater degree of weight loss than LVSG in the long term. Considering the multiple mechanisms by which LRYGB facilitates weight compared to those of LVSG, it seems reasonable that the additional component of malabsorption may account for some of the results observed in this and other studies comparing the weight loss outcomes of each procedure. To date the longest follow up time period described by an RCT is 5 years. Longer term studies are required to better understand this trend, along with improved surveillance and reporting on the number of patients who go on to have further bariatric procedures to manage weight recidivism to allow an accurate assessment of the cost-effectiveness of bariatric surgery as a strategy in the battle against obesity.

Another issue that requires further description in the literature is attrition from longer term studies investigating weight loss outcomes in bariatric patients. It is interesting to note in the present work that of the four studies[19, 20, 23, 25] that report outcomes at 3 to 5 years postoperatively there is an obvious decline in number with each year of follow-up, ranging from 32 to 95%. While some studies manage loss to follow up by reporting results using intention to treat (ITT) statistics[19, 20, 24, 25], others[23] report only time points where 100% follow up is achieved (12 months). Loss to follow up creates major issues in accurately describing long term weight loss outcomes following bariatric procedures, and is an issue that needs innovative measures to address, both to improve the quality of research in this area and to achieve optimal clinical practice, as sustained follow up appears to be related to improved weight outcomes postoperatively[51].

There are a broad range of ethnicities covered by the included studies in this paper, which highlights the issue of an appropriate classification for obesity within different ethnic groups, and the potential for this to alter eligibility criteria for bariatric surgery in patients with diverse ethnic background. There is an increasing acknowledgement that having universal BMI cut offs to define obesity may not adequately reflect risk differences between ethnicity and gender[52]. A number of societies have already adopted ethnic specific BMI ranges in their clinical guidelines and definitions of obesity to reflect the literature in this area since the publication of WHO’s 2004 consensus paper maintaining an international standard[53-55]. These issues highlight the need for adoption of standardized measures of weight loss such as %EWL or %BMI in obesity and bariatric surgery research to ensure a standardized comparison can validly be made between studies of conducted in different ethnic groups and genders.

LIMITATIONS

We acknowledge, there are a number of potential factors that may confound our results obtained and conclusions drawn. First, the included studies covered a diverse range of ethnicities and comorbid conditions. We purposely did not control for these issues in an attempt to better reflect 'real life' clinical practice, however it is possible that with different metabolic responses in some studies with a high proportion of diabetic patients, or with different relative degrees of obesity in different ethnic groups, that this may impact the conclusions drawn. In any case it is likely to have contributed to the heterogeneity inherent in some of the described outcomes. Second is the slightly different surgical techniques described in the methodologies sections of the included studies. This highlights the variation in surgical practice for otherwise standard procedural terminology: this has obvious impacts for the interpretation of weight loss between studies outcomes. Third is the short duration of follow up reported by most studies. Of the nine studies meeting the criteria for inclusion, only three reported outcomes beyond 12 months postoperatively. In seeking long-term solutions for obesity management, it is essential that long-term postoperative outcomes be reported for sufficient durations in sufficient number of patients to allow informed decisions about to be made. Fourth is the potential impact of the moderate methodological quality of the included studies. Finally there remain a relatively small number of RCTs investigating this topic, and even fewer from which the data required to perform meta-analysis is available. This poses a limitation to the statistical power of the analyses performed.

CONCLUSIONS

In conclusion, this systematic review and meta-analysis of RCTs suggests that LRYGB and LVSG are comparable with regards to the weight loss outcomes in the short term, with LRYGB appearing achieving slightly greater weight loss over the longer period of time, however, more RCTs are required to confirm this. Slow weight recidivism is observed after the first postoperative year following both procedures. Long-term reporting of outcomes obtained from well-designed studies using ITT analyses are identified as a major gap in the literature at present. Lastly informed decision making based on true-cost benefits analysis for both of these procedures is required to streamline the best long-term weight loss procedure.

