



A Systematic Review and Meta-Analysis of the Effect of Roux-en-Y Gastric Bypass on Barrett's Esophagus

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Abstract

Background Obesity is associated with a twofold risk of gastroesophageal reflux disease (GERD) and thrice the risk of Barrett's esophagus (BE). Roux-en-Y gastric bypass (RYGB) leads to weight loss and improvement of GERD in population with obesity, but its effect on BE is less clear.

Methods Bibliographic databases were searched systematically for relevant articles till January 31, 2019. Studies evaluating the effect of RYGB on BE with preoperative and postoperative endoscopy and biopsy were included. Study quality was assessed using the Methodological Index for Non-Randomized Studies (MINORS) tool. Meta-analysis was conducted using Mantel-Haenszel, random effects model and presented as risk difference (RD) or odds ratio (OR) with 95% confidence intervals.

Results Eight studies with 10,779 patients undergoing RYGB reported on 117 patients with BE with follow-up of > 1 year. Significant regression of BE after RYGB was observed (RD - 0.56.95% c.i. - 0.69 to - 0.43; $P < 0.001$). Subgroup analysis showed regression of both short-segment BE [ssBE] (RD - 0.51.95% c.i. - 0.68 to - 0.33; $P < 0.001$) and long-segment BE [lsBE] (RD - 0.46.95% c.i. - 0.71 to - 0.21; $P < 0.001$). RYGB also caused improvement in GERD in patients of BE (RD - 0.93, 95% c.i. - 1.04 to - 0.81; $P < 0.001$). RYGB was strongly associated with regression of BE compared with progression (OR 31.2.95% c.i. 11.37 to 85.63; $P < 0.001$).

Conclusions RYGB leads to significant improvement of BE at > 1 year after surgery in terms of regression and resolution of the associated GERD. Both ssBE and lsBE improve after RYGB significantly.

Keywords Gastric bypass · Roux-en-Y gastric bypass · Barrett's esophagus · Gastroesophageal reflux · Meta-analysis

Introduction

Barrett's esophagus (BE) is an acquired condition of the esophagus in which the normal distal squamous epithelial

lining is replaced by the metaplastic columnar epithelium, which is visible endoscopically (≥ 1 cm) above the gastroesophageal junction and confirmed histopathologically from esophageal biopsies [1]. Long-standing

Suggested text for special media/twitter: Roux-en-Y Gastric Bypass leads to regression of Barrett's Esophagus in more than 50% patients.

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gastroesophageal reflux disease (GERD) leads to chronic inflammatory changes in the lower esophagus due to exposure to gastric contents, which may eventually lead to metaplastic transformation [2, 3]. GERD in patients with BE appears to be more severe and more frequently associated with complications like stricture, ulcer, or dysplasia than in patients without columnar mucosa [3]. In spite of the more severe reflux, symptoms of GERD are often less pronounced or even completely absent in patients with BE due to decreased sensitivity of the columnar epithelium to gastric contents. One of the major concerns about BE is its risk of malignant transformation to dysplasia and esophageal adenocarcinoma (EAC). This risk is dependent on the length of BE and long-segment Barrett's esophagus (lsBE), defined as maximal length of BE ≥ 3 cm, and carries a higher risk of malignant transformation than short-segment Barrett's esophagus (ssBE), defined as BE length of < 3 cm [1, 4]. The estimated annual rate of progression of BE to EAC in the western world is 0.07%/year for ssBE and 0.25%/year for lsBE [4].

Another risk factor common to both BE and EAC is obesity. The prevalence of BE is between 0.5 and 2% in an unselected population; however, in those with GERD, the prevalence is higher ranging between 5 and 15% [5, 6]. Studies have confirmed that GERD is approximately twofold more common and BE three times more frequent in the obese population compared with individuals with normal weight [7, 8]. Furthermore, obesity (BMI > 30 kg/m²) increases the risk EAC by a relative risk of 2.4 to 2.8 [9, 10]. Current guidelines on BE advocates regular endoscopic screening with esophageal biopsies to detect field changes or a possible transformation to EAC at an early stage [1, 11].

Roux-en-Y gastric bypass (RYGB) is the second commonest bariatric procedure worldwide [12]. Though its role in the management of obesity and GERD is well established, its effect on BE is not yet fully understood. It also appears to be more effective than sleeve gastrectomy, now the most commonly performed bariatric procedure, in the resolution of GERD [13]. In spite of its well-defined role in inducing weight loss and improving GERD in patients with obesity, there is a paucity of literature on its effect on BE. It can be hypothesized that by reducing reflux, it can potentially lead to regression of BE. Existing literature shows a positive effect of RYGB on BE by inducing its regression, but most studies evaluating this effect are of low quality with few numbers of patients [14, 15]. Lack of routine endoscopic evaluation of the esophagus and stomach prior to bariatric surgery in many bariatric units further makes it extremely difficult to identify patients with BE preoperatively.

The aim of this systematic review and meta-analysis was to evaluate the effect of RYGB on BE.

