Antral resection vs. antral preservation during laparoscopic sleeve gastrectomy for severe obesity: systematic review and meta-analysis

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Abstract:

Background: Laparoscopic sleeve gastrectomy (LSG) is an effective operation for severe obesity. There is controversy as to the optimal technical approach with some advocating sparing of the gastric antrum (antral-preserving, AP) and others supporting commencement of resection close to the pylorus (antral-resecting, AR). The objective of this systematic review was to investigate the effect on peri-operative complications and medium-term outcomes of AR compared to AP.

Methods: We included studies comparing AR (2 to 3cm from pylorus) with AP (> 5cm from pylorus) in patients undergoing primary sleeve gastrectomy for obesity. Medline, EMBASE and Cochrane Review databases from 1946 to April 2017 were searched for studies. Risk of bias within and across studies was assessed using validated scoring systems (Jadad, USPSTF and GRADE).

Results: Eight studies, involving 619 participants, were included: six randomized controlled trials (RCTs) and two retrospective cohort studies. AR was associated with non-significant and significant improvement in weight loss at 12 and 24 month follow-up respectively (12 months: seven studies, 574 subjects, standardized mean difference [SMD] of percentage excess weight loss [%EWL] 0.67 (-0.05 to 1.38); and 24 months: four studies, 412 subjects, SMD of %EWL 0.95 (0.32 to 1.58)), without altering risk of peri-operative bleeding, leak or de novo gastro-oesophageal reflux disease (GORD). Radical antral resection was associated with better weight loss at 24 months after surgery compared to antral preservation, without increased risk of surgical complications.

Discussion:
Limitations of this analysis include study bias (failure to describe method of randomization and/or dropouts), and imprecision due to small overall number of complications. The

cumulative evidence is that radical antral resection leads to improved medium-term weight loss, with no change in surgical risk profile.

Registration:
PROSPERO: CRD42016048657

Main text:

Introduction:

Laparoscopic sleeve gastrectomy (LSG) is an effective operation for morbid obesity, with comparable short-term outcomes to Roux-en-Y gastric bypass (RYGB) for weight loss (1,2) and diabetes resolution (3,4).

In recent years the number of LSG performed has dramatically increased; LSG was the most commonly performed bariatric operation in the USA in 2013 (5). Despite its popularity, the operation is far from standardised and practice varies widely between surgeons (6).

One aspect of controversy is the extent to which the antrum is excised. Proponents of a radical antral resection argue that more restriction leads to better weight loss (7). They point out that since LSG alone is purely restrictive, unlike when it is combined with small intestinal bypass in duodenal switch, the restriction must be profound (8). Opponents stress the importance of preserving the physiological emptying mechanism of the stomach, in order to avoid increased intraluminal pressure (9). Consequences of raised intraluminal pressure could potentially include staple-line leak in the short-term and gastro-oesophageal reflux in the longer term (10).

The objective of this systematic review and meta-analysis was to examine difference in complication rate and weight loss outcomes between antral-sparing (AP) and antral-excising (AR) LSG for obesity.

Methods:

Literature search:

This study was performed following the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) guidelines (11). The study has been registered with the Prospective Register of Systematic Reviews, PROSPERO identification code CRD42016048657. Study titles were searched using MEDLINE (1946 to April 2017) and

Embase (1947 to April 2017) databases using Ovid Online (Ovid Technologies Inc, 2016) in May 2017. Key term combinations were as follows: 'antr* preserv* OR antr* exc* OR antr* resect* OR antr* spar* OR antrectomy' AND 'gastr* adj5 sleeve' AND 'obes*'. No language restrictions were applied. Cochrane database and reference lists of original articles were additionally searched (to April 2017). Published conference abstracts were included where there was sufficient information provided for eligibility to be assessed.

Eligibility criteria:

Studies of participants undergoing primary laparoscopic sleeve gastrectomy for obesity were included. Studies designed to compare the difference in outcome between a radical antral resection (defined as commencing the staple line 2-3cm from the pylorus: AR) and an antral-sparing resection (defined as commencing the staple line >5cm from the pylorus: AP) were included. Retrospective analyses of cohorts in which extent of antral resection was one of several technical and clinical variables were not included.

Outcomes assessed were % excess weight loss (%EWL) at 12 months post-LSG, %EWL at 24 months post-LSG, post-operative staple line bleed, staple line leak, 30-day mortality, and incidence of de novo gastro-oesophageal reflux disease (GORD). Studies which did not report any of these outcomes were excluded.

