Article published online: 2023-05-26

Endoscopic ultrasound-directed transgastric ERCP (EDGE): A multicenter US study on long-term follow-up and fistula closure

OPEN ACCESS

Authors

Prashant Kedia[1], Sardar Shah-Khan[2], Amy Tyberg[3], Monica Gaidhane[1], Avik Sarkar[1], Haroon Shahid[1], Eric Zhao[1], Shyam Thakkar[4], Mason Winkie[4], Matthew Krafft[5], Shailendra Singh[5], Eugene Zolotarevsky[6], Jeremy Barber[6], Mitchelle Zolotarevsky[6], Ian Greenberg[1], Dhiemeziem Eke[1], David Lee[1], Frank Gress[7], Iman Andalib[8], Gregory Bills[9], Patrick Carey[9], Moamen Gabr[10], Michael Lajin[11], Enrique Vazquez-Sequeiros[12], Douglas Pleskow[13], Neal Mehta[13], Allison Schulman[14], Richard Kwon[15], Kevin Platt[16], John Nasr[4], Michel Kahaleh[2]

Institutions

1 Methodist Dallas Medical Center – Gastroenterology, Dallas, Texas, United States
2 Rutgers Robert Wood Johnson Medical School – Gastroenterology, New Brunswick, New Jersey, United States
3 Weill Cornell Medical College – Gastroenterology & Hepatology, New York, New York, United States
4 West Virginia University – Gastroenterology, New Brunswick, New Jersey, United States
5 Ruby Memorial Hospital – Digestive Diseases, Morgantown, West Virginia, United States
6 Spectrum Health Butterworth Hospital – Advanced Endoscopy/Gastroenterology, Grand Rapids, Michigan, United States
7 Icahn School of Medicine at Mount Sinai – Gastroenterology, New York, New York, United States
8 Robert Wood Johnson Health System – Gastroenterology, New Brunswick, New Jersey, United States
9 University of Kentucky Medical Center – Gastroenterology, New Brunswick, Kentucky, United States
10 Tanta University Faculty of Medicine – Gastroenterology and Hepatology – Internal Medicine, Tanta, Egypt
11 Sharp Grassmont Hospital – Gastroenterology/Internal Medicine, Mesa, California, United States
12 University Hospital Ramon y Cajal – Division of Gastroenterology, Madrid, Sapin
13 Beth Israel Deaconess Medical Center – Gastroenterology, Boston, Massachusetts, United States
14 University of Michigan Medicine – Gastroenterology, New Brunswick, Michigan, United States
15 University of Michigan Health System – Gastroenterology, Ann Arbor, Michigan, United States
16 University of Michigan Michigan Medicine – Internal Medicine, Ann Arbor, Michigan, United States

submitted 8.9.2022
accepted after revision 9.3.2023

Bibliography
Endosc Int Open 2023; 11: E529–E537
DOI 10.1055/a-2057-5984
ISSN 2364-3722

Georg Thieme Verlag KG, Rüdigerstraße 14,
70469 Stuttgart, Germany

Corresponding author
Michel Kahaleh, MD, Distinguished Professor of Medicine, Chief of Endoscopy, Rutgers Robert Wood Johnson Medical School, 51 French Street, MEB 479 New Brunswick, New Brunswick, NJ 08901, United States
Fax: +1-732-235-7307
mkahaleh@gmail.com

ABSTRACT

Background and study aims Endoscopic ultrasound-directed transgastric ERCP (EDGE) is a safe and efficacious procedure to treat pancreaticobiliary diseases in Roux-en-Y gastric bypass (RYGB). This multicenter study aimed to determine the long-term outcomes of EDGE focusing on fistula persistence rates and post-procedure weight change.

Patients and methods Information about patients with Roux-en-Y gastric bypass anatomy who underwent EDGE between 2015 and 2021 from 10 institutions was captured in a registry. Patient demographics, procedural details, and clinical outcomes were analyzed.