Methods

Eligibility Criteria

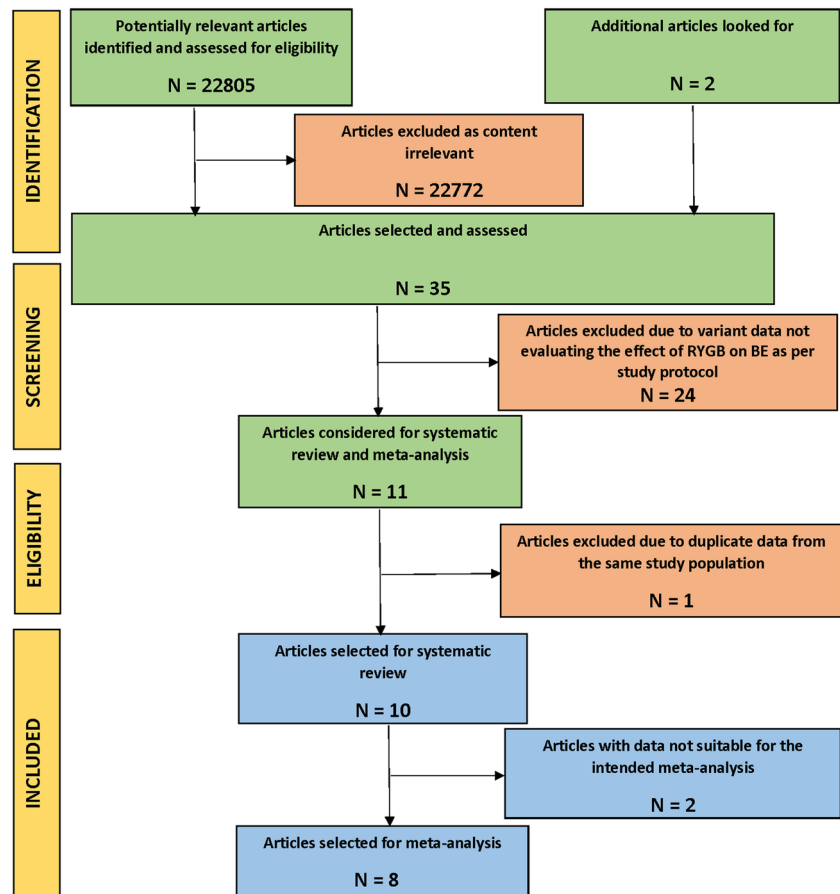
The research question was formulated based on Population, Intervention, Comparison, Outcome, and Study design (PICOS) strategy [16, 17]. The population comprised adult patients undergoing RYGB with known BE diagnosed preoperatively on endoscopy and confirmed histologically. Intervention was RYGB done for the treatment of obesity or obesity-related comorbidities. Comparators were preoperative confirmation of BE on endoscopy and biopsy and postoperative response to RYGB with endoscopy and biopsy at least 1 year after surgery. Outcome of interest was regression of BE.

Data Search and Extraction

Published literature was searched for using MEDLINE, PubMed, Scopus (including Embase), Cochrane Central Register of Controlled Trials (CENTRAL), OpenGray, ScienceDirect, and SpringerLink databases without language restrictions till January 31, 2019. Manual searches were carried out for articles in relevant journals and reference lists in key articles. The retrieved studies were managed using the software, Zotero Standalone (version 4.0.29.10) for Windows (Centre for History and New Media, George Mason University, Fairfax, Virginia, USA). The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines was followed at the time of writing this manuscript [18]. MeSH terms used were “gastric bypass” OR “bariatric surgery” AND “Barrett's esophagus” OR “Gastroesophageal reflux.”

Studies evaluating the effect of RYGB on BE objectively with a preoperative confirmation of BE endoscopically and histologically and assessing the postoperative response to surgery with a repeat endoscopy at > 1 year after surgery were considered for the meta-analysis. Regression of BE was defined as histological regression of intestinal metaplasia to normal squamous mucosa, or from dysplasia to intestinal metaplasia or normal squamous mucosa on postoperative endoscopic biopsy, or disappearance of BE or reduction in the length of BE by at least 3 cm on postoperative endoscopy. Subanalysis based on the length of BE (ssBE [< 3 cm] and lsBE [≥ 3 cm]) was done to evaluate the effect of RYGB on ssBE and lsBE respectively using the same eligibility criteria. Subanalysis was also done to evaluate the effect of RYGB on associated GERD in the selected cohort of patients with BE. Improvement in GERD after RYGB was defined as improvement in symptoms of reflux after surgery, or improvement in endoscopic stigmata of GERD such as esophagitis, esophageal ulcer, and peptic stricture, or improvement in GERD demonstrated by pH study.

Fig. 1 Flow of information in different phases of the systematic review and meta-analysis. RYGB, roux-en-Y gastric bypass; BE, Barrett's esophagus



Progression of BE was defined as dysplastic or cancerous transformation of intestinal metaplasia on postoperative endoscopic biopsy or an increase in the length of BE by 1 cm.

Case reports and reviews, studies reporting BE at only one time point (either preoperative or postoperative) such that a comparison of the outcome before and after RYGB could not be made, studies evaluating the effect of other bariatric procedures

Table 1 Characteristics of studies included for meta-analysis of Barrett's esophagus before and after Roux-en-Y gastric bypass

Year of the study	Study reference	Study type	Total RYGB performed	Number of patients with BE	Age	Gender (M/F)	Follow-up (in months)	Pre-RYGB BMI	Post-RYGB BMI
2006	Csendes et al.	Prospective	557	12	47.4	5:7	24	43.9	29.4
2008	Houghton et al.	Retrospective	1500	5	58.6	3:2	34	43	33
2010	Ben-Meir et al.	Retrospective	5916	14	NA	NA	>12	NA	NA
2012	Braghetto et al.	Prospective	NA	21	53.2	12:9	12	41.5	25.7
2012	Pereira et al.	Retrospective	896	14	47.8	5:9	24	41.8	28.9
2016	Dova et al.	Retrospective	NA	26	52.9	17:9	28.5	43.5	29.1
2017	Gorodner et al.	Retrospective	1681	11	49	6:5	41	44	NA
2018	Andrew et al.	Retrospective	229	14	51.4	3:11	12	46.6	30.3

RYGB, Roux-en-Y gastric bypass; *BE*, Barrett's esophagus; *BMI*, body mass index

Table 2 Response to treatment with Roux-en-Y gastric bypass on Barrett’s esophagus in the studies included for meta-analysis

Study reference	Pre-RYGB BE	Post-RYGB BE	BE regression (%)	Pre-RYGB ssBE	Post-RYGB ssBE	ssBE regression (%)	Pre-RYGB lsBE	Post-RYGB lsBE	lsBE regression (%)	Pre-RYGB GERD	Post-RYGB GERD	Resolution of GERD (%)
Csendes et al.	12	7	5 (47%)	7	3	4 (57%)	5	4	1 (20%)	12	0	12 (100%)
Houghton et al.	5	1	4 (80%)	NA	NA	NA	5	1	4 (80%)	5	0	5 (100%)
Ben-Meir et al.	14	2	12 (86%)	NA	NA	NA	NA	NA	NA	NA	NA	NA
Braghetto et al.	21	8	13 (62%)	NA	NA	NA	21	8	13 (62%)	21	0	21 (100%)
Pereira et al.	14	7	7 (50%)	8	2	6 (75%)	6	5	1 (17%)	14	4	10 (71%)
Dova et al.	26	13	13 (50%)	NA	NA	NA	NA	NA	NA	26	4	21 (81%)
Gorodner et al.	11	7	4 (36%)	9	6	3 (33%)	2	1	1 (50%)	NA	NA	NA
Andrew et al.	14	8	6 (43%)	14	8	6 (43%)	NA	NA	NA	NA	NA	NA

