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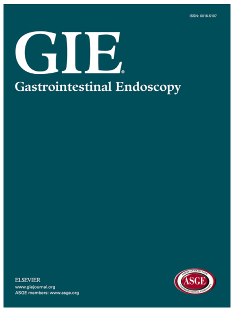

Barrett's esophagus after sleeve gastrectomy: a systematic review and meta-analysis

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Barrett's esophagus after sleeve gastrectomy: a systematic review and meta-analysis

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Short title: Sleeve Gastrectomy and Barrett's Esophagus

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Medical, Lumendi and Microtech. Dr. Ayzengart is a consultant for Bard/Davol. The remaining authors declare that they have no conflict of interest.

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Background and Aims: Sleeve gastrectomy (SG) has seen significant growth in recent years. Gastroesophageal reflux disease (GERD) is a major concern in patients undergoing SG and is the major risk factor for Barrett's esophagus (BE). We aimed to assess the prevalence of BE in patients who had SG.

Methods: We searched major search engines ending in July 2020. We included studies on patients who had esophagogastroduodenoscopy (EGD) after SG. The primary outcome was the prevalence of BE in patients who had SG. We assessed heterogeneity using I^2 and Q statistics. We used funnel plots and classic fail-safe to assess for publication bias. We used random-effects modeling to report effect estimates.

Results: Our final analysis included 10 studies totaling 680 patients who had EGD 6 months to 10 years after SG. The pooled prevalence of BE was 11.6% (95% CI, 8.1 - 16.4%; $p<0.001$; $I^2=28.7\%$). On logistic meta-regression analysis, there was no significant association between BE and the prevalence of postoperative GERD (**β=** 3.5; 95% CI, -18 – 25p; $p=0.75$). There was a linear relationship between the time of postoperative EGD and the rate of esophagitis (**β=** 0.13; 95% CI, 0.06 – 0.20; $p=0.0005$); the risk of esophagitis increased by 13% each year after SG.

Conclusions: The prevalence of BE in patients who had EGD after SG appears to be high. There was no correlation with GERD symptoms. Most cases were observed after 3 years of follow-up. Screening for BE should be considered in patients after SG even in the absence of GERD symptoms postoperatively.

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Introduction

As the epidemic of obesity continues to grip our nation and the world, bariatric surgery has emerged as an effective, yet invasive, approach to help patients with severe obesity[1]. Among the various techniques, sleeve gastrectomy (SG) has seen significant growth in the number of patients[2, 3]. Yet, gastroesophageal reflux disease (GERD) has become a major concern in patients undergoing SG[4]. Many studies have reported a significant increase in GERD symptoms after SG[5, 6]. Several mechanisms have been reported for this phenomenon including loss of angle of His flap valve, decreased pressure at the lower esophageal sphincter, and damage of sling fibers[7].

GERD is the major risk factor for the development of Barrett's esophagus (BE)[8], which is recognized as a precursor for esophageal adenocarcinoma (EAC) [9]. Unfortunately, we have seen trends indicating that the incidence of EAC and of BE has increased in recent years in some Western populations [10, 11].

Obese patients have higher-than-normal prevalence of GERD and hiatal hernias, all of which would be expected to increase the prevalence of BE in this population[8, 12]. Despite all of the above, a meta-analysis of over 13,000 patients who underwent EGD before bariatric surgery found a very low rate of BE at less than 1%[13]. Yet, if patients have worsening GERD after SG, we hypothesize that they would have an increased risk for developing BE. Based on clinical practice guidelines[14], patients whose expected prevalence of BE is above 10% are thought to be at high risk and screening for BE is recommended. Assessing the risk of post-sleeve gastrectomy BE has important clinical implications for all gastroenterologists who may do pre- and postoperative endoscopy, bariatric surgeons who perform the procedure, patients who undergo the procedure, and primary physicians who may need to recommend screening for BE in such patients[15-17]. Therefore, we aimed to conduct a systematic review and meta-analysis of studies that assessed the risk of BE in patients who underwent SG for obesity.

Methods

Study selection

We used our a priori protocol to conduct a literature search with the help of an expert librarian. We included studies if they met the following criteria: (1) randomized trials, prospective, retrospective cohort studies, or meeting abstracts from the last 3 years; (2) patients who underwent sleeve gastrectomy for treatment of obesity; (3) all patients had EGD before sleeve gastrectomy; (4) the study authors invited all patients for EGD, or all consecutive patients underwent EGD at least 6 months after surgery; and (5) BE, if found, was confirmed by biopsy. We excluded studies that (1) perform EGD only on symptomatic patients postoperatively rather than all patients; (2) were case reports or case series; (3) were deemed to be of very poor quality based on the Downs and Black scoring system; or (4) were not available in English. We used the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines for our study.

Search strategy and data extraction

Our literature search was conducted with the help of an expert librarian at Florida State University (RR). We searched MEDLINE (Ovid), Cochrane Library and CENTRAL, Embase, and Web of Science from inception to July of 2020. Details of our literature search are described in Appendix 1. The librarian imported all citations

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into Covidence.org, where all duplicates were removed. Two independent reviewers (Y.Q. and S.P.) conducted the initial review based on our inclusion and exclusion criteria. A third reviewer (B.Q.) with expertise in Barrett's esophagus and systematic reviews resolved all conflicts. We extracted data on study authors, publication year, country, study design, mean age, mean body mass index (BMI), preoperative EGD, time to follow-up EGD, number of patients, number with BE, BE in GERD vs. no GERD, number with de novo GERD, GERD definition, and number with esophagitis before and after surgery.

Outcomes of interest

The primary outcome of interest was the proportion of patients who developed BE after SG. Histologic confirmation was a requirement for diagnosis of BE. This meant that the area of suspected BE underwent biopsy, and histology was consistent with BE based on that intuition's definition of BE. We also stratified BE cases based on GERD symptoms, follow-up time, and presence of esophagitis on follow-up EGD. Secondary outcomes included the prevalence of esophagitis and GERD on follow-up.