Study selection:

Two authors screened all titles and abstracts for relevance. Only clearly irrelevant material was excluded at this stage. Two authors independently screened the full texts, assessing eligibility for inclusion. Any differences were resolved by discussion and consensus. Where necessary, study data was confirmed with the corresponding author.

The following data were retrieved where reported on a piloted spreadsheet: date of publication, study design, randomisation method, number of randomised patients, definition of AR/AP used by study authors, demographics including pre-operative BMI of patients, staple-line leaks, staple-line bleeds, 30-day post-operative mortalities, de-novo GORD, %EWL at 12 months, %EWL at 24 months and other outcomes.

Quality assessment of studies:

Risk of bias was assessed on the study level for all included studies, using the Jadad scoring system for randomised controlled trials (RCTs) (12) and the US Preventive services Task Force (USPSTF) Quality Rating Criteria for cohort studies (13). The Jadad score is a validated tool to assign a score between 0 (weakest) and 5 (strongest) based on the quality of study design and the USPSTF have validated a similar tool for case-control studies where studies are graded 'good', 'fair' or 'poor' depending on fulfilment of internal validity criteria.

Risk of bias across studies was evaluated using guidance from the Grading of Recommendations Assessment, Development and Evaluation working group (GRADE) (14,15). On the basis of overall quality of evidence, confidence in each outcome measure can be classified into one of four levels – high, moderate, low and very low.

Subgroup analysis was planned to investigate causes of heterogeneity, where found to be significant in initial analysis. This was planned for measures of trial quality: RCT or not, and Jadad score. It was also planned for other technical variables that have been associated with differences in likelihood of adverse outcome: bougie size and presence of staple-line reinforcement (SLR) (16).

Statistical analysis:

Meta-analysis was used to evaluate the effect of radical antral resection on %EWL at 12 months, early complications and incidence of de novo GORD. Data was analysed on an intention-to-treat basis where possible. STATA 14 was used to estimate summary measures with 95% confidence intervals: standardised mean differences (SMD) and pooled relative risk (RR) for continuous and dichotomous variables respectively. As AR is considered the intervention, and AP the comparator, RRs are reported as AR/AP ratios.

The I^2-statistic was used to assess the impact of heterogeneity on the analysis. Heterogeneity was considered significant when I^2 was greater than 50%. A random effects model was used to calculate the overall effect. Meta-regression to explore for the cause of heterogeneity, where significant, was planned.

Results:

Study selection:

The search yielded 197 articles. After de-duplication and exclusions (Figure 1), a total of eight studies remained which provided data for a total of 619 patients (7,10,17-22). Table 1 summarises the participants, interventions and outcomes of eligible studies. Given the small number of included studies, tests for funnel plot asymmetry were not performed.

Risk of bias within studies:

Risk of bias according to the Jadad score is summarised in Table 2 for the six randomised controlled trials (RCTs). All RCTs scored 3 or less: this can be attributed to a lack of double-blinding in any of the trials, and to two of the trials consisting of abstracts only, with a consequent lack of methodological detail (18,19).

Two cohort studies were selected for inclusion (17,22). Obeidat et al analysed two consecutive single-centre, single-surgeon cohorts, in which there was an isolated change in practice from 6-cm antral resection (AP) to 2cm antral resection (AR). The two groups were comparable pre-operatively. Yormaz et al analysed two groups of patients for which operative technique was consistent apart from antral length, and who were pre-operatively demographically similar. In this study no information was given regarding how patients were allocated to the two groups but loss to follow-up reasons were given and there was no evidence of systemic bias. Both studies were rated as 'good' according to the USPSTF Quality Rating Criteria.

Weight loss at 12 months post-surgery (12 month %EWL) (Figure 2):

Seven studies reported on this outcome, five of which were RCTs ((7,10,18,20,21). Only one RCT found a statistically significant difference in 12 month %EWL and this was in favour of AR (10). Both cohort studies (17,22) found a statistically significant difference in favour of AR for this outcome.

Meta-analysis for weight loss at 12 months post-surgery demonstrated non-significantly better weight loss for AR both with RCTs only (SMD 0.32, CI -0.02 to 0.67; p=0.68), and also with inclusion of the cohort studies (SMD 0.67; CI -0.05 to 1.38; p=0.67).

