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Efficacy and safety of EUS-directed transgastric ERCP (EDGE) *versus* laparoscopic-assisted ERCP: A systematic review and meta-analysis

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ABSTRACT

The altered anatomy in Roux-en-Y gastric bypass (RYGB) makes conventional endoscopic retrograde cholangiopancreatography (ERCP) a technically challenging procedure. EUS–directed transgastric ERCP (EDGE) and laparoscopic-assisted ERCP (LA-ERCP) are alternative modalities used with comparable efficacy and adverse events in such patients. We conducted a meta-analysis comparing EDGE and LA-ERCP to assess the efficacy and safety in patients with RYGB. We conducted a comprehensive literature search from inception to July 7, 2022, on MEDLINE, EMBASE, Cochrane Register of Controlled Trials, and Web of Science databases using the core concepts of EDGE and LA-ERCP. We excluded case reports, case series (<10 patients), and review articles. Relative risk (RR) was calculated when comparing dichotomous variables, whereas mean difference was calculated for continuous outcomes. A 95% confidence interval (CI) and *P* values (<0.05 considered significant) were also generated. The search strategy yielded a total of 55 articles. We finalized 4 studies with total 192 patients (75 EDGE and 117 LA-ERCP). The rates of technical success were not significantly different for LA-ERCP and EDGE (RR, 0.994; 95% CI, 0.939–1.051; $P = 0.830$, $I^2 = 0\%$) Similarly, no difference in adverse events was noted between the 2 groups (RR, 1.216; 95% CI, 0.561–2.634; $P = 0.620$, $I^2 = 10.67\%$). Shorter procedure time was noted for EDGE compared with the LA-ERCP group (mean difference, 91.53 min; 95% CI, 69.911–113.157 min; $P < 0.001$, $I^2 = 8.32\%$). EDGE and LA-ERCP are comparable in terms of efficacy and safety. In addition, EDGE has overall lower procedural time. Our study suggests that EDGE should be considered as a first-line therapy if expertise available.

Key words: Bariatric surgery; EUS–directed transgastric ERCP (EDGE); Laparoscopic assisted ERCP (LA-ERCP); Roux-en-Y gastric bypass (RYGB)

INTRODUCTION

Roux-en-Y gastric bypass (RYGB) is a commonly performed bariatric surgery in the United States.[1] In patients who have undergone RYGB, conventional endoscopic retrograde cholangiopancreatography (ERCP) is not technically feasible because of altered anatomy. Therefore, other modalities are used to access the biliary system. Standard or balloon enteroscopy-assisted ERCP is one modality used to tackle the problem with long Roux limb; however, its technical success is limited.[2] Laparoscopic-assisted ERCP (LA-ERCP) allowed direct access to the duodenum despite being maximally invasive, and subsequently became the criterion standard ERCP method for RYGB patients.[3,4] Although efficient, LA-ERCP limitations include the need for multispecialty coordination, and surgical adverse events can be seen in as many as 36% of patients.[4,5]

EUS–directed transgastric ERCP (EDGE) is the newest option in the RYGB population.[6] In this method, EUS is used to insert a lumen-apposing metal stent connecting the gastric pouch or proximal efferent limb to the gastric remnant, allowing passage and therefore direct access to the duodenum and the major papilla. The benefits of EDGE over LA-ERCP are the absence of a requirement for surgical intervention, multispecialty coordination, and cost-effectiveness.[7] Within the last few years, single-arm and multiarm studies have emerged regarding adverse events and the efficacy of LA-ERCP and EDGE. A systematic review and meta-analysis of the aforementioned studies by Dhindsa et al.[8] showed technical success rates, clinical success rates, and safety profile of respective EDGE and LA-ERCP techniques. Despite its benefits, the most significant limitation of this meta-analysis was that it mainly included single-arm studies for which comparative efficacy and safety were not assessed, as this was the best data available at the time. Because this meta-analysis was published, new double-armed studies have