CONFLICT OF INTEREST DISCLOSURE

Emma Osland: no conflict of interest disclosed

Rossita Mohamad Yunus: no conflict of interest disclosed

Shahjahan Khan: no conflict of interest disclosed

Breda Memon: no conflict of interest disclosed

Muhammed Ashraf Memon: no conflict of interest disclosed

REFERENCES

1. World Obesity Federation [Internet]. London: About Obesity [updated 2015 Oct 10; cited 2016 January27]. Available from: http://www.worldobesity.org/resources/aboutobesity/

2. Organisation for Economic and Cooperation Development [Internet]. Paris: OBESITY Update June 2014: OECD Directorate for Employment, Labour and Social Affairs; 2014 [updated 2014; cited 2016 January27]. Available from: http://www.oecd.org/health/Obesity-Update-2014.pdf

3. Colquitt JL, Pickett K, Loveman E, Frampton GK. Surgery for weight loss in adults. The Cochrane database of systematic reviews. 2014;8:CD003641. PMID: 25105982.

4. Picot J, Jones J, Colquitt JL, Gospodarevskaya E, Loveman E, Baxter L, et al. The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: a systematic review and economic evaluation. Health technology assessment. 2009 Sep;13(41):1-190 PMID: 19726018.

5. Borisenko O, Adam D, Funch-Jensen P, Ahmed AR, Zhang R, Colpan Z, et al. Bariatric Surgery can Lead to Net Cost Savings to Health Care Systems: Results from a Comprehensive European Decision Analytic Model. Obesity surgery. 2015 Sep;25(9):1559-68. PMID: 25639648.

6. Regan JP, Inabnet WB, Gagner M, Pomp A. Early experience with two-stage laparoscopic Roux-en-Y gastric bypass as an alternative in the super-super obese patient. Obesity surgery. 2003 Dec;13(6):861-4. PMID: 14738671.

7. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Controlled clinical trials. 1996 Feb;17(1):1-12. PMID: 8721797.

8. DerSimonian R, Laird N. Meta-analysis in clinical trials. Controlled clinical trials. 1986 Sep;7(3):177-88. PMID: 3802833.

9. Doi SA, Barendregt JJ, Khan S, Thalib L, Williams GM. Advances in the meta-analysis of heterogeneous clinical trials I: The inverse variance heterogeneity model. Contemporary clinical trials. 2015 Nov;45(Pt A):130-8. PMID: 26003435.

10. Sutton AJ, Abrams KR, Jones D, R., Sheldon TA, Song F. Methods for Meta-analysis in Medical Research. Chichester: John Wiley and Sons Ltd; 2001.

11. Cochran WG. The combination of estimates from different experiments. Biometrics. 1954;10:101-29.

12. Hedges LV. Statistical Methods for meta-analysis. Orlando: Orlando Press; 1985.

13. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Statistics in medicine. 2002 Jun 15;21(11):1539-58. PMID: 12111919.

14. Huedo-Medina TB, Sanchez-Meca J, Marin-Martinez F, Botella J. Assessing heterogeneity in meta-analysis: Q statistic or I2 index? Psychological methods. 2006 Jun;11(2):193-206. PMID: 16784338.

15. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. Bmj. 1997 Sep 13;315(7109):629-34. PubMed PMID: 9310563.

16. Viechtbauer W. Conducting Meta-analyses in R with the metaphor package. J Stat Software; 2010.

17. Fischer L, Wekerle AL, Bruckner T, Wegener I, Diener MK, Frankenberg MV, et al. BariSurg trial: Sleeve gastrectomy versus Roux-en-Y gastric bypass in obese patients with BMI 35-60 kg/m^2- a multi-centre randomized patient and observer blind non-inferiority trial. BMC surgery. 2015;15:87. PMID: 26187377.