For the RCT data alone there was moderate heterogeneity (I^2 = 51.4%) but the effect size was mostly favouring or close to null. For all studies combined heterogeneity was high (I^2 = 93.4%): again both studies found effect sizes favouring the intervention, but the effect size of one study was very large (SMD 2.64; CI 2.20 to 3.08). Removing this study from analysis (Appendix 1) preserved the significant effect in favour of AR but substantially reduced heterogeneity (SMD 0.40, CI 0.12 to 0.69, I^2 =48.2%). The residual heterogeneity could mainly be explained by small study size, with some contribution from study type and age of patients.

<u>Weight loss at 24 months post-surgery (24 month %EWL):</u>

Four studies reported on this outcome, two of which were RCTs (10,19) (Figure 3). Both RCTs found that AR was associated with increased 24 month %EWL than AP although this was only statistically significant in one (10). The two cohort studies (17,22) also both reported significantly greater 24 month %EWL with AR when compared to AP.

Meta-analysis for weight loss at 24 months post-surgery demonstrated increased 24 month %EWL with AR (SMD 0.95; 95% CI 0.32 to 1.58; p=0.003). There was significant heterogeneity for both overall and RCT-only analyses. This can again be explained by different study type and small study size, with a low number of included studies.

<u>Incidence of staple-line leak (figure 4):</u>

Four studies reported incidence of staple-line leak (10,17,20,22). Three showed a trend towards higher risk of leak in patients undergoing AR when compared to AP, however the number of leaks was low (seven in total across all studies), confidence intervals were high and none reached statistical significance.

Meta-analysis for this outcome showed no significant increased risk for leak with AR compared to AP (RR 1.87; 95% CI 0.46 to 7.61), with no significant heterogeneity.

<u>Incidence of staple-line bleed (figure 5):</u>

Five studies reported on staple-line bleed (7,10,17,20,22). No difference was seen between the two surgical approaches in incidence of bleed in any individual study or on meta-analysis (RR 1.27; CI 0.4 to 4.01). Total number of cases of bleed was low.

Incidence of post-operative de novo gastro-oesophageal reflux disease (GORD):

Three studies reported on incidence of GORD (7,10,17) (figure 6): There was no statistically significant difference between the two surgical techniques in terms of GORD incidence demonstrated in any individual study or on meta-analysis (RR 0.69; CI 0.26 to 1.82).

Sub-group analysis and risk of bias across studies:

Sub-group analysis was performed for the factor 'RCT or not' for the outcomes of %EWL (see above). Jadad score was 3 or below for all studies, and so subgroup analysis for this factor was omitted. The other factors initially planned for sub-group analysis (bougie size and SLR) showed too much variability/ insufficient group sizes for this to be useful, given the small overall number of eligible studies.

Risk of bias across studies for each outcome measure is illustrated in table 3.

Discussion:

Eight studies comparing radical antral resection with antral preservation during laparoscopic sleeve gastrectomy for morbid obesity demonstrated a probable improved weight loss with AR (moderate to low quality evidence) and no evidence of difference in rate of staple-line bleed, leak or post-operative de novo GORD (very low quality evidence).

The main strength of this analysis is that it is the first systematic review and meta-analysis of outcomes following the two operative strategies. The search was comprehensive, rigorous pre-defined meta-analysis was performed and quality of evidence has been probed using the GRADE approach. As sleeve gastrectomy becomes increasingly popular as a treatment for obesity, optimizing the operative technique according to judicious appraisal of the available evidence is essential. This analysis demonstrates that AR is associated with improved weight loss, without evidence of increased complications. This is of considerable clinical relevance to surgeons and patients.

The main limitations of this review are those of the primary studies. Small numbers of patients combined with low incidence of complications leads to imprecision in outcome data. There was also considerable risk of bias in the included RCTs with method of randomization not described in several and poor detail regarding dropouts/ withdrawals. As with other surgical RCTs, challenges related to the complexity of surgical interventions are difficult to circumvent (23). In this case, the use of AR or AP is one variable which is likely to interact with other demographic and technical variables to give overall risk of outcome. Although planned, it was not possible to perform subgroup analyses to address some of these potential confounders because of the small numbers of studies and cases eligible for inclusion.

In conclusion, AR is likely to be associated with improved short-medium term excess weight loss following sleeve gastrectomy for morbid obesity when compared with AP. Further research involving larger-scale RCTs are indicated.