Sources of heterogeneity were hypothesized a priori as listed:

1. Variation of GERD definition

2. Variation in follow-up time

3. Variation in the prevalence of GERD in the baseline population

4. Variation in surgical techniques and experience

The following analyses were planned a priori to control for possible heterogeneity: follow-up time (long-term [3 or more years] vs short-term follow-up [<3 years]), and meta-regressions controlling for proportion of GERD, esophagitis, and follow-up time.

Quality assessment

We used the Downs and Black scoring system to assess the quality of each study [21]; however, many questions in the scoring system do not apply to the studies we reviewed. The final score for studies (with a maximum score of 16) was reported, as previously described[13]. Based on this system, we rated studies as high (12–16); moderate (9–11); fair (7–8), and poor (≤6). We also planned to identify and remove possible outliers. We defined these a priori as studies that reported an effect estimate which is ≥10 times higher or lower than expected.

Statistical analysis

We decided to use random effects modeling in all analyses a priori. The primary metameter (effect estimate) of interest was the prevalence of de novo BE after SG and was reported as rated with 95% confidence intervals (CI). We reported the magnitude and direction of effect estimates on Forest plots. Secondary outcomes included the risk difference (RD) in erosive esophagitis (EE) and GERD before surgery compared with after surgery. We defined RD as the proportion of patients with EE after surgery minus the proportion of patients with EE before surgery. Because these patients got pre- and postprocedure EGDs, we used matched proportions. In doing so, we had to assume a correlation coefficient. This was assumed to be 0.5 (halfway between no correlation and complete correlation). We assessed heterogeneity using I^2 and Cochrane's Q statistic. Heterogeneity was defined as low, I^2 ≤50%; moderate, I^2 51%–75%; or high, I^2 >75%. We used both funnel plots and the classic fail-safe test to screen for publication bias. Exploratory logistic meta-regression analyses were used to assess for a possible relationship between prevalence of BE and potential risk factors: duration of follow-up, GERD, and EE. In such cases, we used R^2 analog to report the in-between study variance explained by our model. We used CMA V3 (Biostat, Inc, Englewood, NJ, USA) for all statistical analyses.

Results

Our initial search identified 4,389 studies, of which 4,359 were excluded based on title and abstract. After reviewing 30 full-text articles, 10 studies[15, 17-25], including 2 abstracts, were included in the final analysis totaling 680 patients (**Figure 1**). All patients underwent EGD preoperatively and one had BE before surgery. All studies assessed patients who underwent SG and had EGD after a minimum of 6 months. Seven studies[15, 17, 18, 21-24] assessed patients after a minimum of 3 years. These were referred to as “long-term” follow-up. Three studies[19, 20, 26] assessed patients with EGD within a minimum of 6 months from surgery. These were termed “short-term” follow-up studies. Mean age, BMI, and ratio of females: males were comparable among studies. Study locations included Europe, Canada, Argentina, Chile, India, and Taiwan. Further patient and study characteristics are summarized in **Table 1**.

Prevalence of BE

Overall, there were 680 patients. Of them, 54 patients had BE. All BE cases were non-dysplastic and were de novo. In addition, all cases were observed in studies with long-term follow-up. The pooled prevalence of BE was 11.4% (95% CI, 7.7 -16.6%;

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$p<0.001$) (**Figure 2a**). There was no significant heterogeneity in the model with $I^2=28.7\%$ ($Q=12.6$, $p=0.18$). When we only analyzed the studies that had long-term follow-up, the results were essentially identical with pooled prevalence of BE of 11.5% (95% CI, 7.8% -16.7%) $p<0.001$; $I^2=46\%$; and $Q=11.2$.

BE and GERD symptoms

We further assessed the prevalence of BE in patients with or without postoperative GERD symptoms based on three long-term studies[15, 17, 18]. Overall, 7 patients had BE without postoperative GERD symptoms. The pooled rate on meta-analysis was 10.3% (95% CI, 5% - 20%; $p<0.001$). The pooled rate of BE in patients with GERD symptoms was 18.2% (95% CI, 12.4% - 26%). There was no significant difference in the odds of having BE based on GERD symptoms (OR =1.74; 95% CI, 0.52 – 5.89; $p=0.37$) (**Figure 2b**). There was no significant heterogeneity ($I^2=52\%$, $Q=4.2$).

Only one study[17] reported the rate of columnar lined esophagus (CLE, as seen endoscopically). In this study the rate of CLE was high (50%, n=10). But only 3 of these patients were confirmed on biopsies.

These results were also confirmed on multivariable logistic meta-regression analysis, controlling for mean age and follow-up time, which showed no significant association between the prevalence of BE and the prevalence of postoperative GERD (**β= 3.5;** 95% CI, -18 – 25; $p=0.75$). However, there was a significant association between mean age and GERD prevalence, when controlling for GERD and follow-up time (**β= 0.8;** 95% CI, 0.3 – 1.4; $p=0.0028$). R^2 analog was 1. This indicates that the model explained most of the heterogeneity between studies.

On multivariable logistic meta-regression analysis, there was also no significant association between the prevalence of BE and the duration of follow-up (**β**=-0.02; 95% CI, -0.3 – 0.3; p=0.874), or the prevalence of postoperative esophagitis (**β=** 1; 95% CI, -4.1 – 6; p=0.70).

Esophagitis after SG

Seven studies reported esophagitis before and after SG at various follow-up intervals. The study by Tai et al[26] was excluded from this analysis because the surgeons were reported to be in their initial learning curve, which could skew data from experienced centers. For Soricelli et al, the rate of preoperative esophagitis was extracted from a prior study[6] of the same cohort. In 5 studies[15, 18, 21-23] with long-term follow-up, the relative increase in the rate of esophagitis was 86% (64% – 109%), p<0.001, I^2=47% Q=7.6 (p=0.107). This means that there is an 86% increase in the risk of esophagitis on long-term follow-up after SG. For short-term studies[19, 20], there was a 35% increase (14% – 57%), p<0.001, I^2=0, Q=0.5. This difference between short-term and long-term studies was statistically significant (p=0.001, **Figure 3A**).