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Table 1

Baseline data of the included studies and rates of achieving technical success

Authors	Total (*N*)	LA-ERCP	EDGE	Age (LA-ERCP *vs.* EDGE), y		Sex (LA-ERCP *vs.* EDGE)		Procedure Indication (LA-ERCP *vs.* EDGE)		Technical Success of Achieving Therapeutic ERCP (*n/N*)	
				LA-ERCP	EDGE	LA-ERCP	EDGE	LA-ERCP	EDGE	LA-ERCP	EDGE
Kedia et al.[12]	72	43	29	55.75 (13.57)	57.25 (13.57)	F: 36 M: 7	F: 25 M: 4	B: 36 P: 7	B: 23 P: 6	42/43	28/29
Wang et al.[15]	60	42	18	50.6 (15.9)	59.3 (6.5)	F: 38 M: 4	F: 16 M: 2	B: 35 P: 7	B: 14 P: 4	41/42	18/18
Kochhar et al.[13]	44	18	26	60.78 (12.67)	60.77 (11.44)	F: 12 M: 6	F: 20 M: 6	B: 17 P: 2 Others: 2	B: 22 P: 4	17/18	26/26
Kröll et al.[14]	19	14	2	47.75 (12.71)	50.5 (0.89)	F: 3 M: 11	F: 2 M: 0	B: 14 P: 0	B: 2 P: 0	14/14	2/2

B: biliary; EDGE: EUS-directed transgastric ERCP; ERCP: endoscopic retrograde cholangiopancreatography; F: female; LA-ERCP: laparoscopic-assisted ERCP; M: male; P: pancreatic.

emerged comparing EDGE to LA-ERCP. Our study aimed to pool the data from these new studies to compare EDGE to LA-ERCP in terms of efficacy and adverse events.

METHODS

Search strategy

The "Meta-analysis of observational studies (MOOSE)" guidelines for the systematic review were used to plan the study.[9] A comprehensive literature search from inception to July 7, 2022, was conducted using the MEDLINE, EMBASE, Cochrane Register of Controlled Trials, and Web of Science databases. An experienced librarian (W.L.-S.) assisted with the search methodology. The core concepts of EDGE and LA-ERCP and their medical subject heading terms in various combinations were used for the aforementioned databases (Supplementary Table 1, http://links.lww.com/ENUS/A355). We added manual searching and cross-referencing to the computerized literature search.

Inclusion and exclusion criteria

We limited the screening to include randomized controlled trials and comparative observational studies assessing the incidence of adverse events, technical, and clinical success rate in EDGE *versus* LA-ERCP. Abstracts were included as we anticipated a lower number of overall full-text studies. We excluded case reports, case series (<10 patients), editorials, guidelines, and review articles.

Screening and data extraction

Two independent investigators (M.K.G. and H.H.) conducted the screening and data extraction. Conflict resolution was achieved through mutual discussion. Initially, titles, and abstracts were screened followed by full texts. Data pertaining to technical and clinical success rate, adverse events, length of hospital stay, and procedure time were recorded using Microsoft Excel (Microsoft, Redmond, Washington).

Data synthesis and statistical analysis

Statistical analysis was performed with Open meta-analyst (CEBM; University of Oxford, Oxford, United Kingdom). We calculated the pooled rates of each outcome. Dichotomous variables were compared using relative risk (RR), and continuous variables were assessed using mean difference (MD) along with a 95% confidence interval (CI) and *P* value (<0.05 was considered statistically significant). We used the random-effects model and DerSimonian-Laird method for pooling data. Study heterogeneity was calculated with the I^2 statistic values of 0%, 25%, 50%, and 75% as absent, low, moderate, and high heterogeneity.[10]

Bias assessment

Risk of bias assessment for the studies was used with the Newcastle-Ottawa Scale.[11] Funnel plot was used for qualitative