Figure 1: PRISMA flow diagram to illustrate study selection

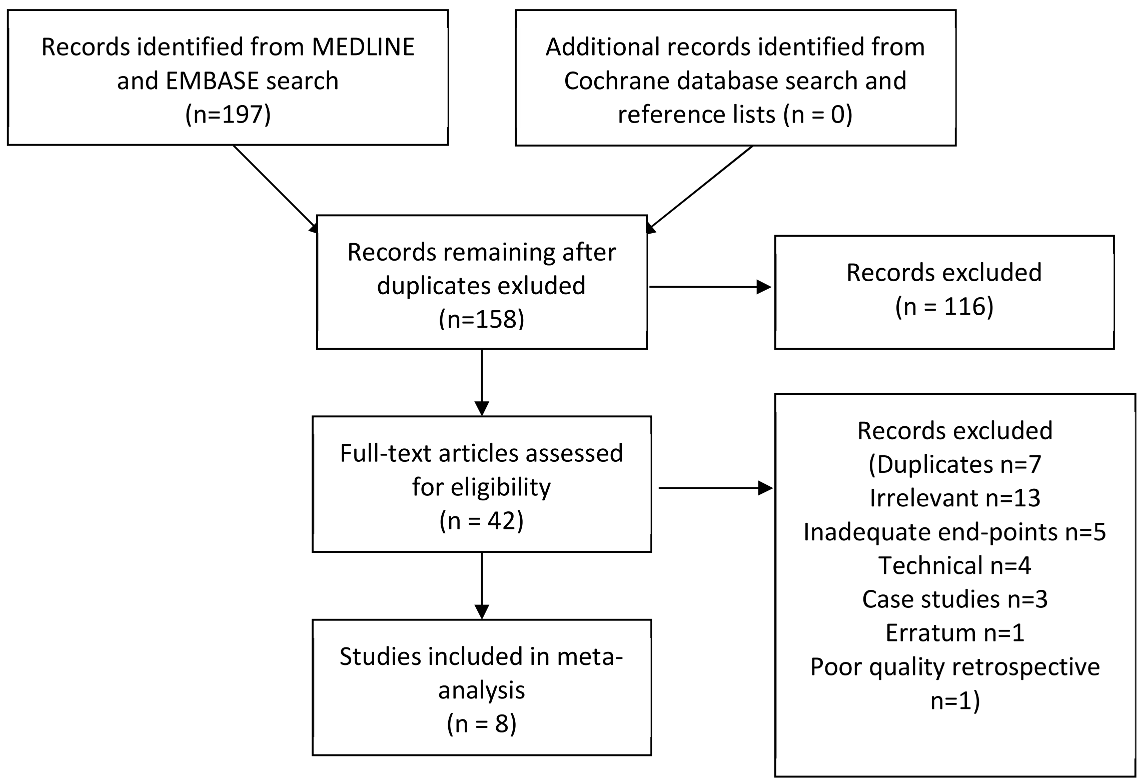


Figure 2: Weight loss at 12 months post-surgery

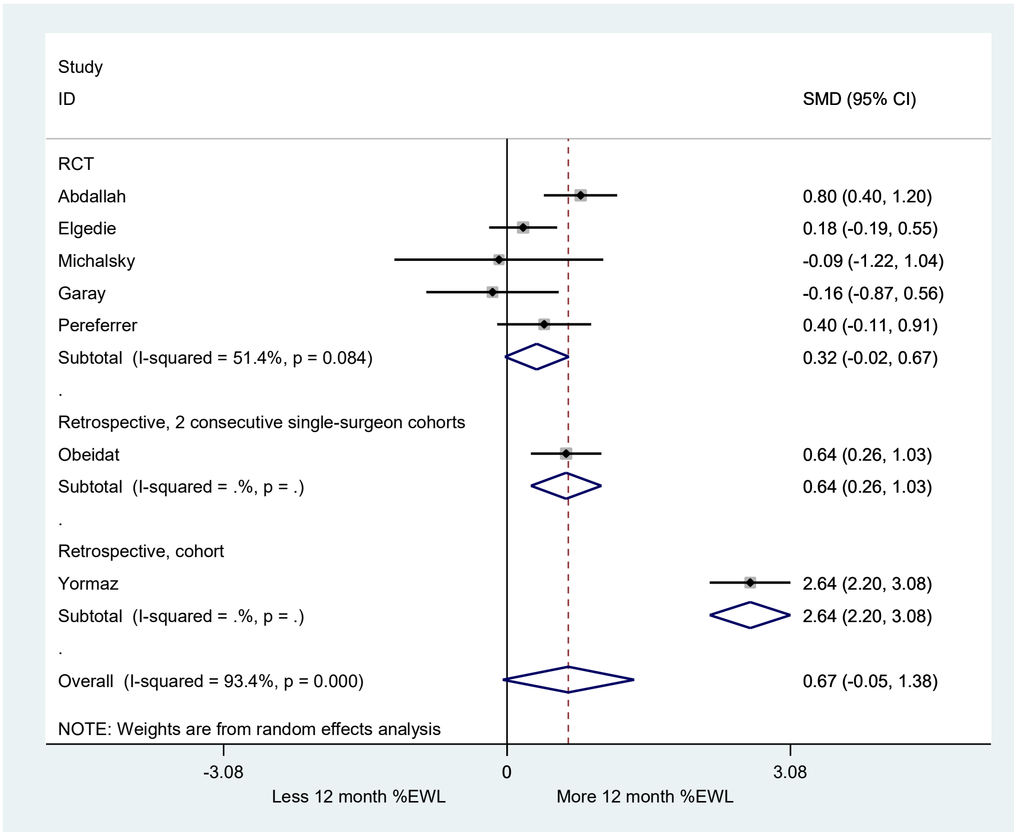


Figure 3: Weight loss at 24 months post-surgery

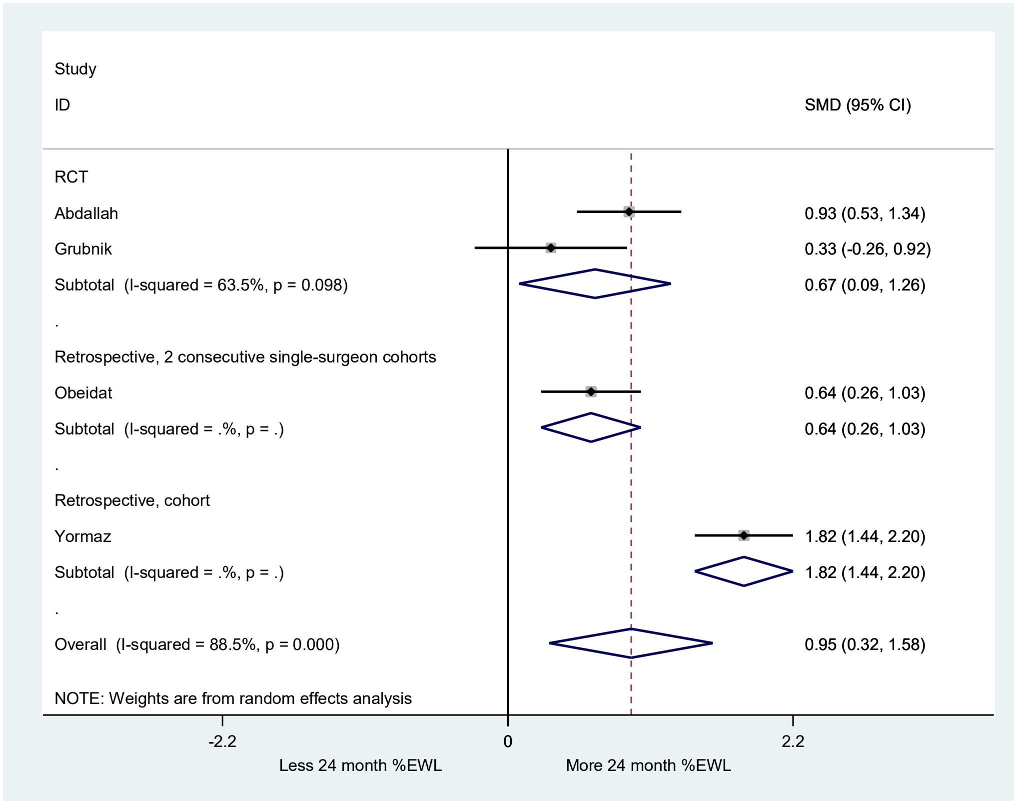


Figure 4: Incidence of staple-line leak

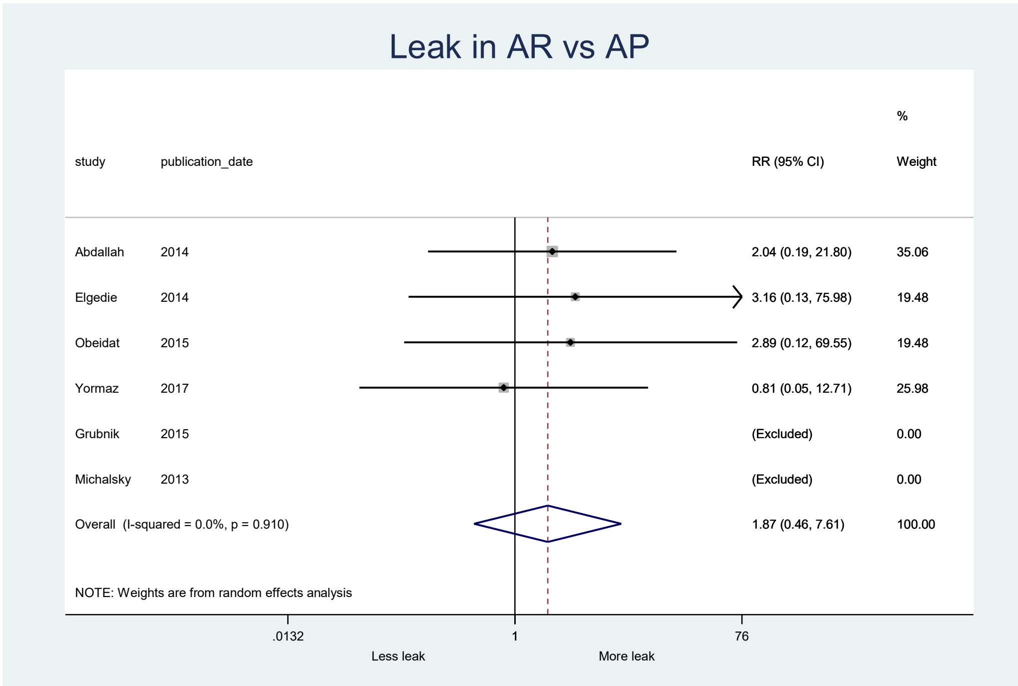


Figure 5: Incidence of staple-line bleed

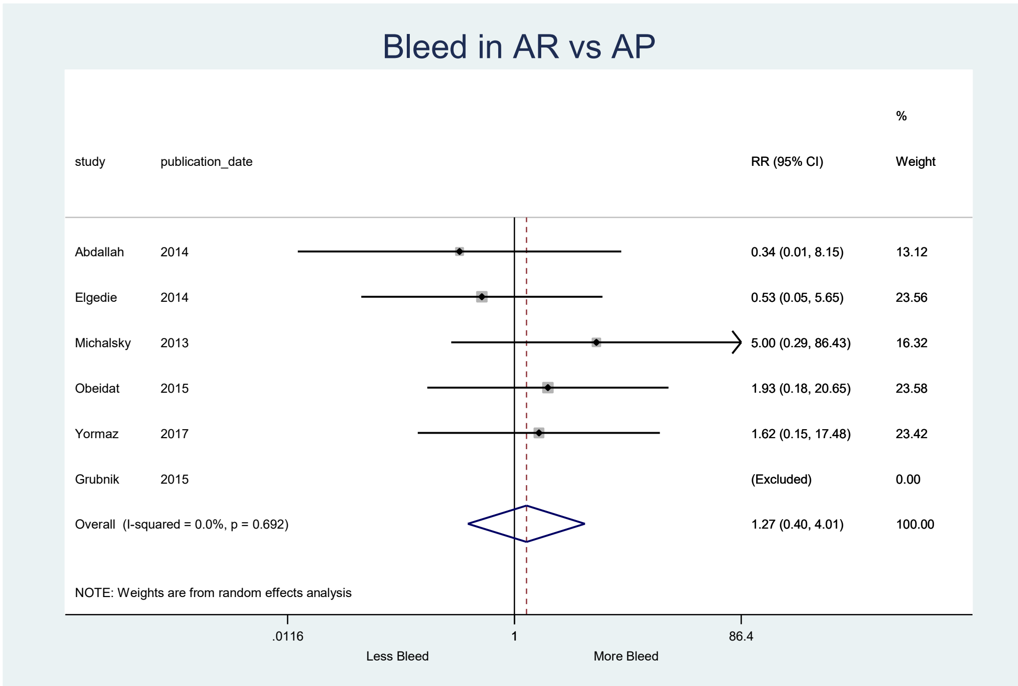


Figure 6: Incidence of post-operative de novo gastro-oesophageal reflux disease

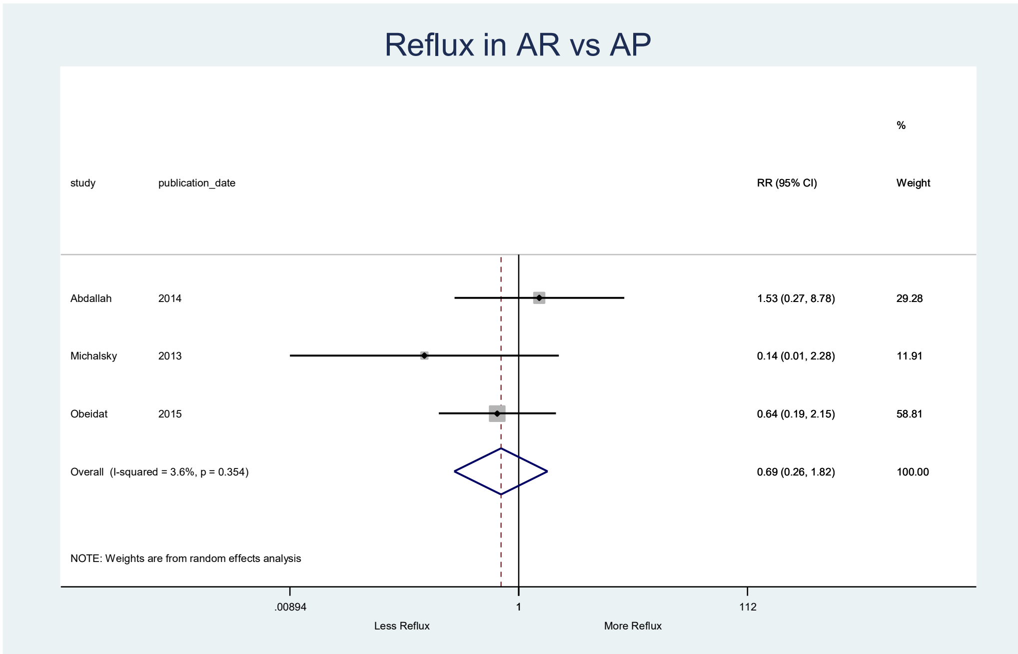