On univariate logistic meta-regression analysis, there was a linear relationship between the time of postoperative EGD and the rate of esophagitis (**β=** 0.08; 95% CI, 0.007 – 0.16; p=0.048). This indicates that the risk of esophagitis increases by 8% each year after SG. The study by Csendes et al was acting as an outlier. When this was excluded from the meta-regression the results the association between EE and

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follow-up time was more pronounced: (**β=** 0.13; 95% CI, 0.06 – 0.20; p=0.0005, **Figure 3B**). Funnel plot showed some risk of publication bias (Figure 3C). A classic fail-safe test showed that we would need to identify 208 additional "null" studies in order for the combined p-value to exceed 0.05. On meta-regression, the size of bougie used intraoperatively was not associated with the rate of esophagitis (**β=** 0.036; 95% CI, -0.02 – 0.09; p=0.186).

GERD after SG

Eight studies reported the rate of GERD after SG. One study by Dimbezel et al[23] did not have a clear definition of how GERD was identified preoperatively so this was excluded from this analysis. As expected, the definition of GERD varied greatly by study, as detailed in **Table 1**. As a result, significant heterogeneity was noted in the magnitude of postoperative GERD. However, all studies showed the effect estimate to be in the same direction: a significant increase in the prevalence of GERD postoperatively with odds ratios (OR) ranging from 1.6 to 49 as detailed in **Figure 4A**. Four studies[17, 20, 22, 26] reported on de novo GERD after SG. Among those who had no GERD symptoms before surgery, the rate of having GERD postoperatively was 45% (95% CI, 35% – 55%), I^2=51%, Q=6.1, p=0.106 (**Figure 4B**). Use of proton pump inhibitors before and after SG was reported in only 2 of the included studies. Sebastianelli et al[15] reported an increase in PPI use from 22% preoperatively to 76% postoperatively.

Similarly, Soricelli et al[18] reported an increase in PPI use from 24% preoperatively to 73% postoperatively.

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Considerations: bias and quality assessment

Based on Down & Black, all studies were of adequate quality to be included in the study (Table 1). Publication bias was assessed using funnel plots. This showed no evidence of publication bias (**Figure 2C**), but there was some asymmetry noted due to the 3 studies with zero prevalence of BE. Using the classic fail-safe test, we need to identify 340 additional "null" studies in order for the combined p-value to exceed 0.05. When removing one study at a time from the analysis, we found no evidence of overdue effect on the final results of our study.

Discussion

SG has gained wider acceptance as an effective bariatric procedure for patients with severe obesity[2]. However, our study shows that the prevalence of BE is high on long-term follow-up after surgery. On meta-analysis of all existing studies, we found that the prevalence of BE was about 11.6%. Furthermore, we found that BE was not limited to patients with GERD symptoms only. BE appeared around 3 years after SG and continued to be detected at 10 years after the procedure.

Previous meta-analyses[4, 27] focused on GERD and EE after SG. In a meta-analysis by Yeung et al[27], the authors conducted a subanalysis in which they reported the pooled prevalence of BE to be around 8%. However, the results were limited by the very high heterogeneity of 92%, making the pooled estimate grossly uninterpretable. An abstract by Horter et al focused on prevalence of BE after SG[28]. Although the study has not been yet published, we noted that heterogeneity was also high at 88% making interpretation difficult. Despite that, the pooled prevalence of BE in long term studies was 13.3% which is similar to our report of 11.6%. We believe that our results are in fact more accurate for several reasons. Firstly, we had a strict a priori protocol with clear inclusion criteria. Specifically, if a study did not ask all, or consecutive patients, to enroll, then the patients who were missed on follow-up EGD may be different from the ones who had no EGD. Including such studies will skew the results. An example of this is the study by Braghetto[29]. After the first year of follow-up, EGD was only done “selectively.” As a result, about 47% of patients did not have follow-up EGD at 3 years, and >70% did not have follow-up at 5 years. In such cases, the reported rates of BE, and esophagitis, may be greatly misleading. Such studies were excluded from our analysis.

Clinical Implications

To our knowledge, this is the largest evidence-based study to assess the risk of BE after SG as a primary outcome. There are several important clinical implications to our findings. First, due to the growth popularity and demand for SG, bariatric surgeons, primary care providers, and gastroenterologists need to be aware of these potential adverse outcomes. Our data warrant a discussion with patients regarding the risks and benefits of screening for BE after SG. Based on ASGE guidelines[14], screening for BE may be indicated in any patient population in which the prevalence of BE is over 10%. Note that 11.6% of cases are all de novo; none of the patients who had SG had BE at the screening EGD before the procedure. In our previous meta-

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analysis[13], we studied over 13,000 patients who had EGD before bariatric surgery and showed that despite their obesity, the risk of BE in this patient population was very low (<1%). The above data would suggest that screening might be more useful if started around 3 years after SG. More data on this issue will be needed before such recommendations are adopted into clinical guidelines.

Second, although BE may take several years to develop, the risk of esophagitis appears to increase by 13% each year based on our regression analysis. Many patients with BE and esophagitis may be asymptomatic. Although these secondary results require further investigation, our results indicate that early post-SG acid suppression may be considered to mitigate the risk of GERD and ultimately the risk of BE and EAC.

Last, the elevated risk of BE due to SG should be discussed with patients at the time of surgical referral. Patients at increased risk of BE should be given the option to have an alternative procedure. These patients may include those with GERD, documented esophagitis, family history of BE or EAC, males, and smokers.