18. Biter LU, Gadiot RP, Grotenhuis BA, Dunkelgrun M, van Mil SR, Zengerink HJ, et al. The Sleeve Bypass Trial: a multicentre randomized controlled trial comparing the long term outcome of laparoscopic sleeve gastrectomy and gastric bypass for morbid obesity in terms of excess BMI loss percentage and quality of life. BMC obesity. 2015;2:30. PubMed PMID: 26316928.

19. Yang J, Wang C, Cao G, Yang W, Yu S, Zhai H, et al. Long-term effects of laparoscopic sleeve gastrectomy versus roux-en-Y gastric bypass for the treatment of Chinese type 2 diabetes mellitus patients with body mass index 28-35 kg/m^2. BMC surgery. 2015;15:88. PMID: 26198306.

20. Zhang Y, Zhao H, Cao Z, Sun X, Zhang C, Cai W, et al. A randomized clinical trial of laparoscopic Roux-en-Y gastric bypass and sleeve gastrectomy for the treatment of morbid obesity in China: a 5-year outcome. Obesity surgery. 2014 Oct;24(10):1617-24. PMID: 24827405.

21. Helmio M, Victorzon M, Ovaska J, Leivonen M, Juuti A, Jaser N, et al. SLEEVEPASS: a randomized prospective multicenter study comparing laparoscopic sleeve gastrectomy and gastric bypass in the treatment of morbid obesity: preliminary results. Surgical endoscopy. 2012 Sep;26(9):2521-6. PMID: 22476829.

22. Helmio M, Victorzon M, Ovaska J, Leivonen M, Juuti A, Peromaa-Haavisto P, et al. Comparison of short-term outcome of laparoscopic sleeve gastrectomy and gastric bypass in the treatment of morbid obesity: A prospective randomized controlled multicenter SLEEVEPASS study with 6-month follow-up. Scandinavian journal of surgery. 2014 Feb;103(3):175-81. PMID: 24522349.

23. Peterli R, Borbely Y, Kern B, Gass M, Peters T, Thurnheer M, et al. Early results of the Swiss Multicentre Bypass or Sleeve Study (SM-BOSS): a prospective randomized trial comparing laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass. Annals of surgery. 2013 Nov;258(5):690-4; PMID: 23989054.

24. Karamanakos SN, Vagenas K, Kalfarentzos F, Alexandrides TK. Weight loss, appetite suppression, and changes in fasting and postprandial ghrelin and peptide-YY levels after Roux-en-Y gastric bypass and sleeve gastrectomy: a prospective, double blind study. Annals of surgery. 2008 Mar;247(3):401-7. PMID: 18376181.

25. Kehagias I, Karamanakos SN, Argentou M, Kalfarentzos F. Randomized clinical trial of laparoscopic Roux-en-Y gastric bypass versus laparoscopic sleeve gastrectomy for the management of patients with BMI < 50 kg/m2. Obesity surgery. 2011 Nov;21(11):1650-6. PMID: 21818647.

26. Keidar A, Hershkop KJ, Marko L, Schweiger C, Hecht L, Bartov N, et al. Roux-en-Y gastric bypass vs sleeve gastrectomy for obese patients with type 2 diabetes: a randomised trial. Diabetologia. 2013 Sep;56(9):1914-8. PMID: 23765186.

27. Vix M, Liu KH, Diana M, D'Urso A, Mutter D, Marescaux J. Impact of Roux-en-Y gastric bypass versus sleeve gastrectomy on vitamin D metabolism: short-term results from a prospective randomized clinical trial. Surgical endoscopy. 2014 Mar;28(3):821-6. PMID: 24196556.

28. de Barros F, Setubal S, Martinho JM, Monteiro AB. Early Endocrine and Metabolic Changes After Bariatric Surgery in Grade III Morbidly Obese Patients: A Randomized Clinical Trial Comparing Sleeve Gastrectomy and Gastric Bypass. Metabolic syndrome and related disorders. 2015 Aug;13(6):264-71. PMID: 25919069.