RYGB, Roux-en-Y gastric bypass; *BE*, Barrett’s esophagus; *ssBE*, short-segment Barrett’s esophagus; *lsBE*, long-segment Barrett’s esophagus; *NA*, not available

on BE, studies evaluating the effect of RYGB on GERD only without evaluation of BE, or data on intestinal metaplasia of the cardia and not BE, or studies with data not suitable for meta-analysis of the effect of RYGB on BE were excluded.

Selection of studies was done by two independent reviewers utilizing a blinded model. Studies with post-RYGB data at one or more than one time point were also included for comparison with pre-RYGB data. Disagreement in the selection of studies between the two reviewers was resolved with consensus and additional opinion utilizing Cohen’s kappa statistical model [19].

Data was extracted by four reviewers into tables using SPSS (version 24) for Windows (International Business

Machines Corporation). All attempts were made to retrieve missing information as per the study protocol by contacting the primary authors of the included studies.

Assessment of Risk of Bias

Assessment of risk of bias in the included studies was done by three reviewers utilizing the methodological index for non-randomized studies (MINORS) criteria [20]. Assessment of risk of bias was blinded, and all disagreements were resolved with consensus and opinion from additional reviewers utilizing Cohen’s kappa statistical model [19].

Table 3 Assessment of risk of bias in studies included for meta-analysis of Barrett’s esophagus before and after Roux-en-Y gastric bypass

Year of the study	Study reference	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Quality (score)
2006	Csendes et al.	2	2	2	2	0	2	1	0	Intermediate [11]
2008	Houghton et al.	2	0	0	2	0	2	0	0	Low [6]
2010	Ben-Meir et al.	2	0	0	2	0	2	1	0	Low [7]
2012	Braghetto et al.	2	1	2	2	0	2	2	0	Intermediate [11]
2012	Pereira et al.	2	0	0	2	0	2	0	0	Low [6]
2016	Dova et al.	2	0	0	2	0	2	1	0	Low [7]
2017	Gorodner et al.	2	0	0	2	0	2	1	0	Low [7]
2018	Andrew et al.	2	0	0	2	0	2	1	0	Low [7]

Q1. Did the study have a clearly stated aim? Q2. Were consecutive patients included? Q3. Was the data collected prospectively? Q4. Were endpoints appropriate to the study? Q5. Was there an unbiased assessment of endpoints? Q6. Was the follow-up period adequate? Q7. Was loss to follow-up less than 5%. Q8. Was there a prospective calculation of study size? 0, not reported; 1, reported but inadequate; 2, reported and adequate. Overall score, > 12; high quality, 8–12; intermediate quality, < 8, low

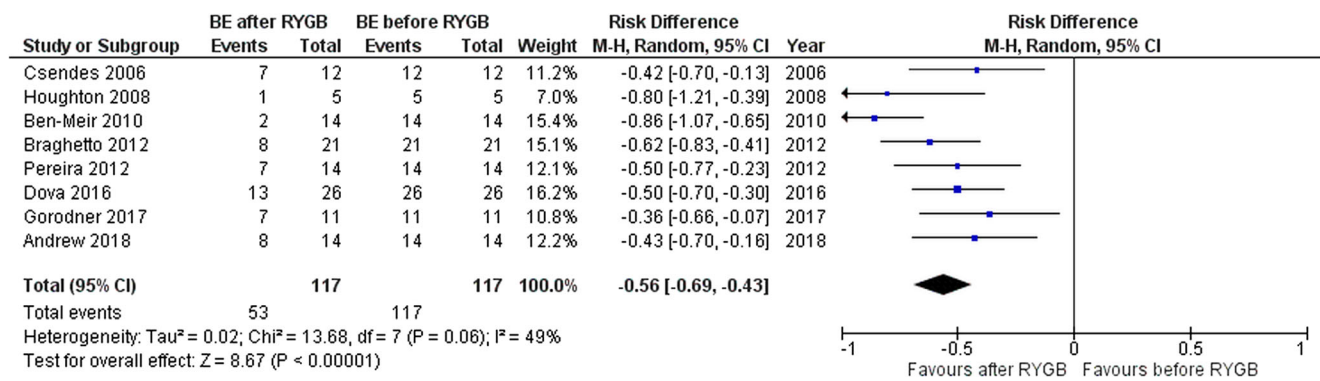


Fig. 2 Forest plot for Barrett's esophagus before and after Roux-en-Y gastric bypass. A Mantel-Haenszel, random-effects model is used for meta-analysis. Risk difference is shown with 95% confidence intervals. RYGB, Roux-en-Y gastric bypass; BE, Barrett's esophagus

Statistical Analysis

Outcome of the meta-analysis was measured using forest plots [21]. Funnel plots were used to draw conclusions about publication bias and heterogeneity at different time frames [22]. These were formulated with respect to individual outcome measures rather than to assess the overall quality of the studies included in the meta-analysis. Funnel plots and forest plots were generated using the software, Review Manager (RevMan version 5.3.5) (Cochrane Collaboration, Oxford, UK) [21, 22]. The experimental group of the meta-analysis was BE after RYGB, and the control group was BE before RYGB. The magnitude of the experimental effect was calculated in terms of risk difference (RD) and confidence intervals set at 95% to reflect a significance level of 0.05. The same statistical principles were applied for subgroup analysis done to evaluate the effect of RYGB based on the length of BE (ssBE [< 3 cm] and lsBE [≥ 3 cm]), and on GERD.

Regression of BE was also compared with progression of BE in the selected group of sample and data presented as odds ratio (OR) with confidence intervals set at 95% to establish significance at < 0.05 .

