

Safety and Efficacy of EDGE in Roux-en-Y Gastric Bypass Patients: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Endoscopic Retrograde Cholangiopancreatography (ERCP) in Roux-en-Y gastric bypass patients is very challenging. Access to the excluded stomach or jejunum using Endoscopic Ultrasound (EUS) guided Lumen-Apposing Metal Stents (LAMS) and performing ERCP is becoming more available.

Methods: We conducted a systematic review and meta-analysis with two authors independently reviewing electronic databases (PubMed, Embrace, and Cochrane Library) from inception through June 2022. Fixed and random effects models were used to calculate the weighted mean (WM), pooled proportions, and confidence intervals (CI).

Results: On initial search, 457 articles were found, of which 63 were selected and reviewed. Data was extracted from 11 studies (n= 543) examining EDGE procedure in Roux-en-Y gastric bypass patients. The primary outcome was successful LAMS placement with a pooled rate of 97.84% (95% CI = 96.46 to 98.89). Successful ERCP through the LAMS was calculated as the secondary outcome. This gave a pooled proportion of 95.57% (95% CI = 93.11 to 97.51). The pooled proportion of patients who underwent ERCP in one session was 46.89 % (95% CI = 42.59 to 51.22), and in two different sessions was 53.45 % (95% CI = 49.13 to 57.75). This pooled analysis noted a persistent fistula after stent removal in 14.02 % of patients (95% CI = 11.12 to 17.18). Procedure-related complications such as stent migration were reported in 7.72% of patients (95% CI = 5.63 to 10.09), and perforation was seen in 4.33 % of patients (95% CI = 2.67 to 6.36). The pooled analysis of other complications included bleeding that was seen in 1.83 % of patients (95% CI = 0.79 to 3.27), post-ERCP pancreatitis in 2.43 % of patients (95% CI = 1.18 to 4.11), and infection in 1.04 % of patients (95% CI = 0.27 to 2.27). The pooled estimates calculated with fixed and random effects models were the same. Publication bias calculated using the Harbord-Egger bias indicator gave a value of 2.60 ($p = 0.16$). The Begg-Mazumdar indicator gave Kendall's tau b value of 0.07 ($p = 0.90$).

Conclusions: EDGE is a minimally invasive procedure with a high technical success rate in patients requiring biliary intervention after Roux-en-Y gastric bypass. There are minimal intra and post-procedural complications. So, EDGE can be used as the first-line therapy in this patient population.

Keywords

Endoscopic ultrasound, Gastric bypass procedure, Endoscopic ultrasound-guided axios stent, EUS guided ERCP, Post bypass ERCP.

Synopsis

EUS-guided LAMS placement is a successful and safe method

to perform ERCP in patients with gastric bypass surgery. It has minimal intra-procedural and post-procedural complications.

Introduction

Bariatric surgeries are becoming more popular and available due to the obesity epidemic and the failure of non-surgical weight loss reduction techniques [1-3]. Bariatric surgeries help control

obesity and complications associated with obesity increasingly [1,4]. About 36% of patients who undergo RYGB were noted to develop gallstones, of which 5.3% require ERCP [5-7]. Therefore, there is a greater need to create different diagnostic and therapeutic techniques to treat patients with altered anatomy.

Patients who undergo Roux-en-Y bypass surgery have specific challenges when these patients require ERCP for biliary intervention [8,9]. These techniques are challenging due to the difficulty of maneuvering through the anastomoses and identifying and gaining access to the ampulla [10]. Endoscopic Ultrasound-directed trans-gastric ERCP (EDGE) is emerging as an alternative to enteroscopy and laparoscopy-assisted ERCP in patients with Roux-en-Y bypass anatomy [11,12]. Laparoscopic-assisted ERCP has a higher technical success when compared to enteroscopy-assisted ERCP (95% vs 63%) [8,13,14]; however, it has very high complication rates of up to 15 % and requires multiple interdisciplinary teams [1,2,8]. EDGE accesses the excluded stomach from the gastric pouch with a lumen apposing metal stents. Followed by ERCP performed through the LAMS [10,12,13]. This technique has a higher success rate with minimal complications. Here, we conducted a meta-analysis and systematic review to assess the safety and efficacy of this technique.