None of the studies reported on the rate of progression of BE into dysplasia. However, there would be no reason for us to assume the BE after SG would behave differently from BE in other patients. We know, for instance, that cases of EAC and gastric cancers have been reported in patients after SG[7, 30]. Additionally, cases of cancer after SG may be diagnosed at later stages because patients have common upper GI

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symptoms and may present for evaluation at later stages. Therefore, we have to assume that BE in this population has to be considered seriously.

In addition, there could be clinical implications for endoscopic sleeve gastroplasty (ESG). This procedure has been gaining traction among gastroenterologists and surgeons[31]. The procedure mimics SG but is done through an endoscope by plicating the wall of stomach on itself to reduce its size. Although ESG mimics SG in its technique, the effect of ESG on GERD, EE and BE has not been well studied. Fayad et al[32] conducted a case-control retrospective study of 83 ESG patients and 54 SG patients. They found that the risk of reflux was lower in the ESG group. However, the true effect of ESG on GERD and EE has not yet been established. We hope that our results will serve as a motivation to clinicians and researchers in the field of ESG to design and conduct research studies that investigate this topic and provide much needed answers.

Besides the risk of BE aft3er SG, the risk of EE is also of significant interest and shares the same pathophysiology with BE and GERD. Although this was not a primary outcome of our study, it was one of the secondary outcomes planned a priori. We reported the increased risk using the prevalence of EE before and after the procedure. This gives the reader and the patient a better understanding of the magnitude of risk for developing esophagitis after SG. The data we found on EE were compelling. In the long-term studies, the relative increase in EE was 87%. In the short-term studies, the relative increase was 35%. One study[26] was removed from this analysis. However, the effect estimate of removed studies was very high in favor of

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more EE after SG. Furthermore, our meta-regression showed a 13% increase in the risk of esophagitis every year postoperatively. Although some literature continues to debate the risk of GERD and EE after SG[33], the data from our study show a consistent and substantial trend toward more EE after SG. In fact, as we showed above, we will need to identify 208 additional studies that show no elevation in the risk of EE after SG to negate the results of our study, which would be highly unlikely. As a secondary outcome, our study also assessed the risk of GERD. As we expected, the definition of GERD varied greatly by study. Thus, we could not pool the estimates. However, all studies showed a higher prevalence of GERD after SG compared with before the procedure. Moreover, among patients who had no diagnosis of GERD before procedure, as much at 40% of them developed de novo GERD.

Strengths and Limitations

Our study has several strengths. It is the first study to focus on BE as a primary outcome. Our literature search was broad and inclusive. Heterogeneity was minimal in most of our analyses. Additionally, we had a strict definition of studies to be included. This resulted in a more reliable analysis of studies with interpretable effect estimates. When heterogeneity was significant, as the case with GERD, the effect estimates were not pooled.

A potential limitation of our study is the relatively small sample size. Despite our comprehensive search, only a few studies reported the outcomes of interest based on our a priori inclusion criteria. Although we recognize that larger studies will be

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helpful in confirming our results, we also note that our results showed that we would need a large number of “null” studies to negate the results of our analyses.

Additionally, our primary outcome was BE. As a result, some of the secondary outcome results should be used with caution, as we did not set out to find the risk of EE or GERD. However, the trends noted in our study regarding secondary outcomes are consistent and profound, and are in line with previous studies.

Last, we used funnel plots to assess for publication bias despite having less than ten studies. This can cause the power of the test to be low. To adjust for this, we have also reported the results of the classic fail-safe, which showed a low risk of publication bias.

Conclusions

Patients who undergo SG are at increased risk of developing BE. Larger studies are needed to understand the pathophysiology of this phenomenon. Gastroenterologists, primary care providers, and bariatric surgeons should be aware of the above data. Careful discussion with patients regarding the risks of SG before the procedure, and the risk-benefit assessment of screening for BE after SG, should be considered.

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Figure legends

Fig. 1: Flow chart of study selection.

Fig. 2: A, The prevalence of BE in patients with follow-up EGD. B, The odds of having Barrett's esophagus in patients with GERD symptoms compared with those without with or without GERD. C, Funnel plot assessing publication bias.

Fig. 3: A, Relative risk increase in the rate of esophagitis after SG compared with pre-operative rate of esophagitis. B, Meta-regression of the risk difference of esophagitis based on follow-up times. C, Funnel plot assessing publication bias.

Fig. 4: A, Forest plot of the odds ratios of having GERD after SG compared with before. B, Pooled rate of Denovo GERD in patients who had no GERD symptoms preoperatively.

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Table 1 Patient and study characteristics of the 10 studies included in the analysis.