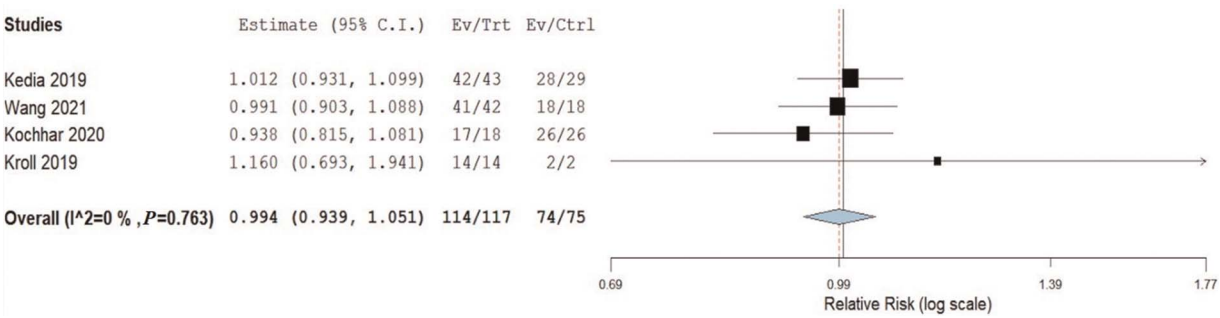

Figure 1. Technical success between EUS-directed transgastric ERCP (EDGE) and laparoscopic-assisted ERCP.

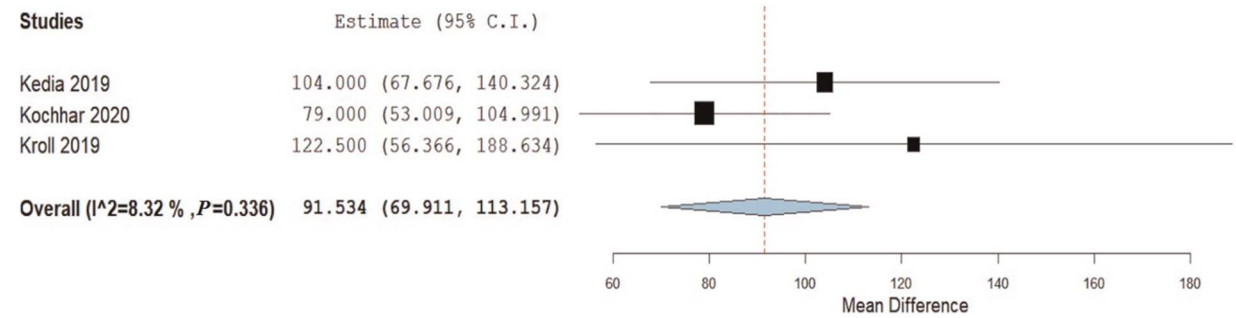

Figure 2. Procedure time between EUS-directed transgastric ERCP (EDGE) and laparoscopic-assisted ERCP.

and the Egger regression test for quantitative analysis for publication bias with a *P* value of <0.05, considered significant for the latter.

RESULTS

The search strategy yielded a total of 55 articles. After removing duplicates, 35 studies were analyzed. Four studies with 192 subjects were selected for final inclusion after implementing strict inclusion and exclusion criteria (Supplementary Figure 1, http://links.lww.com/ENUS/A355).[12–15] The studies were published between 2019 and 2021 and included 75 EDGE and 117 LA-ERCP patients [Table 1]. The mean age ranged from 47.75 to 60.78 years [Table 1]. One hundred fifty-two (77.9%) of the subjects were female (89 in the LA-ERCP group and 63 in the EDGE group), and 40 were male (28 in the LA-ERCP group and 12 in the EDGE group; Table 1).

Efficacy

All studies reported the technical success of reaching the excluded stomach and performing a successful ERCP. The technical success rates were comparable between LA-ERCP and EDGE (RR, 0.994; 95% CI, 0.939–1.051; $P = 0.830$, $I^2 = 0\%$; Table 1, Figure 1). All studies except that of Wang et al.[15] reported the procedure time of EDGE and LA-ERCP. There was a statistically significant MD of 91.534 minutes between the procedures favoring the EDGE as a less time-consuming procedure (95% CI, 69.911–113.157; $P < 0.001$ $I^2 = 8.32\%$; Figure 2).