Methods

Selection Criteria

ERCP through EUS-guided LAMS placement in Roux-en-Y bypass patients were selected.

Inclusion Criteria

Studies that used EUS-guided LAMS placement followed by ERCP through the LAMS were included.

Exclusion Criteria

Studies that did not use EUS-guided LAMS or ERCP were excluded.

Data Collection

We conducted a systematic review and meta-analysis with two authors independently reviewing electronic databases, including PubMed (167), Embrace (139), and Cochrane Library (151). We mentioned the numbers from the initial search reference articles from inception through June 2022.

The major gastroenterology journals were searched manually for abstracts regarding the topic. The terms used to search for articles included endoscopic ultrasound-guided LAMS placement, ERCP through LAMS, and EDGE in gastric bypass patients. The data searched and extracted was reviewed by both the authors and mutually agreed upon before analysis. Cohen's k was used to quantify the agreement among the reviewers for the data collected.

Quality of Studies

The quality of the clinical trials with control and treatment groups was assessed. We used several criteria to determine the quality of the study (such as randomization and biases, including selection

bias). Most of the studies did not have a control group; therefore, the criteria needed to be more applicable as there is no consensus on assessing these studies.

Statistical Analysis

The meta-analysis was conducted by calculating the pooled proportions of the outcomes individually. We calculated the pooled proportion of patients with successful EUS-guided LAMS placement. The outcome we measured included the pooled proportion of patients with successful ERCP through LAMS. Patients who underwent ERCP in a single session and multiple sessions were also calculated. The arcsine-based transformation model, such as the Freeman-Turkey variant, was used to transform these pooled data into a quantity. The inverse arcsine variance weights were used for the fixed effects model, and DerSimonian-Laird weights were used for the random effects model. These models were used to calculate the pooled proportion as the back-transform for the weighted mean of the transformed proportions [15]. The point estimates about each study's pooled estimate summary were shown using the Forest plots. The width of the point estimates in the forest plots indicated the weight assigned to that study. The effect of publication and selection bias was tested using the Harbord-Egger bias indicator [16,17] and the Begg-Mazumdar bias indicator [18,19]. We constructed funnel plots using the standard error and diagnostic odds ratio to evaluate potential publication bias.

Microsoft Excel was used to collect data and for all the analyses.

Results

Upon initial search, we found 457 articles about the EDGE procedure in Roux-en-Y gastric bypass patients. Out of those, 63 articles were relevant to the topic. We selected 11 studies (n=543) that met the inclusion criteria for this study. These selected articles were published and available as full-text articles. Figure 1 shows the search data. The pooled estimates were calculated using the fixed effect model.

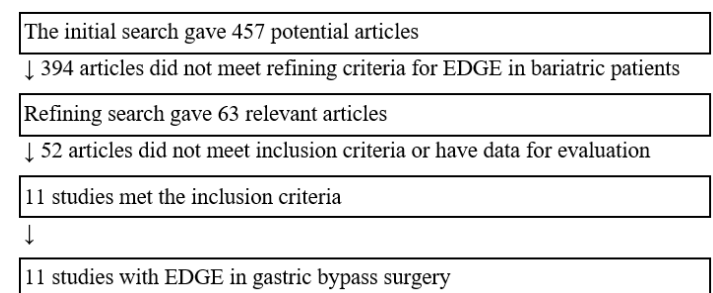


Figure 1: Search results for the meta-analysis.

This meta-analysis includes 543 patients, with 74 males and 298 females. Among these, 34 patients had biliary stricture, 135 had choledocholithiasis, 24 had cholangitis, 29 had recurrent pancreatitis, and 24 had pancreatic lesions. The primary outcome was successful LAMS placement with a pooled rate of 97.84% (95% CI = 96.46 to 98.89). The forest plot in Figure 2 shows

this pooled analysis. Successful 15 mm LAMS placement was seen in a proportion of 73.80% (95% CI = 69.28 to 78.08). The similar success rate with a 20 mm LAMS had a pooled proportion of 43.62% (95% CI = 37.76 to 49.56). Transgastric fistula was created in a pooled analysis of 58.26% (95% CI = 54.12 to 62.36) and transjejunal fistula in 45.24% (95% CI = 40.98 to 49.53). LAMS was sutured in 17.72% of the patients (95% CI = 14.17 to 21.58). Successful ERCP through the LAMS was calculated as the secondary outcome. This gave a pooled proportion of 95.57% (95% CI = 93.11 to 97.51). The forest plot in Figure 3 shows this pooled analysis. The pooled proportion of patients who underwent ERCP in one session was 46.89% (95% CI = 42.59 to 51.22), and in two different sessions was 53.45% (95% CI = 49.13 to 57.75).