Study	Type of study	Publication	Country	Mean age (SD or range)	Mean BMI	% male	% Excess WL	% TBWL	Bougie size (FR)	Time to EGD or follow-up time	Number patients	# BE	BE with GERD	BE without GERD	Type of BE	Preop EE	Post op EE	Definition of GERD	Preop GERD	Postop GERD	DeNovo GERD	D&B
Sebastianelli 2019	Prospective	Manuscript	Multinational	41 ±11	46 ± 8	0.27	58% ± 27	25%	NA	78 ± 15 (months)	90	17	16 of 68	1 of 22	NDBE	9	37	Montreal consensus	20	68	NC	14
Felsenreich 2017	Prospective	Manuscript	Austria	38.4 ± 12.4	49.5 ± 9.6	0.21	NA	NA	42-48	10 years	20	3	1 of 10	2 of 10	NDBE	NA	6	Reflux Symptoms Index	0	10	10 of 26	13
Soricelli 2018	Prospective	Manuscript	Italy	NA	NA	NA	NA	NA	48	66 (41 - 89) months	144	19	15 of 101	4 of 43	NDBE	NA	86	Visual Analog Scale	59	101	NC	9
Elkassem 2018	Prospective	Abstract	Canada	47.8	49.1	NA	NA	26%	NA	At least 3 year	21	3	NA	NA	NA	10	16	NC			NC	/
Tai 2013	Prospective	Manuscript	Taiwan	37.2 ± 12.7	36.3 ± 4.1	0.29	NA	NA	36	12 (12-21) months	66	0	/	/	/	11	44	Reflux Disease Questionnaire	8	47	26 of 58	12
Sharma 2014	Prospective	Manuscript	India	35.8 (19-60)	47.8	0.31	64.3% ± 18.4	NA	36	6 months	32	0	/	/	/	6	8	Scintigraphy, Severity Symptoms, and Carlson Dent	8	25	NC	12
Viscido 2018	Prospective	Manuscript	Argentina	40 ± 9	47 ± 16	0.34	64% ± 9.4	NA	42	18 months	109	0	/	/	/	22	37	Montreal Consensus	36	48	27 of 73	10
Csendes 2019	Prospective	Manuscript	Chile	38 + 10.2	38.6 + 2.9	0.22	NA	NA	38	95 + 15 months	104	4	/	/	/	14	33	Burning symptoms	44	69	31 of 53	12
Dimbezel 2020	Prospective	Manuscript	France	49.6 + 11.7	40 + 1.9	0.12	/	/	/	62.4 months	40	4	/	/	/	1	18	No clearly defined preop	18	13	/	11
Lallemand 2019	Prospective	Abstract	France	43 + 12	49.4 + 7.4	/	/	/	/	5 years	54	4	/	/	/	/	/	Unclear	/	/	/	/

WL: weight loss; TBWL: total body weight loss; EGD: esophagogastroduodenoscopy; BE: Barrett's esophagus; GERD: gastroesophageal reflux disease; op: operative, EE: erosive esophagitis; D&B: Downs and Black score; NA: not available; NC: not clear

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Appendix: search strategy for our search

Ovid MEDLINE(R) and In-Process & Other Non-Indexed Citations and Daily (1946 to present)
Search run July 2020

1. Barrett Esophagus/
2. (Barrett$ adj1 (esophagus or oesophagus)).ti,ab.
3. (barrett esophag$ or barrett's esophag$ or barretts esophag$ or barrett oesophag$ or barrett's oesophag$ or barretts oesophag$).ti,ab.
4. (esophag$ or oesophag$ or esophagoscop$ or oesophagoscop$).ti,ab.
5. ((esophagogastric or oesophagogastric or gastro-esophageal or gastroesophageal or gastro-oesophageal or gastrooesophageal or esophageal or esophagus or oesophag$) and (inflamed or inflammation or inflammatory or irritat$ or erythem$ or erythaem$ or inflitrat$ or ulcer or ulcers or ulcerat$ or dyspla$ or hyperplas$ or metaplas$)).ti,ab.
6. (reflux or heartburn or GER or GERD or dyspepsi$).ti,ab.
7. exp esophagitis/
8. 1 or 2 or 3 or 4 or 5 or 6 or 7
9. exp Bariatric Surgery/ or exp Obesity/su
10. (jejunoileal bypass$ or vertical banded gastroplast$ or gastric bypass$ or stomach bypass$ or Roux-En-Y or "fobi" or biliopancreatic diversion or gastric band$ or AGB or biliopancreatic diversion$ or gastroplasty or gastroplasties or gastric stapl$ or stomach stapl$ or bariatric$ or "lap. band" or lap-band or "lap band" or gastric partition$ or sleeve gastrectom$).ti,ab.
11. 9 or 10
12. ("weight loss" or "weight reduction" or obesity or bariatric).ti,ab.
13. exp bariatric medicine/
14. 12 or 13
15. (surgery or surgeries or surgical or operation or operations or operative).ti.
16. 14 and 15
17. 11 or 16
18. (prevalence or incidence or epidemiol* or survey or "rapid assessment" or "situation assessment" or "situational assessment" or RAR or cohort or surveillance or seroprevalence or seroincidence or seroepidemiol* or screening).ti,ab,kw. or exp epidemiologic methods/ or exp epidemiologic studies/ or exp sentinel surveillance/ or exp seroepidemiologic studies/ or exp cohort studies/ or exp cross-sectional studies/ or exp longitudinal studies/ or exp follow-up studies/ or exp prospective studies/
19. 8 and 17 and 18

Embase (Elsevier) (1947 – present)
Search run July 2020

1. 'Barrett esophagus'/exp OR ((Barrett* NEAR/1 esophagus) OR (Barrett* NEAR/1 oesophagus) OR "barrett esophag*" OR "barrett?s esophag*" OR "barretts esophag*" OR "barrett oesophag*" OR "barrett?s oesophag*" OR "barretts oesophag*"):ti,ab OR ((esophagi* OR oesophag* OR esophagoscop* OR oesophagoscop*)):ti,ab OR ((esophagogastric OR oesophagogastric OR gastro-

esophageal OR gastroesophageal OR gastro-oesophageal OR gastrooesophageal OR esophageal OR esophagus OR oesophag*) AND (inflamed OR inflammation OR inflammatory OR irritat* OR erythem* OR erythaem* OR inflitrat* OR ulcer OR ulcers OR ulcerat* OR dyspla* OR hyperplas* OR metaplas*)):ti,ab OR (reflux OR heartburn OR GER OR GERD OR dyspepsi*):ti,ab OR 'esophagitis'/exp