Table 1: characteristics of included studies

Reference (full-length paper unless otherwise indicated)	Number treated	Number completing study (number in intervention group – AR)	Definition of intervention (AR) and comparator (AP) in cm from pylorus	Pre-operative BMI in kg/m2 mean (SD)	Staple line reinforcement	Bougie size	Mean %Excess weight loss (SD) at 12 months post-surgery (all patients)	Mean %Excess weight loss (SD) at 24 months post-surgery (all patients)	Total early mortality (% of cases)	Total Leak (% of cases)	Total Bleed (% of cases)	Total de novo GORD (% of cases)	Jadad score
Abdallah	105	105 (52)	2cm vs 6cm	51.7 (7.5)	Not routine	38F	57.8 (16)	66.5 (12.7)	1 (1.0)	3 (2.9)	1 (1.0)	5 (4)	3
Elgeidie	114	106 (55)	2cm vs 6cm	44.8	Not routine	38F	66.1	Not given	1	1 (0.9)	3 (2.7)	Not given	2
Garay (abstract)	30	30 (14)	2cm vs 5cm	Not given	Not detailed	Not detailed	57.7	Not given	Not given	Not given	Not given	Not given	1

Grubnik *(abstract)	45	45 (22)	2cm vs 6cm	49.6 (6.8)	Not detailed	Not detailed	Not detailed	56.4	0 (0)	0 (0)	0 (0)	Not given	1
Michalsky	12	12 (6)	2.5cm vs 6cm	41.4	Not routine	36F	61.8	Not detailed	0 (0)	0 (0)	2 (16.7)	3 (25)	2
Obeidat	125	110 (56)	2cm vs 6cm	46.1 (7.9)	Oversewn	38F	72.9 (23.5)	73.2 (27.3)	0 (0)	1 (1.0)	3 (2.7)	10 (9)	NA (cohort study)
Pereferrer	60	59 (30)	3cm vs 8cm	51.1	Seamguard	38F	60.5[&]	Not detailed	0 (0)	Not detailed	Not detailed	Not detailed	3
Yormaz	168	152 (84)	2cm vs 6cm	48.8 +/- 5.3	V-loc wound closure device	36F	56.3		0 (0)	2	3	Not detailed	NA (cohort study)

* No leak or bleed assumed from statement in abstract 'no serious postoperative complications in both groups'. Author uncontactable to clarify.