Tests for heterogeneity using tau [2], Cochran's Q (chi [2]), and I^2 [2] are incorporated in the forest plots [23]. Studies were assumed to be heterogeneous at the outset; hence, a Mantel-Haenszel, random-effects model was used for meta-analysis

instead of the fixed-effect model to allow the outcome measures to vary in a normal distribution between studies.

Data Availability

All data generated or analyzed during this study are included in this published article.

Results

Description of the Studies

Figure 1 summarizes the flow of information in different phases of the review. A Cohen's kappa score of 1 was achieved between the two primary reviewers.

Eight studies [24–31] with more than 10,779 patients undergoing RYGB identified a total of 117 patients suitable for meta-analysis of the effect of RYGB on BE. Six out of the eight studies [24, 25, 27, 28, 30, 31] categorized the effect of RYGB based on the length of BE (ssBE or lsBE). While all eight studies evaluated the effect of RYGB on BE, four studies evaluated the effect on ssBE [24, 28, 30, 31], five studies on lsBE [24, 25, 27, 28, 30], and five studies on GORD [24, 25, 27–29]. Regression of BE was analyzed in terms of histological regression from intestinal metaplasia to cardiac mucosa in all the included studies [24–31]. In addition, five studies [24, 25, 29–31]

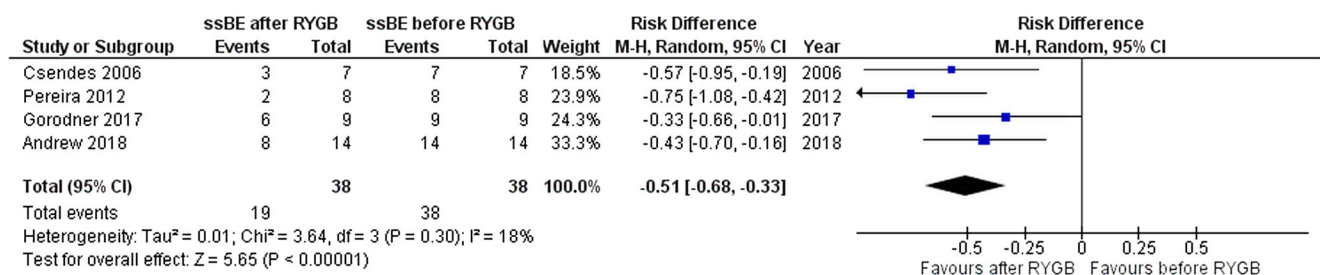


Fig. 3 Forest plot for short-segment Barrett's esophagus before and after Roux-en-Y gastric bypass. A Mantel-Haenszel, random-effects model is used for meta-analysis. Risk difference is shown with 95% confidence intervals. RYGB, Roux-en-Y gastric bypass; ssBE, short-segment Barrett's esophagus

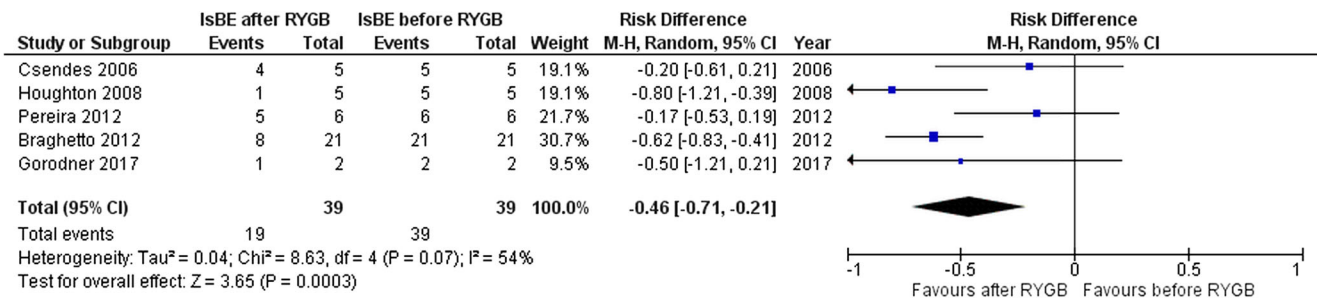


Fig. 4 Forest plot for long-segment Barrett’s esophagus before and after Roux-en-Y gastric bypass. A Mantel-Haenszel, random-effects model is used for meta-analysis. Risk difference is shown with 95% confidence intervals. RYGB, Roux-en-Y gastric bypass; lsBE, long-segment Barrett’s esophagus

also evaluated histological regression from low-grade dysplasia to intestinal metaplasia. Regression in terms of reduction in the length of BE was also evaluated in three out of eight studies [25, 26, 30]. Demographics of the patients in studies included for the meta-analysis are summarized in Table 1. The response of BE, ssBE, lsBE, and GERD to RYGB is summarized in Table 2.

Five [24, 25, 29–31] studies included a total of 10 patients with dysplastic BE (low-grade dysplasia or indeterminate dysplasia) of which six (60%) downgraded to intestinal metaplasia with no evidence of dysplasia or non-metaplastic cardiac mucosa. Seven [24, 25, 27–31] out of the eight studies showed no progression of non-dysplastic BE to dysplasia or dysplastic BE to a higher grade in any patient in while one study [26] showed progression of BE to dysplasia in two out of 14 patients (14.2%) after RYGB.

Two studies [14, 15] initially included in this review were excluded from the meta-analysis due to data not being compatible to conduct the meta-analysis. Both showed regression of BE after RYGB.

Assessment of Risk of Bias

A kappa score of 0.9 was achieved in the assessment of risk of bias between the three reviewers. Risk of bias was found to be relatively high across studies. Six out of eight studies were found to be of “low” quality [25, 26, 28–31] while 2 studies

were found to be of “intermediate” quality [24, 27]. Assessment of risk of bias of the included studies as per MINORS criteria is summarized in Table 3.