2. 'Bariatric Surgery'/exp OR 'Obesity'/exp su OR ("jejunoileal bypass*" OR "vertical banded gastroplast*" OR "gastric bypass*" OR "stomach bypass*" OR Roux-En-Y OR fobi OR "biliopancreatic diversion" OR "gastric band*" OR AGB OR "biliopancreatic diversion*" OR gastroplasty OR gastroplasties OR "gastric stapl*" OR "stomach stapl*" OR bariatric* OR "lap. band" OR lap-band OR "lap band" OR "gastric partition*" OR "sleeve gastrectom*"):ti,ab OR (('bariatrics'/exp OR ("weight loss" OR "weight reduction" OR obesity OR bariatric):ti,ab) AND (surgery OR surgeries OR surgical OR operation OR operations OR operative):ti)
3. ((prevalence or incidence or epidemiology or survey or surveillance or screening or seroprevalence or seroincidence or cohort or "rapid assessment" or "situation assessment" or "situational assessment" or "RAR"):ti,ab,kw or 'seroepidemiology'/exp or 'seroprevalence'/exp or 'epidemiology'/exp or 'prevalence'/exp or 'epidemiological data'/exp or 'incidence'/exp or 'observational study'/exp or 'cohort analysis'/exp)
4. #1 AND #2 AND #3

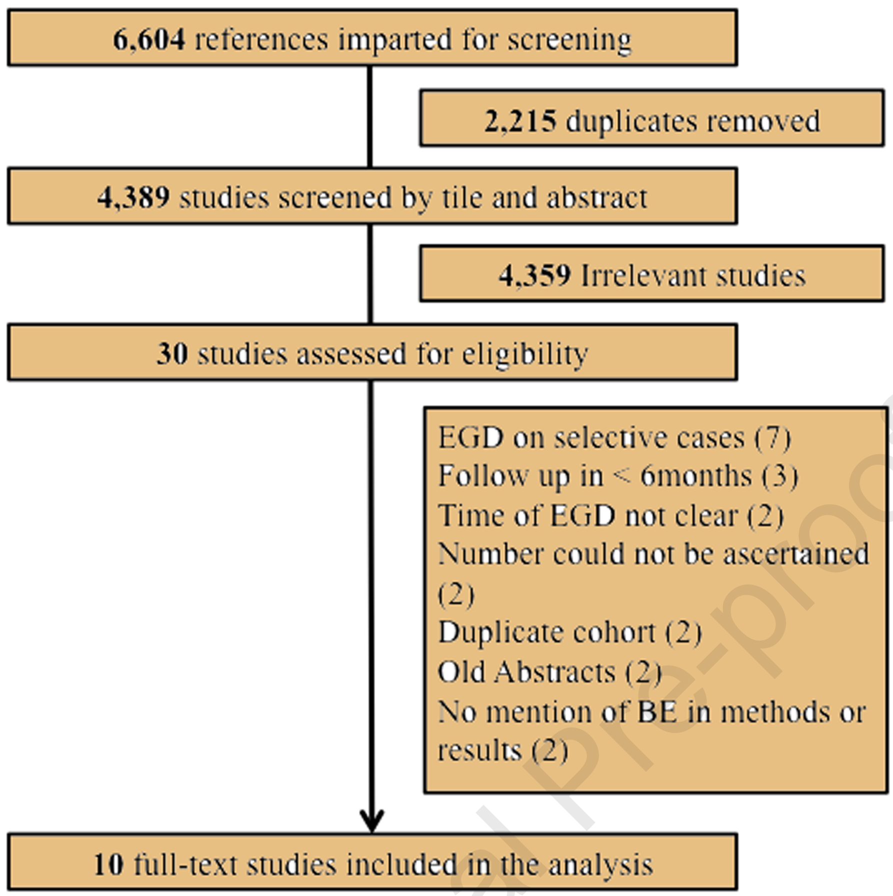
Web of Science
Science Citation Index Expanded (SCI-EXPANDED) --1900-present
Conference Proceedings Citation Index- Science (CPCI-S) --1993-present
Search run July 2020

TS= ("Barrett Esophagus" OR (Barrett* NEAR/1 esophagus) OR (Barrett* NEAR/1 oesophagus) OR "barrett esophagi*" OR "barrett's esophag*" OR "barretts esophagi" OR "barrett oesophag*" OR "barrett's oesophag*" OR "barretts oesophag*" OR esophag* OR oesophag* OR esophagoscop* OR oesophagoscop* OR ((esophagogastric OR oesophagogastric OR gastro-esophageal OR gastroesophageal OR gastro-oesophageal OR gastrooesophageal OR esophageal OR esophagus OR oesophag*) AND (inflamed OR inflammation OR inflammatory OR irritat* OR erythem* OR erythaem* OR inflitrat* OR ulcer OR ulcers OR ulcerat* OR dyspla* OR hyperplas* OR metaplas*)) OR reflux OR heartburn OR GER OR GERD OR dyspepsi*)
TS= ("Bariatric Surgery" OR (Obesity NEAR/3 surgery) OR (Obese NEAR/3 surgery) OR "jejunoileal bypass*" OR "vertical banded gastroplast*" OR "gastric bypass*" OR "stomach bypass*" OR Roux-En-Y OR fobi OR "biliopancreatic diversion" OR "gastric band*" OR AGB OR "biliopancreatic diversion*" OR gastroplasty OR gastroplasties OR "gastric stapl*" OR "stomach stapl*" OR bariatric* OR "lap. band" OR lap-band OR "lap band" OR "gastric partition*" OR "sleeve gastrectom*" OR (("weight loss" OR "weight reduction" OR obesity OR bariatric OR "bariatric medicine") AND (surgery OR surgeries OR surgical OR operation OR operations OR operative)))
TS=(prevalence OR incidence OR epidemiol* OR survey OR "rapid assessment" OR "situation assessment" OR "situational assessment" OR RAR OR cohort OR

surveillance OR seroprevalence OR seroincidence OR seroepidemiol* OR screening OR "epidemiologic methods" OR "epidemiologic studies" OR "sentinel surveillance" OR "seroepidemiologic studies" OR "cohort studies" OR "cross-sectional studies" OR "longitudinal studies" OR "follow-up studies" OR "prospective studies")
#1 AND #2 AND #3

Cochrane Library and Central Register of Controlled Trials (CENTRAL)
Search run on July 2020