[&] %EWL using IDW based on Metropolitan life tables (2 calculations of EWL using different IDW were given in this paper)

Table 2: risk of bias in included randomised controlled trials (Jadad score)

Reference	Described as randomised?	Adequate method of randomisation? (One point deducted if inappropriate)	Described as double-blind?	Adequate method of double-blinding? (One point deducted if inappropriate)	Description of dropouts/ withdrawals?	Jadad score
Abdallah	Yes	Yes	No	No	No dropouts	3
Elgeidie	Yes	Yes	No	No	Yes	3
Garay	Yes	Not described	No	No	No statement	1
Grubnik	Yes	Not described	No	No	No statement	1
Michalsky	Yes	Not described	No	No	No withdrawals	2
Pereferrer	Yes	Yes	No	No	Yes	3

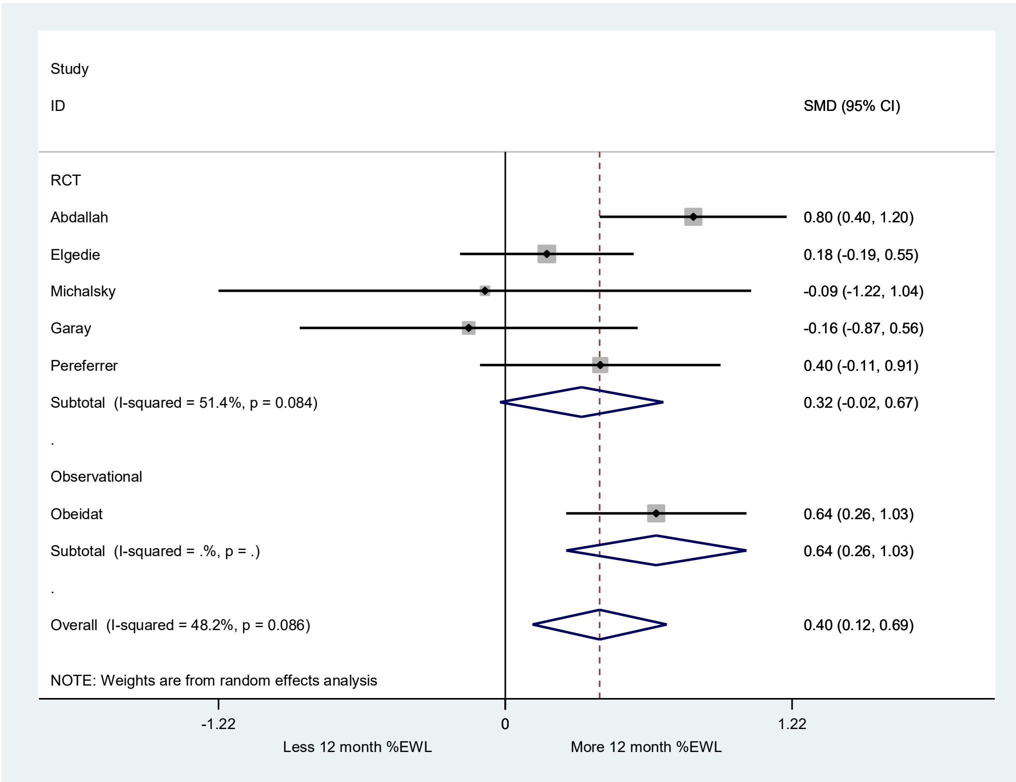
Table 3: GRADE evidence profile:

Outcome	Risk of bias*	Inconsistency	Indirectness	Imprecision**	Publication bias	Classification
12 month %EWL	Serious limitations	Serious limitations (inconsistent Forrest plot estimates)	No serious limitations	No serious limitations	Undetected	Low
24 month %EWL	Serious limitations	Serious limitations (heterogeneity)	No serious limitations	No serious limitations	Undetected	Moderate
Staple-line leak	Serious limitations	No serious limitations	No serious limitations	Very serious limitations	Undetected	Very low
Staple-line bleed	Serious limitations	No serious limitations	No serious limitations	Very serious limitations	Undetected	Very low
GORD	Serious limitations	No serious limitations	No serious limitations	Very serious limitations	Undetected	Very low

* For most studies there was an inadequate method of randomization (if at all) and no blinding in any study

** For dichotomous outcomes the number of events was very low so results are imprecise

Appendix 1: Weight loss at 12 months post-surgery with one retrospective study (Yormaz et al) removed



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