29. Yip S, Plank LD, Murphy R. Gastric bypass and sleeve gastrectomy for type 2 diabetes: a systematic review and meta-analysis of outcomes. Obesity surgery. 2013 Dec;23(12):1994-2003. PMID: 23955521.

30. Zhang Y, Wang J, Sun X, Cao Z, Xu X, Liu D, et al. Laparoscopic sleeve gastrectomy versus laparoscopic Roux-en-Y gastric bypass for morbid obesity and related comorbidities: a meta-analysis of 21 studies. Obesity surgery. 2015 Jan;25(1):19-26. PMID: 25092167.

31. Zhang C, Yuan Y, Qiu C, Zhang W. A meta-analysis of 2-year effect after surgery: laparoscopic Roux-en-Y gastric bypass versus laparoscopic sleeve gastrectomy for morbid obesity and diabetes mellitus. Obesity surgery. 2014 Sep;24(9):1528-35. PMID: 24913240.

32. Li JF, Lai DD, Lin ZH, Jiang TY, Zhang AM, Dai JF. Comparison of the long-term results of Roux-en-Y gastric bypass and sleeve gastrectomy for morbid obesity: a systematic review and meta-analysis of randomized and nonrandomized trials. Surgical laparoscopy, endoscopy & percutaneous techniques. 2014 Feb;24(1):1-11. PMID: 24487151.

33. Li J, Lai D, Wu D. Laparoscopic Roux-en-Y Gastric Bypass Versus Laparoscopic Sleeve Gastrectomy to Treat Morbid Obesity-Related Comorbidities: a Systematic Review and Meta-analysis. Obesity surgery. 2016 Feb;26(2):429-42. PMID: 26661105.

34. Li JF, Lai DD, Ni B, Sun KX. Comparison of laparoscopic Roux-en-Y gastric bypass with laparoscopic sleeve gastrectomy for morbid obesity or type 2 diabetes mellitus: a meta-analysis of randomized controlled trials. Canadian journal of surgery Journal canadien de chirurgie. 2013 Dec;56(6):E158-64. PMID: 24284156.

35. Cooper TC, Simmons EB, Webb K, Burns JL, Kushner RF. Trends in Weight Regain Following Roux-en-Y Gastric Bypass (RYGB) Bariatric Surgery. Obesity surgery. 2015 Aug;25(8):1474-81. PMID: 25595383.

36. Braghetto I, Csendes A, Lanzarini E, Papapietro K, Carcamo C, Molina JC. Is laparoscopic sleeve gastrectomy an acceptable primary bariatric procedure in obese patients? Early and 5-year postoperative results. Surgical laparoscopy, endoscopy & percutaneous techniques. 2012 Dec;22(6):479-86. PMID: 23238373.

37. Dykstra MA, Switzer NJ, Sherman V, Karmali S, Birch DW. Roux en Y gastric bypass: how and why it fails? Surgery: Current Research. 2014;4(2):165-9.

38. Lee WJ, Almulaifi A. Recent advances in bariatric/metabolic surgery: appraisal of clinical evidence. Journal of biomedical research. 2015 Apr;29(2):98-104. PMID: 25859263.

39. Guijarro A, Suzuki S, Chen C, Kirchner H, Middleton FA, Nadtochiy S, et al. Characterization of weight loss and weight regain mechanisms after Roux-en-Y gastric bypass in rats. American journal of physiology Regulatory, integrative and comparative physiology. 2007 Oct;293(4):R1474-89. PMID: 17626126.

40. Meguid MM, Glade MJ, Middleton FA. Weight regain after Roux-en-Y: a significant 20% complication related to PYY. Nutrition. 2008 Sep;24(9):832-42. PMID: 18725080.

41. Langer FB, Reza Hoda MA, Bohdjalian A, Felberbauer FX, Zacherl J, Wenzl E, et al. Sleeve gastrectomy and gastric banding: effects on plasma ghrelin levels. Obesity surgery. 2005 Aug;15(7):1024-9. PMID: 16105401.