#1 [mh ^"Barrett Esophagus"]
#2 ((Barrett* NEAR1 esophagus) OR (Barrett* NEAR1 oesophagus)):ti,ab
#3 (barrett esophag* OR barrett's esophag* OR barretts esophag* OR barrett oesophag* OR barrett's oesophag* OR barretts oesophag*):ti,ab
#4 (esophag* OR oesophag* OR esophagoscop* OR oesophagoscop*):ti,ab
#5 ((esophagogastric OR oesophagogastric OR gastro-esophageal OR gastroesophageal OR gastro-oesophageal OR gastrooesophageal OR esophageal OR esophagus OR oesophag*) AND (inflamed OR inflammation OR inflammatory OR irritat* OR erythem* OR erythaem* OR inflitrat* OR ulcer OR ulcers OR ulcerat* OR dyspla* OR hyperplas* OR metaplas*)):ti,ab
#6 ("reflux" OR "heartburn" OR "GER" OR "GERD" OR "dyspepsi*"):ti,ab
#7 [mh esophagitis]
#8 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
#9 [mh "Bariatric Surgery"] OR [mh Obesity] su
#10 ("jejunoileal bypass*" OR "vertical banded gastroplast*" OR "gastric bypass*" OR "stomach bypass*" OR "Roux-En-Y OR fobi" OR "biliopancreatic diversion" OR "gastric band*" OR "AGB" OR "biliopancreatic diversion*" OR "gastroplasty" OR "gastroplasties" OR "gastric stapl*" OR "stomach stapl*" OR "bariatric*" OR "lap. band" OR "lap-band" OR "lap band" OR "gastric partition*" OR "sleeve gastrectom*"):ti,ab
#11 #9 OR #10
#12 ("weight loss" OR "weight reduction" OR "obesity" OR "bariatric"):ti,ab
#13 [mh "bariatric medicine"]
#14 #12 OR #13
#15 (surgery OR surgeries OR surgical OR operation OR operations OR operative):ti
#16 #14 AND #15
#17 #11 OR #16
#18 (prevalence OR incidence OR epidemiol* OR survey OR "rapid assessment" OR "situation assessment" OR "situational assessment" OR RAR OR cohort OR surveillance OR seroprevalence OR seroincidence OR seroepidemiol* OR screening):ti,ab,kw OR [mh "epidemiologic methods"] OR [mh "epidemiologic studies"] OR [mh "sentinel surveillance"] OR [mh "seroepidemiologic studies"] OR [mh "cohort studies"] OR [mh "cross-sectional studies"] OR [mh "longitudinal studies"] OR [mh "follow-up studies"] OR [mh "prospective studies"]
#19 #8 AND #17 AND #18



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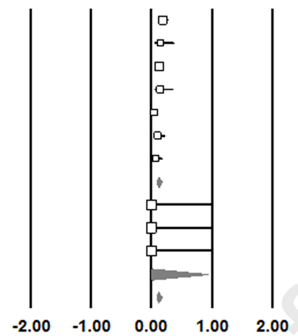
Group by Follow up	Study name	Event rate	Lower limit	Upper limit	*P* Value
Long	Sebastianelli 2019	0.189	0.121	0.283	.000
Long	Felsenreich 2017	0.150	0.049	0.376	.006
Long	Soricelli 2018	0.132	0.086	0.198	.000
Long	Elkassem 2018	0.143	0.047	0.361	.004
Long	Csendes 2019	0.038	0.015	0.098	.000
Long	Dimbezel 2020	0.100	0.038	0.238	.000
Long	Lallemand 2019	0.074	0.028	0.181	.000
Long		0.115	0.078	0.167	.000
Short	Tai 2013	0.000	0.000	1.000	.379
Short	Sharma 2014	0.000	0.000	1.000	.420
Short	Viscido 2018	0.000	0.000	1.000	.353
Short		0.000	0.000	0.931	.131
Overall		0.114	0.077	0.166	.000

Statistics for each study

Event rate and 95% CI



Meta Analysis

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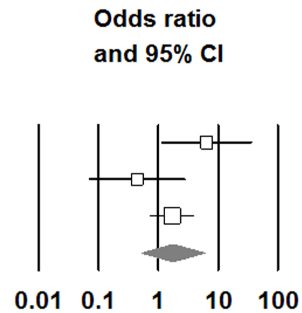
Study name	Odds ratio	Lower limit	Upper limit	*P* Value
	Statistics for each study			
Sebastianelli 2019	6.46	1.13	36.84	.036
Felsenreich 2017	0.44	0.07	2.86	.393
Soricelli 2018	1.70	0.72	4.03	.227
	1.74	0.52	5.89	.370



Meta Analysis

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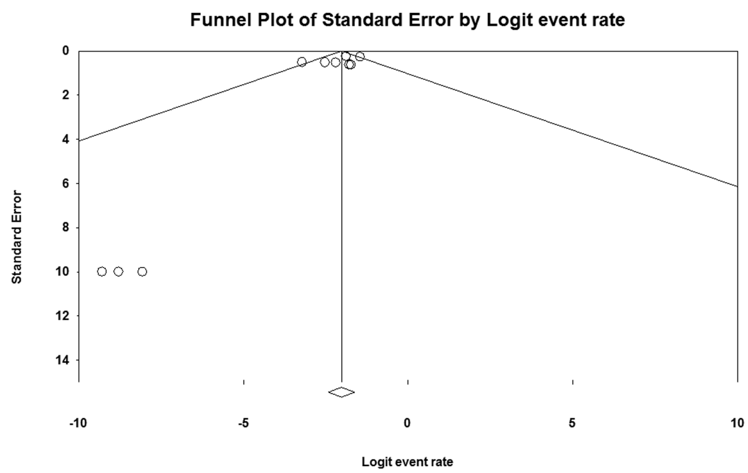