Adverse events

Different sets of adverse events were reported in EDGE and LA-ERCP [Table 2]. LA-ERCP–specific adverse events included cellulitis and intraperitoneal abscess, whereas EDGE-specific adverse events included stent dislodgement. Some adverse events like cholangitis, bleeding, perforation, and pancreatitis were common between the 2 procedures. After pooling data of all adverse events, there was no statistical difference between the 2 modalities (RR, 1.216; 95% CI, 0.561–2.634; $P = 0.620$, $I^2 = 10.67\%$; Figure 3). Kedia et al.[12] reported adverse events like perforation, severe pancreatitis, and wound dehiscence requiring a second visit to the operating room as serious. Wang et al.[15] classified adverse events as mild, moderate, and severe, however, did not define adverse events. In the subgroup of serious adverse events reported in Kedia et al. and Wang et al., no statistical difference was observed between EDGE and LA-ERCP, either (RR, 1.077; 95% CI, 0.237–4.894; $P = 0.920$, $I^2 = 0\%$; Figure 4). Bleeding was reported by Kedia et al. and Kochhar et al.,[13] and no statistical significance was observed between EDGE and LA-ERCP, either (RR, 0.702; 95% CI, 0.120–4.120; $P = 0.695$, $I^2 = 0\%$; Figure 5). Lastly, there was no statistical significance in the length of hospital stay between the 2 modalities (MD, 1.330; 95% CI, 0.632–3.292; $P = 0.184$, $I^2 = 79.64\%$; Figure 6).

Risk of Bias

We used the Newcastle-Ottawa Scale to calculate the risk of bias as shown in Table 3. The score for studies ranged from 5 to 7, with an average score of 6.5. Because of a limited number of studies, funnel plot and the Egger regression test were not performed.

Table 2

Adverse events seen in EUS-directed transgastric ERCP versus laparoscopic-assisted ERCP

	Perforation		Pancreatitis			Bleeding				Cholangitis		Others	
	LA-ERCP	EDGE	LA-ERCP	EDGE	Stent Dislodgement*	LA-ERCP	EDGE	Intraperitoneal Abscess†	Cellulitis†	LA-ERCP	EDGE	LA-ERCP	EDGE
Kedia et al.[12]	2/43	1/29	0/43	2/29	3/29	1/43	1/29	2/43	1/43	NR	NR	2/43	0/29
Wang et al.[15]	1/42	0/18	5/42	0/18	1/18	0/42	0/18	1/42	2/42	NR	NR	5/42	0/18
Kochhar et al.[13]	0/18	0/26	1/18	0/26	1/26	1/18	2/26	0/18	0/18	NR	NR	1/18	0/26
Kröll et al.[14]	NR	0/2	1/14	0/2	0/2	NR	0/2	0/14	0/14	1/14	0/2	0/14	0/2

EDGE: EUS-directed transgastric ERCP; ERCP: endoscopic retrograde cholangiopancreatography; LA-ERCP: laparoscopic-assisted ERCP; NR: not reported; Others: wound dehiscence, abdominal wall seroma, abdominal wall seroma, severe abdominal pain (unclear etiology), partial small bowel obstruction, intra-abdominal infection.

*Adverse event seen only in LA-ERCP.

†Adverse event seen only in EDGE.

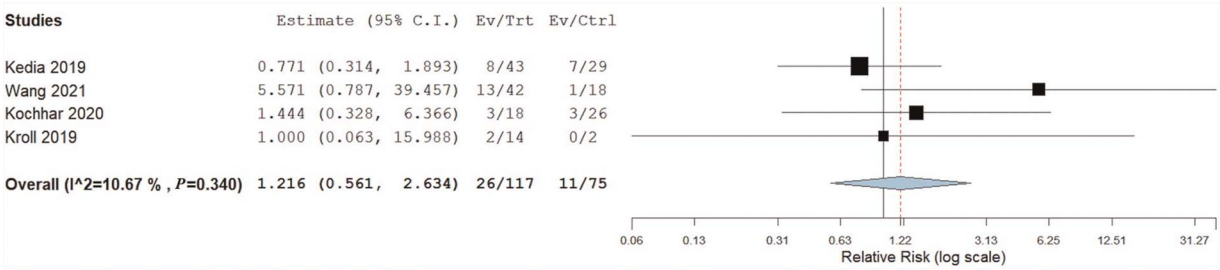

Figure 3. Adverse events between EUS-directed transgastric ERCP (EDGE) and laparoscopic-assisted ERCP.