Results One hundred seventy-two patients were included in the study (mean age 60, 25% male). Technical success

of lumen-apposing metal stent (LAMS) placement was 171 of 172 (99.4 %) while clinical success of intervention was 95%. The mean procedure time was 65 minutes. The most commonly reported complication was stent dislodgement/migration (n = 29, 17). Mean length of time of LAMS duration was 69 days. Mean follow-up time was 6 months. Endoscopic fistula closure was performed in 40 % of patients (69/172) at the time of LAMS removal. Persistence of fistula was observed in 19 of 62 patients (31 %) assessed. Length of LAMS indwell time (days) was a predictor of persistent fistula. The average weight gain while the LAMS was in place was 12 lb in 63 patients (36.6 %); 59.4 % of patients gained < 5 lb.

Conclusions EDGE is a safe and efficacious procedure for RYGB patients requiring ERCP. Post-procedure evaluation and management of the enteral fistula varies widely among centers currently and would benefit from further standardization. Fistula persistence appears to be uncommon and can be managed endoscopically but may be related to length of indwell times of the LAMS.

Introduction

Obesity has become a major epidemic in the United States, with an age-adjusted prevalence of over 40 % among adults [1]. With this rise in obesity comes an increase in rates of bariatric surgery, including the Roux-en-Y gastric bypass (RYGB) procedure. Over the past decade, there have been an estimated 40,000 to 65,000 RYGB procedures performed every year in the United States [2]. While effective as a treatment for obesity, RYGB does have its complications, including a high prevalence of subsequent gallstone disease. Rapid weight loss can contribute to the development of gallstones by increasing the lithogenicity of bile [3]. Approximately 13 % of post-bariatric patients can develop gallbladder sludge within 6 to 18 months after surgery [4], and up to 30 % of patients can develop gallstones within 24 months [5, 6].

Endoscopic retrograde cholangiopancreatography (ERCP) is frequently needed in these patients to manage choledocholithiasis resulting from their gallstone disease. However, performing traditional ERCP in patients with RYGB anatomy is technically challenging. Multiple techniques have been developed to help overcome this, including enteroscopy-assisted ERCP and laparoscopy-assisted ERCP. Laparoscopy-assisted ERCP has demonstrated excellent technical and clinical success rates; however, it is limited by not being fully endoscopic, with the additional need for a surgeon and additional operating room costs and surgical risks. Enteroscopy-assisted ERCP, although fully endoscopic, has demonstrated lower rates of technical success rates and longer procedure times, and is thus not the ideal procedure of choice as well. There was a need for a more successful, completely endoscopic, and minimally invasive technique, and thus the novel endoscopic ultrasound-directed transgastric ERCP (EDGE) procedure was created [7].

EDGE is a minimally invasive, completely endoscopic approach using endoscopic ultrasound to create a temporary fistula by placing a lumen-apposing metal stent (LAMS) that connects either the gastric pouch or the proximal jejunum to the excluded stomach. This allows endoscopists the ability to then perform conventional anterograde ERCP utilizing a standard duodenoscope passed through the LAMS [7]. Since its inception, EDGE has gained popularity, and multiple studies have demonstrated high technical and clinical success rates, ranging from 98 % to 100 % and 91 % to 100 %, respectively [8–12]. Furthermore, these studies also reported acceptable safety profiles with low rates of adverse events (AEs). Therefore, the efficacy and safety of EDGE have now been well reported. However, data on long-term outcomes of EDGE remain sparse. In particular, current data for rates of fistula persistence are limited, and data regarding post-procedural weight change are highly variable with mixed results. Therefore, the purpose of this larger, multicenter study was to re-examine the efficacy and safety profile of EDGE, and to further assess its long-term outcomes, with a particular focus on rates of fistula persistence and weight change.