Meta-Analysis of the Effect of Roux-en-Y Gastric Bypass on Barrett’s Esophagus

Meta-analysis of the effect of RYGB on histological regression of BE (117 patients; n = 8) is shown in Fig. 2. Subgroup analysis of the effect of RYGB on ssBE (38 patients; n = 4) and lsBE (39 patients; n = 5) are shown in Figs. 3 and 4, respectively. Analysis of the effect of RYGB on GERD in patients with BE (78 patients; n = 5) is shown in Fig. 5.

BE showed significant regression on postoperative endoscopy at > 1 year after RYGB (RD - 0.56, 95% c.i. - 0.69 to - 0.43; P < 0.001). On subgroup analysis, significant regression of ssBE (RD - 0.51, 95% c.i. - 0.68 to - 0.33; P < 0.001) and lsBE (RD - 0.46, 95% c.i. - 0.71 to - 0.21; P < 0.001) was observed after RYGB. RYGB also led to a significant improvement in GERD (RD - 0.93, 95% c.i. - 1.04 to - 0.81; P < 0.001) at > 1 year after surgery.

Sixty-four out of 117 (54.7%) patients showed histological regression of BE while 2 patients (1.7%) showed progression. RYGB was strongly associated with regression of BE in the postoperative period compared with progression (OR 31.2, 95% c.i. 11.37, to 85.63; P < 0.001) on meta-analysis (Fig. 6).

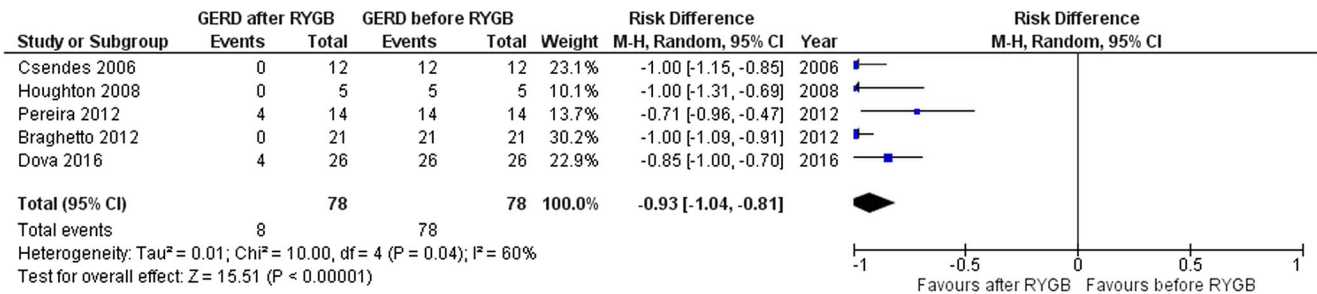


Fig. 5 Forest plot for gastroesophageal reflux disease in patients with Barrett’s esophagus before and after Roux-en-Y gastric bypass. A Mantel-Haenszel, random-effects model is used for meta-analysis. Risk

difference is shown with 95% confidence intervals. RYGB, Roux-en-Y gastric bypass; GERD, gastroesophageal reflux disease

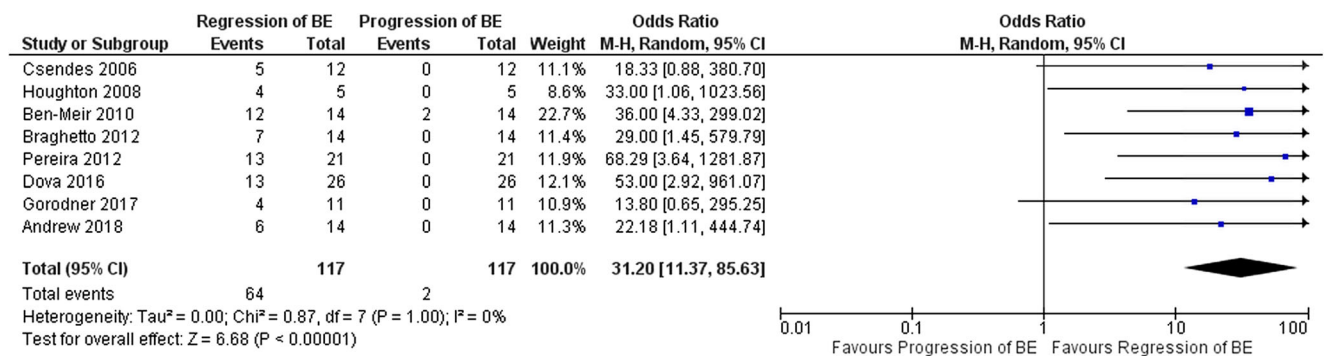


Fig. 6 Forest plot for regression and progression of Barrett’s esophagus after Roux-en-Y gastric bypass. A Mantel-Haenszel, random-effects model is used for meta-analysis. Odds ratio is shown with 95% confidence intervals. BE, Barrett’s esophagus

Assessment of Heterogeneity and Publication Bias

The funnel plots for the assessment of heterogeneity and publication bias are shown in Fig. 7. Funnel plots indicate variable asymmetry and are likely due to publication bias or “small study effects” due to inclusion of a large number of studies with small sample size.

Discussion

This meta-analysis of 8 studies (117 patients) [24–31] showed that BE undergoes significant regression at > 1 year after RYGB on endoscopy and biopsy. This effect is observed in both ssBE and lsBE, as shown in a subgroup analysis. RYGB also resulted in significant resolution of GERD in patients with