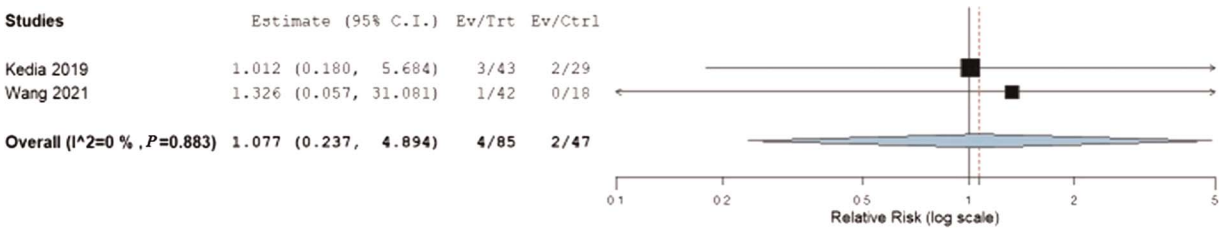

Figure 4. Severe adverse events between EUS-directed transgastric ERCP (EDGE) and laparoscopic-assisted ERCP.

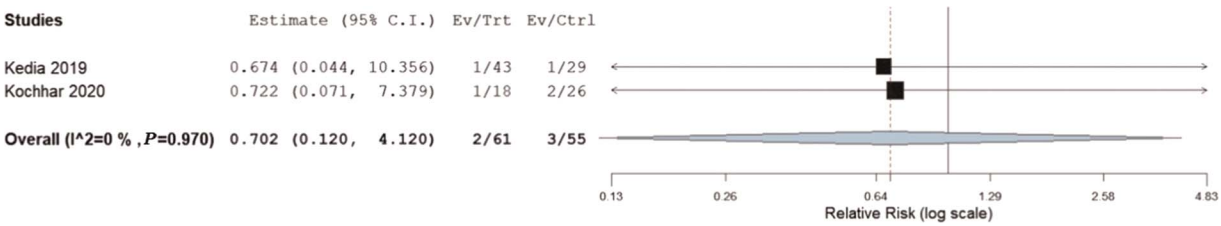

Figure 5. Bleeding rates between EUS-directed transgastric ERCP (EDGE) and laparoscopic-assisted ERCP.

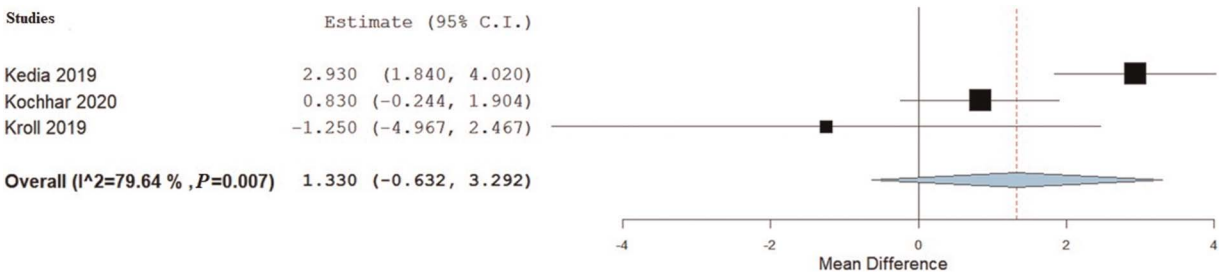

Figure 6. Length of hospital stay between EUS-directed transgastric ERCP (EDGE) and laparoscopic-assisted ERCP.