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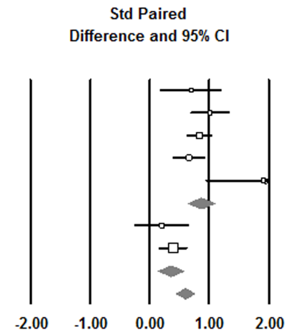
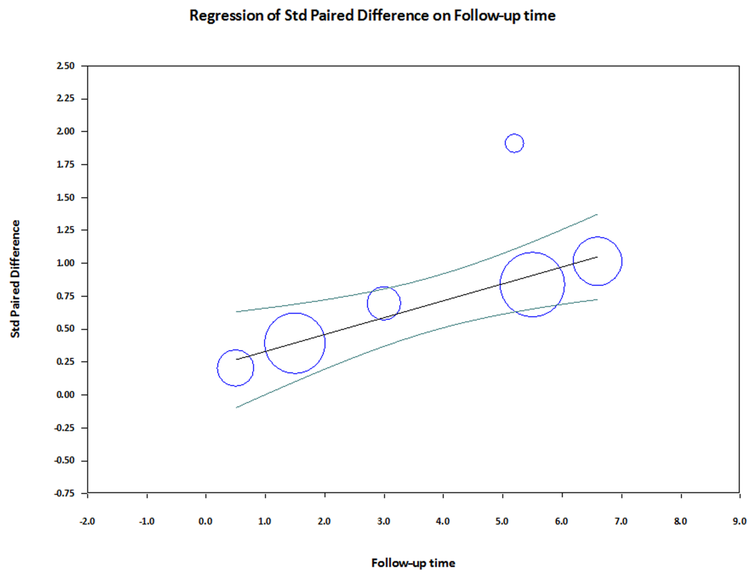
Group by Follow up	Study name	Std Paired Difference	Lower limit	Upper limit	*P* value
Long	Elkassem 2018	0.69	0.18	1.21	.009
Long	Sebastianelli 2019	1.01	0.68	1.34	.000
Long	Soricelli 2018	0.84	0.62	1.05	.000
Long	Csendes 2019	0.66	0.38	0.94	.000
Long	Dimbezel 2020	1.91	0.94	2.88	.000
Long		0.86	0.64	1.09	.000
Short	Sharma 2014	0.20	-0.26	0.67	.395
Short	Viscido 2018	0.39	0.15	0.63	.001
Short		0.35	0.14	0.57	.001
Overall		0.60	0.44	0.75	.000



Meta Analysis



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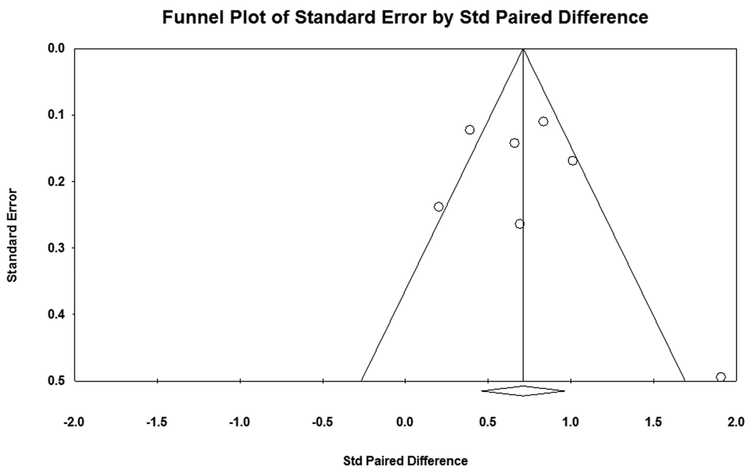

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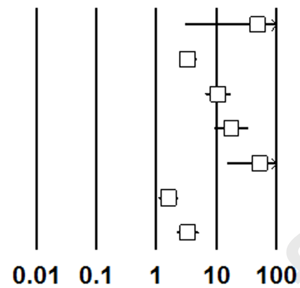
Study name	Statistics for each study			
	Odds ratio	Lower limit	Upper limit	*P* value
Felsenreich 2017	49.0	3.0	803.5	.006
Soricelli 2018	3.4	2.4	4.8	.000
Sebastianelli 2019	10.8	6.6	17.6	.000
Tai 2013	17.9	9.3	34.7	.000
Sharma 2014	53.6	15.4	186.2	.000
Viscido 2018	1.6	1.1	2.4	.019
Csendes 2019	3.4	2.2	5.1	.000

Odds ratio and 95% CI

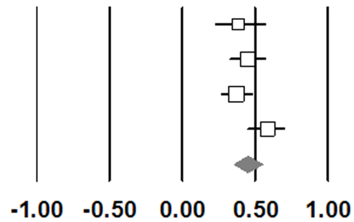


Meta Analysis

Journal Pre-proof

Study name	Statistics for each study			
	Event rate	Lower limit	Upper limit	*P* value
Felsenreich 2017	0.38	0.22	0.58	.244
Tai 2013	0.45	0.33	0.58	.432
Viscido 2018	0.37	0.27	0.49	.028
Csendes 2019	0.58	0.45	0.71	.219
	0.45	0.35	0.55	.320

Event rate and 95% CI



Meta Analysis

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Lead Author: **Bashar Qumseya, MD, MPH, FASGE**

Article: **Barrett's esophagus post Sleeve Gastrectomy: a systematic review and meta-analysis**

Date: **6/9/2020**

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ASGE
GASTROINTESTINAL ENDOSCOPY

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Acronyms

Sleeve gastrectomy (SG)

Gastroesophageal reflux disease (GERD)

Barrett's esophagus (BE)

Esophagogastroduodenoscopy (EGD)

Esophageal adenocarcinoma (EAC)

Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA)

95% confidence intervals (CI)

Erosive esophagitis (EE)

Risk difference (RD)

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