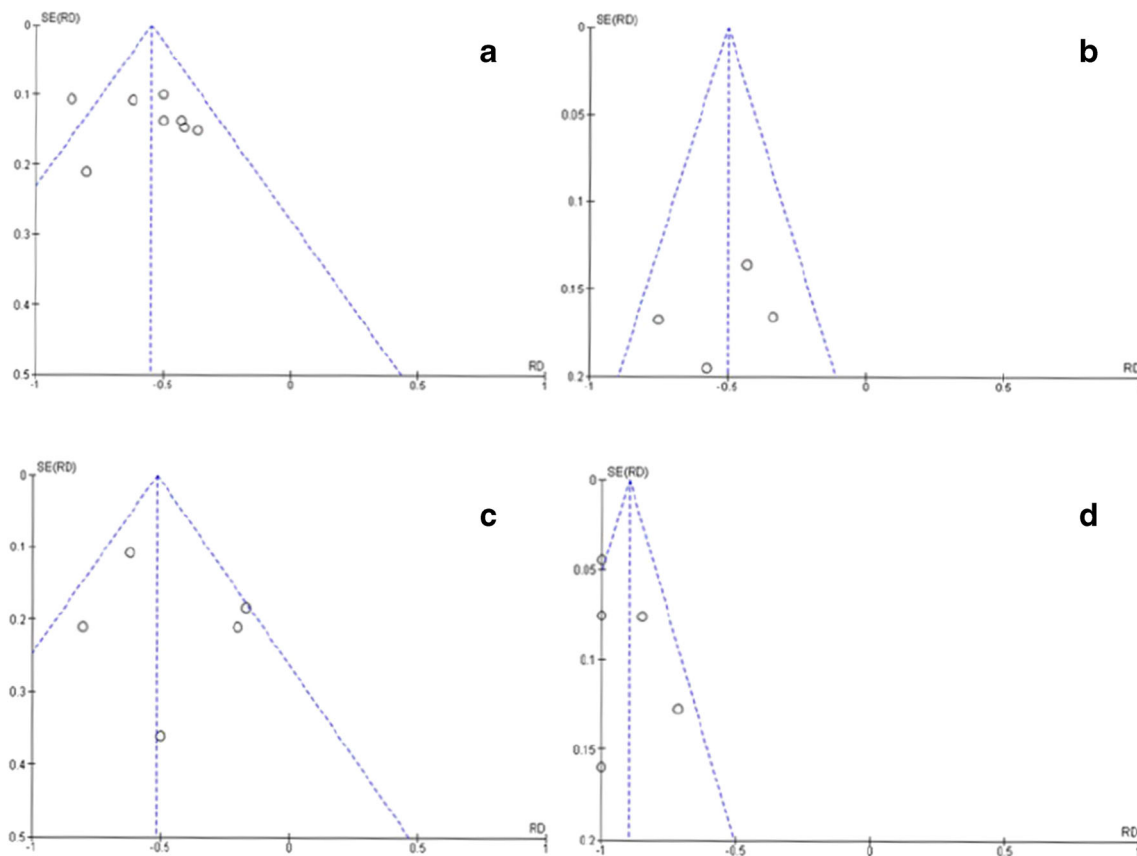


Fig. 7 Funnel plot of studies included in the meta-analysis of Barrett esophagus before and after Roux-en-Y gastric bypass (a), short-segment Barrett’s esophagus before and after Roux-en-Y gastric bypass (b), long-segment Barrett’s esophagus before and after Roux-en-Y gastric bypass (c), and gastroesophageal reflux disease in patients of Barrett’s esophagus before and after Roux-en-Y gastric bypass (d)

BE at > 1 year after surgery. The odds of BE regressing after RYGB was 31 times higher than progression after surgery.

Existing guidelines on BE endorse regular surveillance and management of BE in an unselected cohort of patients; however, there is no universal recommendation that caters to the management of BE in the obese population [1, 10]. Proton pump inhibitors (PPI), endoscopic therapy with radiofrequency ablation (RFA), endoscopic mucosal resection (EMR), and traditional anti-reflux surgery are the common interventions offered in BE. PPI therapy for symptomatic control, followed by repeat endoscopy, is usually offered to patients of BE without significant risk factors like dysplasia [1, 32]. More aggressive endoscopic therapy like RFA [33, 34] and EMR [1, 35, 36] are reserved for BE with dysplasia. Anti-reflux surgery has shown promising results in the regression of BE in about one-third of patients in retrospective studies [37–39]. However, this view has been disputed by a randomized controlled trial [40] which concludes that anti-reflux surgery is no more effective than PPI therapy and does not lead to regression of BE, which can even progress to dysplasia after surgery. One study found the progression rate of BE after traditional anti-reflux surgery to be 0.8%/year [41]. Neither of these modalities address the issue of excess weight which is regarded as one of the primary reasons behind failure of traditional anti-reflux surgery in obese individuals [42–44].

RYGB seems to be an attractive option in morbidly obese individuals with GERD as it can address reflux and its consequences along with inducing weight loss. According to a study on obese patients with GERD who failed traditional anti-reflux surgery, RYGB when used as a salvage procedure produced symptomatic improvement from GERD in 100% patients with complete resolution in 78% [42]. However, there is a scarcity of literature on the effect of RYGB on BE. The results of this meta-analysis show that there is a 56% regression of BE and 93% improvement in GERD after RYGB at > 1 year after surgery. This further lends support to the view that RYGB should be utilized as the therapy of first choice in suitable morbidly obese patients with GERD.

Another area of debate is the utilization of routine endoscopic assessment of the esophagus and stomach before bariatric surgery. Since obesity is a risk factor for GERD, hiatus hernia, BE, and EAC, routine preoperative screening before bariatric surgery can potentially diagnose abnormalities which may alter the course of management. The European Association of Endoscopic Surgery (EAES) guidelines [45] advocate routine preoperative endoscopy in all patients undergoing bariatric surgery. In contrast, the American Society for Gastrointestinal Endoscopy (ASGE) guidelines [46] recommend preoperative endoscopic evaluation in symptomatic patients only. In our study, BE was diagnosed in 117 out of more than 10,779 patients who underwent RYGB with a selective incidence of less than 1.08%. In a multicenter study [47]

on 3219 patients evaluating the role of upper gastrointestinal endoscopy in bariatric surgery, endoscopy was found to be normal in 66% patients who were asymptomatic compared with only 9% in those who had upper gastrointestinal symptoms and the authors concluded that preoperative endoscopy should be considered only in symptomatic patients before bariatric surgery. Similar findings were observed in a study from the USA [48] that found an abnormality detection rate of 61.6% on preoperative endoscopy before bariatric surgery; however, this altered the surgical strategy in only 1.7% patients, and the authors concluded that endoscopic screening before bariatric surgery picks up abnormalities, but the diagnosis of these findings rarely changes the surgical strategy. Furthermore, on cost analysis, the cost of performing routine endoscopy prior to bariatric surgery per clinically important lesion detected that altered surgical management was approximately US\$34,800 per lesion [48]. Based on the findings of these studies, and a detection rate of BE of less than 1.08% of all RYGB patients in this meta-analysis, it can be argued that endoscopic screening should be limited to patients with upper gastrointestinal symptoms only.