Patients and methods

This study was an international, multicenter, retrospective cohort study. Data were obtained from a total of 10 institutions (9 United States, 1 European). Information on patients with RYGB anatomy who underwent EDGE for treatment of pancreaticobiliary disease between January 2015 and December 2021 was captured in a dedicated registry. The decision to perform EDGE at these institutions was based on endoscopists' preferences after discussion of risks, benefits, and alternatives of various pancreaticobiliary access routes with their patients. These patients' charts were then analyzed to obtain information regarding patient demographics, procedural details, and clinical outcomes.

Study outcomes and analysis

Patient demographics, including age and gender, were recorded. Clinical specifics such as procedure indication and acuity of procedure were obtained. Information regarding procedural details was collected, including type of fistula created, technical success of LAMS placement, LAMS luminal diameter size, number of sessions, procedure time, and clinical success (defined as successful ERCP with completion of the intended intervention). AEs including stent migration and bleeding were also recorded. Furthermore, data regarding post-procedure outcomes were obtained. They included follow-up time, method of fistula closure (if attempted), method of fistula reassessment (if assessed), persistence of fistula (if assessed), and method of repeat closure. Weight before and after LAMS placement was recorded as well. Descriptive statistics such as measures of frequency, mean, and range were conducted. Mann-

Whitney analyses, logistic regression and Fisher's exact test were conducted.

All data analyses were conducted using MedCalc V18.9 (MedCalc Software, Ostend, Belgium). Survey data were gathered in a dedicated registry (NCT05041608) approved by WCG IRB.

Typical procedure technique

The excluded stomach was located endosonographically with a linear echoendoscope from the remnant gastric pouch or the jejunal limb and then accessed with a 19G EUS needle. Contrast, along with 120 mL of water, was injected through the 19G needle to confirm the position within and distend the excluded stomach. The fistula tract was either created over a.035-inch guidewire, or freehand using the cautery-enhanced LAMS (Axios; Boston Scientific). The LAMS was then deployed with the distal end in the excluded stomach and the proximal flange into the remnant gastric pouch or jejunum. Over a guidewire, the lumen of the stent was then dilated with a dilating balloon to the diameter of the stent. This allows for the antegrade passage of a duodenoscope through the LAMS into the stomach remnant and to the ampulla, where conventional ERCP could be performed either during the index procedure (single-session EDGE) or during the subsequent procedure(s) (staged EDGE). Once ampullary access was no longer required, the LAMS was removed. The fistula was either allowed to close spontaneously or closed using an over-the-scope clip (OTSC)/ endoscopic suturing/or Argon plasma coagulation (APC) depending on the endoscopist's preference. Assessment for persistence of the fistula, and method by which do this, was also based on the endoscopist's preference.

Results

Patient and procedure characteristics

A total of 172 patients were identified in this study. The mean age of the patients was 60 years, and 43 (25 %) were male. The average American Society of Anesthesiology score was 3. The mean time since initial RYGB was 12 years. The primary procedure indication was biliary stricture in 82 % of patients (▶ **Table 1**). Most of the procedures (60 %) were done acutely as an inpatient, with the remaining 40 % done electively. A total of 125 patients (73 %) underwent gastro-gastric fistula creation, with proximal flange deployment of the LAMS in the gastric pouch, while the remaining patients underwent jejuno-gastric fistula creation, with proximal flange deployment in the blind jejunal limb in 35 patients (20 %) and in the efferent jejunal limb in 12 patients (7 %) (▶ **Table 1**). A majority (88 %) of procedures were electrocautery-assisted, and 25 % were wire-assisted. A 20-mm AXIOS stent was used in 140 patients (81 %), while a 15-mm AXIOS stent was used in the other 32 patients (19 %). LAMS was balloon dilated in 148 cases (86 %), with a range of dilation from 12 to 20 mm. The LAMS was fixated (suture) upon placement in 32 cases (19 %). Mean procedure time was 65 minutes.

▶ **Table 1** Demographics and procedure characteristics.