proportion of 23.95% (95% CI = 19.16 to 29.11). The pooled analysis of patients requiring other modalities to help with fistula closure was calculated. Clips were used in 4.62% of patients (95% CI = 2.82 to 6.82), OVESCO in 6.56% of patients (95% CI = 4.54 to 8.93), and Apollo suture in 31.06% of patients (95% CI = 26.82 to 35.46). Procedure-related complications such as stent migration were noted in 7.72% of patients (95% CI = 5.63 to 10.09), and perforation was seen in 4.33% of patients (95% CI = 2.67 to 6.36). The pooled analysis of other complications included bleeding that was seen in 1.83% of patients (95% CI = 0.79 to 3.27), post-ERCP pancreatitis in 2.43% of patients (95% CI = 1.18 to 4.11), and infection in 1.04% of patients (95% CI = 0.27 to 2.27). Weight changes in patients who underwent EDGE procedures were studied in 6 of the 11 studies included in this paper with a mean follow-up of 6 months. A weight gain of 0.9 - 1.7 kgs was noted in a pooled proportion of 20.15% of patients (95% CI = 15.04 to 31.82). Weight loss of 1 - 8.6 kgs was measured in a pooled proportion of 36.84% of patients (95% CI = 24.71 to 48.37). The publication bias calculated using the Harbord-Egger bias indicator yielded a value of 2.60 (p = 0.16). The Begg-Mazumdar indicator produced Kendall's tau b value of 0.07 (p = 0.90). Figure 4 shows the funnel plots for publication bias. An interobserver variability for data collection among the reviewers gave a Cohen's k value of 1.0.

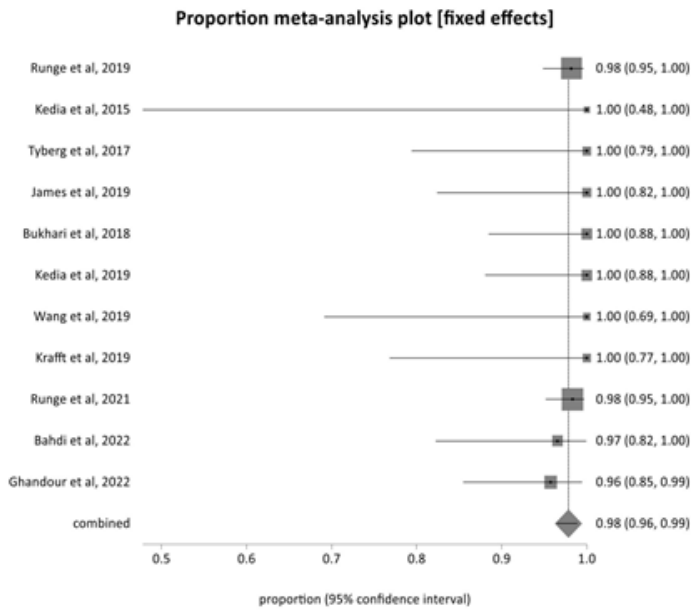


Figure 2: Pooled percentage of patients with successful LAMS placement.