This review has many strengths. It is the first meta-analysis on the effect of RYGB on BE providing a high-level evidence on this topic. This analysis on 117 patients is the largest among existing literature and suggests that RYGB should be the preferred bariatric procedure in suitable, obese patients with BE as one out of two patients show regression of BE at > 1 year after surgery. The results of this study also showed comparable results for ssBE (regression rate of 51%) and lsBE (regression rate of 46%) at > 1 year after RYGB, a 93% improvement in GERD symptoms after RYGB in obese patients with BE, and 31 times odds of regression of BE after RYGB compared with progression.

The aim of this study was to perform a meta-analysis of the effect of RYGB on BE in obese population based on the existing scientific literature. A limitation of this meta-analysis is the relatively low quality of literature available on this topic. Only 117 patients from 8 studies with BE were identified to have undergone RYGB, but this could be due to a relatively low rate of detection of BE before bariatric surgery and the lack of routine endoscopic screening before bariatric surgery in most units. There is a possibility of an inter-observer variation in the diagnosis of BE between the studies included for this meta-analysis leading to observer bias. Variation in the histopathological diagnosis of BE by the pathologists examining the specimen in the studies included could also confound the results. There was some missing information in the individual studies despite our attempts at contacting the authors. Postoperative use of PPI, although clearly mentioned in only one study, could potentially confound

the results of this meta-analysis. Also, this meta-analysis pertains to only obese patients with BE undergoing RYGB and the results of this study cannot be extrapolated to non-obese individuals. Another limitation of the study was that patients who failed to show a regression of BE after RYGB were not followed up in the long term. Well-controlled prospective studies with long-term follow-up are felt necessary to fully understand the effect of RYGB on BE.

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Authors' Contributions K.M suggested the importance of carrying out this research. M.T.A and K.M. conducted the literature search and were involved in the selection of studies. M.T.A, K.M, F.R, and V.J were involved in extraction of data. M.T.A, O.A, and A.M were involved in data analysis and interpretation. M.T.A, P.J, and D.W performed the assessment of risk of bias in the included studies. All authors contributed to the write-up, corrections, validation, and final approval of the manuscript.

Compliance with Ethical Standards

Ethics Approval The study protocol was approved by the research committee of Obesity Service, Luton and Dunstable University Hospital, including research methodology and analysis plan detailed in the manuscript.

Competing Interests The authors declare that they have no competing interests in relation to this manuscript.

Consent to Participate We declare that consent to participate is not applicable to this study.

Consent to Publish We declare that consent to publish is not applicable to this study.

References

- Fitzgerald RC, di Pietro M, Ragunath K, et al. British Society of Gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus. *Gut*. 2014;63:7–42.
- Moersch RN, Ellis Jr FH, Mc DJ. Pathologic changes occurring in severe reflux esophagitis. *Surg Gynecol Obstet*. 1959;108:476–84.
- Stein HJ, Siewart JR. Barrett's esophagus: pathogenesis, epidemiology, functional abnormalities, malignant degeneration, and surgical management. *Dysphagia*. 1993;8(3):276–88.
- Hamade N, Vennelaganti S, Parasa S, et al. Lower annual rate of progression of short-segment vs long-segment Barrett's esophagus to esophageal adenocarcinoma. *Clin Gastroenterol Hepatol*. 2019;17(5):864–868.
- Runge TM, Abrams JA, Shaheen NJ. Epidemiology of Barrett's esophagus and esophageal adenocarcinoma. *Gastroenterol Clin N Am*. 2015;44(2):203–31.
- Westhoff B, Brotze S, Weston A, et al. The frequency of Barrett's esophagus in high-risk patients with chronic GERD. *Gastrointest Endosc*. 2005;61(2):226–31.
- Braghetto I, Csendes A. Patients having bariatric surgery: surgical options in morbidly obese patients with Barrett's esophagus. *Obes Surg*. 2016;26:1622–6.
- Nandurkar S, Locke 3rd GR, Fett S, et al. Relationship between body mass index, diet, exercise and gastro-oesophageal reflux symptoms in a community. *Aliment Pharmacol Ther*. 2004;20(5):497–505.
- Kubo A, Corley DA. Body mass index and adenocarcinomas of the esophagus or gastric cardia: a systematic review and meta-analysis. *Cancer Epidemiol Biomark Prev*. 2006;15:872–8.
- Hampel H, Abraham NS, El-Serag HB. Meta-analysis: obesity and the risk for gastroesophageal reflux disease and its complications. *Ann Intern Med*. 2005;143:199–211.
- Sampliner RE. Practice guidelines on the diagnosis, surveillance, and therapy of Barrett's esophagus. *Am J Gastroenterol*. 1998;93:1028–32.
- Angrisani L, Santonicola A, Iovino P, et al. Bariatric surgery and endoluminal procedures: IFSO worldwide survey 2014. *Obes Surg*. 2017;27(9):2279–89.
- Zhang N, Maffei A, Cerabona T, et al. Reduction in obesity-related comorbidities: is gastric bypass better than sleeve gastrectomy? *Surg Endosc*. 2013;27(4):1273–80.
- Park C, Portenier D. Reflux, Barrett's esophagus & bariatric surgery: working towards a clinical pathway for the management of a pre-cancerous condition in bariatric surgery patients. *Surg Obes Relat Dis*. 2015;11(6):S118.
- Cobey F, Oelschlager B. Complete regression of Barrett's esophagus after Roux-en-Y gastric bypass. *Obes Surg*. 2005;15:710–2.
- O'Connor D, Green S, Higgins JPT. Defining the review question and developing criteria for including studies. *Cochrane Handbook for Systematic Reviews of Interventions*, Version 5.1.0: The Cochrane Collaboration; 2013. Available at - https://handbook-5-1.cochrane.org/chapter_5/5_defining_the_review_question_and_developing_criteria_for.htm. Accessed 27 Feb 2019.
- Centre for reviews and dissemination. *Systematic reviews: CRD's guidance for undertaking reviews in healthcare*. York: University of York; 2009. Available at - <https://www.york.ac.uk/crd/guidance/>. Accessed 27 Feb 2019.
- Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analysis: the PRISMA statement. *BMJ*. 2009;339:b2535.
- Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Meas*. 1960;20(1):37–46.
- Slim K, Nini E, Forestier D, et al. Methodological index for non-randomized studies (minors): development and validation of a new instrument. *ANZ J Surg*. 2003;73(9):712–6.
- Lewis S, Clarke M. Forest plots: trying to see the wood and the trees. *BMJ*. 2001;322(7300):1479–80.
- Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315(7109):629–34.
- Higgins JPT, Thompson SG, Deeks JJ. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557–60.
- Csendes A, Burgos AM, Smok G, et al. Effect of gastric bypass on Barrett's esophagus and intestinal metaplasia of the cardia in patients with morbid obesity. *J Gastrointest Surg*. 2006;10(2):259–64.
- Houghton SG, Romero Y, Sarr MG. Effect of Roux-en-Y gastric bypass in obese patients with Barrett's esophagus: attempts to eliminate duodenogastric reflux. *Surg Obes Relat Dis*. 2008;4(1):1–4.
- Ben-Meir A, Sonpal I, Salomone MG. Roux-en-Y gastric bypass (RYGB) improves Barrett's esophagus. *Surg Obes Relat Dis*. 2010;6(3):S48–9.
- Braghetto I, Korn O, Csendes A, et al. Laparoscopic treatment of obese patients with gastroesophageal reflux disease and Barrett's esophagus: a prospective study. *Obes Surg*. 2012;22(5):764–72.