Table 3

Newcastle-Ottawa Scale for illustration of quality of studies

	Selection				Comparability	Exposure		
Study	Is the Case Definition Adequate?	Representativeness of Cases?	Selection of Controls	Definition of Controls	Comparability Based on Design or Analysis	Ascertainment of Exposure	Same Method of Ascertainment of Cases/Controls?	Nonresponse Rate?	Quality Score
Kedia et al.[12]	1	1	0	1	1	1	1	1	7
Wang et al.[15]	1	1	0	1	1	1	1	1	7
Kochhar et al.[13]	1	1	0	1	1	1	1	1	7
Kröll et al.[14]	1	1	0	0	1	1	1	1	5

DISCUSSION

This systematic review and meta-analysis demonstrates the superiority of EDGE over LA-ERCP in terms of shorter procedure duration. In terms of technical success and adverse events, the 2 modalities showed comparable rates.

The results of our study have important implications as the obesity epidemic continues in the United States and globally.[16] Four of 10 Americans are obese, and it is forecasted that by 2030, more than half of US adults will be obese.[16,17] Bariatric surgery is the most effective and sustainable modality for the treatment of obesity.[18,19] RYGB is the preferred bariatric procedure in patients with uncontrolled diabetes mellitus, severe gastroesophageal reflux, and bile reflux, and is the most common bariatric procedure after gastric sleeve.[20] Baseline obesity and subsequent rapid weight loss lead to an increased risk of forming gallstones after RYGB; which is seen in one-third of patients as early as 6 months after the procedure.[21,22] Therefore, there is a pressing need to find the ideal intervention between LA-ERCP and EDGE in the RYGB population.

Our study demonstrated a significantly longer procedure duration (difference of 91.5 minutes) in LA-ERCP compared with EDGE. LA-ERCP procedure requires multispecialty coordination between surgery and gastroenterology. This not only equals a significantly higher duration of procedure as illustrated in our study, but it also means higher cost and utilization of health care resources. James et al.[7] in its base case analysis showed that the use of the EDGE modality resulted in $4877 per patient with $5188 per quality-adjusted life year. LA-ERCP demonstrated total costs of $28,310 per patient with $34,259 per quality-adjusted life year. In this meta-analysis, we did not perform a cost-effectiveness analysis because of the paucity of data; however, we expect similar results to James et al.

Our meta-analysis showed statistically comparable rates of adverse events between LA-ERCP and EDGE with similar rates of perforation, pancreatitis, and bleeding. Some adverse events were unique to each technique such as stent dislodgement in ERCP and intraperitoneal abscess as seen with LA-ERCP.

Our study has limitations. First, all studies were retrospective and observational, which, because of their inherent design, have numerous biases including selection and confounding bias. Despite that, these were the highest quality literature available to date. Second, the total number of subjects was not robust, which limited the strength of the analysis. Nevertheless, all included studies included a direct comparison between EDGE and LA-ERCP, which allowed comparative meta-analysis in contrast to prior meta-analysis. Third, we were not able to perform a funnel plot for bias analysis because the number of studies was inadequate. Fourth, we were unable to compare each adverse event individually because some adverse events were procedure specific and not all studies measured the same events. However, we were able to compare total, severe, and bleeding adverse events because they were ubiquitously reported. Lastly, we were unable to provide subgroup analysis in terms of indication of procedure because of a lack of stratified data. This may not be important in technical success but may have implications for adverse event rates.

In conclusion, LA-ERCP and EDGE are comparable in terms of efficacy and safety, with the exception of procedure duration where EDGE is superior serving as a cost-effective alternative and

potentially decreasing total hospitalization length. Our study suggests that EDGE should be used as first-line therapy if available. Future high-quality randomized controlled trials of large numbers are needed to minimize bias and increase the strength of the data.

Conflict of Interest

Douglas G. Adler is the Co-Editor-in-Chief of the journal. This article was subject to the journal's standard procedures, with peer review handled independently of the editor and his research group.

Author Contributions

Manesh Kumar Gangwani & Hossein Haghbin contributed to study conception and draf write up; Fnu Priyanka & Yousaf Hadi contributed to material preparation and data collection; Dushyant Singh Dahiya contributed to methodology and write up; Faisal Kamal contributed to results and analysis; Wade Lee-Smith contributed to search strategy and design; Ali Nawras contributed to review of manuscript and discussion; Muhammad Aziz contributed to data analysis; Douglas G. Adler contributed to overall review, editing and finalization. All authors read and approved the final manuscript.

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