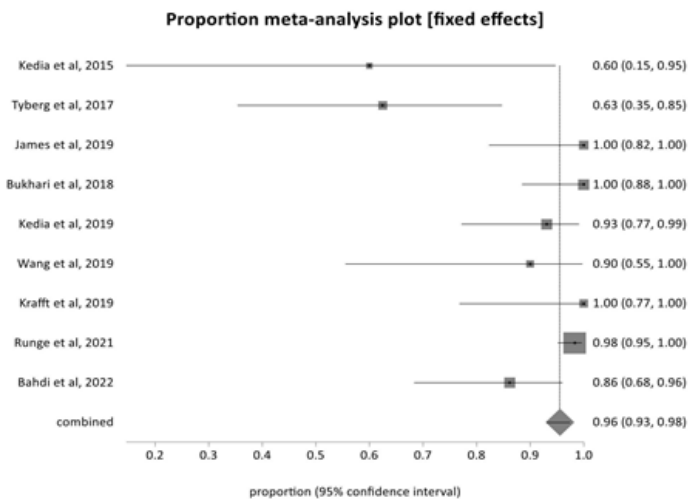


Figure 3: Pooled percentage of patients with successful ERCP.

This pooled analysis noted a persistent fistula after stent removal in 14.02% of patients (95% CI = 11.12 to 17.18). Spontaneous fistula closure upon LAMS removal was calculated with a pooled

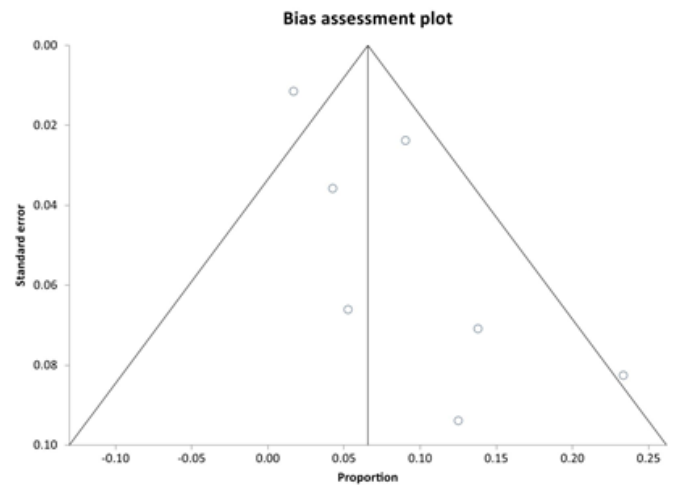


Figure 4: Funnel plot showing publication bias.

Discussion

Bariatric procedures are becoming more popular as they reduce obesity and its related complications. Due to a significant increase in bariatric surgery, there is an increase in performing endoscopic interventions in patients with altered anatomy [1]. About 50% of post-bariatric surgery patients can develop gallstones in 2 years [20,21]. Biliary interventions in patients who have undergone Roux-en-Y bypass are very challenging. Many surgical and endoscopic techniques, such as laparoscopic-assisted ERCP (LA-ERCP) and external EDGE or enteroscopy-assisted ERCP (e-ERCP), have been used. However, these techniques require a multi-disciplinary approach and a high intra-procedural complication rate [22-24]. EDGE is used more commonly in these patients and can be

performed in one sitting without requiring a multi-disciplinary team. EDGE is performed by creating an endoscopic fistula to the excluded stomach via EUS-guided LAMS placement; ERCP is then performed through the LAMS. In this meta-analysis, we looked at this procedure's efficacy and the associated risks in patients with altered anatomy.

Overall, we found that about 97% of patients in this study had successful LAMS placement with either a 15 mm LAMS or a 20 mm LAMS. Successful ERCP through the LAMS was around 96%, similar to patients undergoing LA-ERCP or e-ERCP. Some medical institutes still use LA-ERCP and e-ERCP as first-line therapy, especially in patients with cholangitis who require emergent biliary drainage [22]. However, these procedures are very time-consuming and need a multispecialty team of doctors with higher procedural complication rates. This meta-analysis found that EDGE has similar success with fewer adverse events, as noted in a comparative retrospective study by Kedia et al. in 2019. This study included a total of 71 patients, of which 29 patients underwent EDGE and 43 patients underwent LA-ERCP. There was a 98% success rate in both patient groups. However, the adverse events were lower in the EDGE group when compared to the LA-ERCP group [25].

Similarly, 2018, Bukhari et al. did a multicenter retrospective study comparing EDGE and e-ERCP. They included 60 patients, with 30 in each group, and had a 100% success rate in the EDGE group compared to 97% in the e-ERCP group. Procedure-related complications were also significantly lower in the EDGE group [26].