42. Pedersen SD. The role of hormonal factors in weight loss and recidivism after bariatric surgery. Gastroenterology research and practice. 2013;2013:528450. PMID: 24250335.

43. Ryan KK, Tremaroli V, Clemmensen C, Kovatcheva-Datchary P, Myronovych A, Karns R, et al. FXR is a molecular target for the effects of vertical sleeve gastrectomy. Nature. 2014 May 8;509(7499):183-8. PMID: 24670636.

44. Kohli R, Myronovych A, Tan BK, Salazar-Gonzalez RM, Miles L, Zhang W, et al. Bile Acid Signaling: Mechanism for Bariatric Surgery, Cure for NASH? Digestive diseases. 2015;33(3):440-6. PMID: 26045281.

45. Belgaumkar AP, Vincent RP, Carswell KA, Hughes RD, Alaghband-Zadeh J, Mitry RR, et al. Changes in Bile Acid Profile After Laparoscopic Sleeve Gastrectomy are Associated with Improvements in Metabolic Profile and Fatty Liver Disease. Obesity surgery. 2015 Sep 4. PMID: 26337697.

46. Freire RH, Borges MC, Alvarez-Leite JI, Toulson Davisson Correia MI. Food quality, physical activity, and nutritional follow-up as determinant of weight regain after Roux-en-Y gastric bypass. Nutrition. 2012 Jan;28(1):53-8. PMID: 21885246.

47. Kofman MD, Lent MR, Swencionis C. Maladaptive eating patterns, quality of life, and weight outcomes following gastric bypass: results of an Internet survey. Obesity. 2010 Oct;18(10):1938-43. PMID: 20168309.

48. Himes SM, Grothe KB, Clark MM, Swain JM, Collazo-Clavell ML, Sarr MG. Stop regain: a pilot psychological intervention for bariatric patients experiencing weight regain. Obesity surgery. 2015 May;25(5):922-7. PMID: 25750006.

49. Schwartz J, Chaudhry UI, Suzo A, Durkin N, Wehr AM, Foreman KS, et al. Erratum to: Pharmacotherapy in Conjunction with a Diet and Exercise Program for the Treatment of Weight Recidivism or Weight-Loss Plateau Post-Bariatric Surgery: A Retrospective Review. Obesity surgery. 2016 Feb;26(2):452-8. PMID: 26615406.

50. Schwartz J, Suzo A, Wehr AM, Foreman KS, Mikami DJ, Needleman BJ, et al. Pharmacotherapy in Conjunction with a Diet and Exercise Program for the Treatment of Weight

Recidivism or Weight Loss Plateau Post-bariatric Surgery: a Retrospective Review. Obesity surgery. 2016 Feb;26(2):452-8. PMID: 26615406.

51. Spaniolas K, Kasten KR, Celio A, Burruss MB, Pories WJ. Postoperative Follow-up After Bariatric Surgery: Effect on Weight Loss. Obesity surgery. 2016 Jan 12 Epub ahead of print. PMID: 26757922.

52. Carpenter CL, Yan E, Chen S, Hong K, Arechiga A, Kim WS, et al. Body fat and body-mass index among a multiethnic sample of college-age men and women. Journal of obesity. 2013:790654. PMID: 23691288.

53. Misra A, Chowbey P, Makkar BM, Vikram NK, Wasir JS, Chadha D, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. The Journal of the Association of Physicians of India. 2009 Feb;57:163-70. PMID: 19582986.

54. Consultation WHOE. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet. 2004 Jan 10;363(9403):157-63. PMID: 14726171.

55. International Diabetes Federation [Internet]. Brussels: The IDF consensus worldwide definition of metabolic syndrome. 2006. [updated 2006; cited 2016 March 4] Available from: https://www.idf.org/webdata/docs/MetS_def_update2006.pdf