28. Pereira N, Csendes A, Smok G, et al. Effects of gastric bypass for morbid obesity on Barrett esophagus. *Rev Chilena Cirugía*. 2012;64(2):155–60.
29. Dova G, Caro LE, Brasesco O, et al. Effects of gastric bypass in obese patients with Barrett's esophagus. *Gastrointest Endosc*. 2016;83(5):AB551.
30. Gorodner V, Buxhoeveden R, Clemente G, et al. Barrett's esophagus after roux-en-Y gastric bypass: does regression occur? *Surg Endosc*. 2017;31(4):1849–54.
31. Andrew B, Alley JB, Aquiar CE, et al. Barrett's esophagus before and after Roux-en-Y gastric bypass for severe obesity. *Surg Endosc*. 2018;32(2):930–6.
32. Nguyen DM, El-Serag HB, Henderson L, et al. Medication usage and the risk of neoplasia in patients with Barrett's esophagus. *Clin Gastroenterol Hepatol*. 2009;7:1299–304.
33. Shaheen NJ, Sharma P, Overholt BF, et al. Radiofrequency ablation in Barrett's esophagus with dysplasia. *N Engl J Med*. 2009;360:2277–88.
34. Gray NA, Odze RD, Spechler SJ. Buried metaplasia after endoscopic ablation of Barrett's esophagus: a systematic review. *Am J Gastroenterol*. 2011;106:1899–908.
35. Mino-Kenudson M, Brugge WR, Puricelli WP, et al. Management of superficial Barrett's epithelium-related neoplasms by endoscopic mucosal resection: clinicopathologic analysis of 27 cases. *Am J Surg Pathol*. 2005;29:680–6.
36. Pouw RE, Seewald S, Gondrie JJ, et al. Stepwise radical endoscopic resection for eradication of Barrett's oesophagus with early neoplasia in a cohort of 169 patients. *Gut*. 2010;59:1169–77.
37. Simonka Z, Paszt A, Abraham S, et al. The effects of laparoscopic Nissen fundoplication on Barrett's esophagus: long-term results. *Scand J Gastroenterol*. 2012;47:13–21.
38. Hofstetter WL, Peters JH, DeMeester TR, et al. Long-term outcome of antireflux surgery in patients with Barrett's esophagus. *Ann Surg*. 2001;234:532–8.
39. Guruski RR, Peters JH, Hagen JA, et al. Barrett's esophagus can and does regress after antireflux surgery: a study of prevalence and predictive features. *J Am Coll Surg*. 2003;196(5):706–12.
40. Parrilla P, Martinez de Haro LF, Ortiz A, et al. Long-term results of a randomized prospective study comparing medical and surgical treatment of Barrett's esophagus. *Ann Surg*. 2003;237:291–8.
41. Zehetner J, DeMeester SR, Ayazi S, et al. Long-term follow-up after anti-reflux surgery in patients with Barrett's esophagus. *J Gastrointest Surg*. 2010;14:1483–91.
42. Kellogg TA, Andrade R, Maddaus M, et al. Anatomic findings and outcomes after antireflux procedures in morbidly obese patients undergoing laparoscopic conversion to Roux-en-Y gastric bypass. *Surg Obes Relat Dis*. 2007;3(1):52–7.
43. Morgenthal CB, Lin E, Shane MD, et al. Who will fail laparoscopic Nissen fundoplication? Preoperative prediction of long-term outcomes. *Surg Endosc*. 2007;21(11):1978–84.
44. Perez AR, Moncure AC, Rattner DW. Obesity adversely affects the outcome of antireflux operations. *Surg Endosc*. 2001;15:986–9.
45. Sauerland S, Angrisani L, Belachew M, et al. Obesity surgery: evidence-based guidelines of the European Association for Endoscopic Surgery (EAES). *Surg Endosc*. 2005;19:200–21.
46. Anderson MA, Gan SI, Fanelli RD, et al. Role of endoscopy in the bariatric surgery patient. *Gastrointest Endosc*. 2008;68:1–10.
47. Abd EME, Alfalah H, Asker WA, et al. Place of upper endoscopy before and after bariatric surgery: a multicenter experience with 3219 patients. *World J Gastrointest Endosc*. 2016;8(10):409–17.
48. Gomez V, Bhalla R, Heckman MG, et al. Routine screening endoscopy before bariatric surgery: is it necessary? *Bariatric Surg Pract Patient Care*. 2014;9(4):143–9.

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