The biggest concern with the EDGE technique is the risk of stent migration as an endoscope is passed through the LAMS. This risk was higher in the initial studies, as noted by Kedia et al. in 2015. The study included five patients and used a 15 mm LAMS with 100 % successful ERCP; however, 3 of the five patients had stent dislodgement during the procedure, suspected to be due to stent over-dilation [9]. At the time, this was still a novel technique, but in subsequent studies, this risk decreased with under-dilation of the 15 mm LAMS or alternative use of a 20 mm LAMS to minimize the risk of stent migration [10,14]. Extensive retrospective studies published by Rungi et al. in 2019 and 2021, including 166 and 178 patients, respectively, had 16 patients with stent migration [11,14]. This is thought to be due to the more liberal use of 20 mm LAMS and skillful manipulation by endoscopists, as EDGE is being performed in many centers.

Another technique to decrease the risk of stent migration was using endoscopic suturing of the LAMS before ERCP. In 2022, Ghandour et al. included 47 patients in a retrospective study, of which 17 patients had LAMS suturing with 0 stent migration and 30 patients without LAMS sutures; five patients were noted to have stent migration [13]. This technique can also be used case-by-case to stabilize the LAMS if there is concern for stent migration. EDGE can be performed in a single session or as double sessions based on the patient's clinical scenario and fistula maturation. James et al. and Krafft et al. 2019 compared the outcomes of

single-session EDGE versus double-session EDGE [5,10]. In these studies, emergent EDGE was done in one sitting for patients with Cholangitis with a 97% success rate and minimal to no stent migration. This was later confirmed in 2022 by Bahdi et al. and Ghandour et al., who included 29 and 47 patients, of which 17 patients in each group underwent single-session EDGE. There was only one patient in the single session EDGE with stent migration compared to 6 patients in the double session EDGE with stent migration [8,13]. All these studies imply that there is not much difference in the outcome and procedural adverse effects in both single session versus double session EDGE. Either can be done based on the clinical illness and endoscopist's comfort level during the procedure [4,21].

Persistent fistula and weight gain are significant concerns in patients undergoing EDGE after bariatric surgery, especially in patients with longer LAMS indwelling time [7,23,27]. In this meta-analysis, the average time for stent removal varied from 42 days to 84 days [13,25]. Most patients had spontaneous fistula closure upon LAMS removal [8,10,13,25]; however, a small patient population required additional endoscopic intervention for fistula closure. These techniques included closure with clips, OVESCO, endoscopic suture, and APC to promote fistula closure, which accounted for about 30 % of the patients [1,5,8-14,25,26]. Some of the studies looked into weight changes, and about 20 % of the patients had a weight gain of 0.9 - 1.7 kgs, and 37% had a weight loss of 1 - 8.6 kgs at follow-up visits [1,5,8,25]. This suggests that EDGE does not increase the risk of weight gain in the bariatric population. Other procedure-related complications, including perforation, post-ERCP pancreatitis, infection, and bleeding, were less than 5%, making this a very safe procedure with high success rates [1,5,8-14,25,26].

There are some limitations to this meta-analysis, including smaller sample sizes and the retrospective nature of most of the studies, with only two prospective studies available so far. There is no comparison between the outcomes in patients who underwent transgastric and transduodenal fistula access for ERCP. Not all studies compared the outcomes with LA-ERCP or e-ERCP and included only the EDGE group, which might raise the question of selection bias. Weight changes were also measured only at short interval follow-ups and were not included in all the literature available. Therefore, longer follow-up intervals to assess the long-term effects of EDGE on weight changes need to be studied in post-bariatric groups of patients. This meta-analysis and systematic review calculated bias using Egger and Begg-Mazumdar bias indicators that showed no statistically significant bias. Furthermore, funnel plots were used to represent publication bias among the studies included in the present analysis, as shown in Figure 4.

Conclusion

EDGE is a minimally invasive procedure with a high technical success rate in patients requiring biliary intervention after Roux-en-Y gastric bypass. There are minimal intra and post-procedural complications. So, EDGE can be used as the first-line therapy in this patient population.

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