Gender	43 males (25 %)
Age (average)	60 years
ASA (1–4)	3
Weight at the time of EDGE (in pounds)	Average 197 lb (range 123–401)
Procedure indication	▪ Biliary stricture 141 (82 %) ▪ Cholangitis 6 (3.5 %) ▪ Pancreatic stricture 11 (6.4 %) ▪ Other 14 (8.1 %)
Inpatient Outpatient	▪ 103 (60 %) ▪ 69 (40 %)
Location of LAMS proximal flange deployment	
▪ Gastric pouch	125 (73 %)
▪ Blind jejunal limb	35 (20 %)
▪ Efferent jejunal limb	12 (7 %)
Size of AXIOS stent	
▪ 20-mm-diameter stent	140 (81 %)
▪ 15-mm-diameter stent	32 (19 %)
Electrocautery-assisted?	
▪ Yes	152 (88 %)
▪ No	20 (12 %)
Was LAMS balloon-dilated after deployment?	
▪ Yes	148 (86 %)
▪ No	24 (14 %)
Was the LAMS fixated upon placement?	
▪ Yes	32 (19 %)
▪ No	140 (81 %)
Single-session vs staged (two-step) EDGE?	
▪ Single-session	75 (44 %)
▪ Staged	97 (56 %)
Success rates	
▪ Technical success of LAMS placement	171 (99.4 %)
▪ Clinical success of ERCP completion	163 (95 %)

ASA, American Society of Anesthesiologists; EDGE, endoscopic ultrasound-directed transgastric ERCP; LAMS, lumen-apposing metal stent; ERCP, endoscopic retrograde cholangiopancreatography.

Technical and clinical success

Overall technical success of LAMS placement was achieved in 171 of 172 patients (99.4 %). In the one unsuccessful case, the LAMS stent was unable to be placed because the excluded stomach was pushed too far away. Single-session EDGE was per-

▶ **Table 2** Adverse events.

Stent dislodgement/migration[1]	28 (16.3 %)
Bleeding	11 (6 %)
Ulceration	4 (2 %)
Pancreatitis	2 (1 %)
Abdominal pain	2 (1 %)
Cholangitis	1 (1 %)

[1] One case required surgical removal due to migration to the terminal ileum causing small bowel obstruction

formed in 75 patients (44 %), and staged EDGE was performed in 97 patients (56 %). If staged, the mean number of days between part 1 (fistula formation) and part 2 (ERCP intervention) was 19 days. Clinical success, defined as successful ERCP with completion of the intended pancreaticobiliary intervention, was achieved in 163 patients (95 %).

Adverse events

The most common complication was stent migration/dislodgement, reported in 28 cases (16.3 %) (▶ **Table 2**), with only one (3.2 %) meeting criteria for severe (13). Of these, 19 (68 %) occurred peri-procedurally, with 17 managed with bridging stents and two requiring surgical intervention. The other 9 (32 %) occurred post-procedurally (median of 2 days after procedure), with 11 managed with either repositioning/replacement/allowance to pass enterally, and one requiring surgical removal due to migration to the terminal ileum causing small bowel obstruction. A subgroup analysis did not reveal any statistically significant predictors of stent migration based on technical aspects of the EDGE procedure (▶ **Table 3**). Bleeding occurred in 11 patients (6 %), all of which were managed endoscopically. Other AEs included ulceration (2 %), abdominal pain (1 %), pancreatitis (1 %), and cholangitis (< 1 %).

Fistula reassessment

At the time of data collection, LAMS removal had been performed in 142 of 172 patients (83 %). The mean duration of LAMS indwell time was 69 days. The fistula was actively closed at the time of LAMS removal in 49 % of cases (n = 69), with suturing being used in 52 cases, APC in 39 cases, and OTSC in 17 cases (▶ **Table 4**). If suturing was utilized, the number of sutures used ranged from 1 to 3, and all cases utilizing OTSC used a 12-mm clip.

Mean follow-up time post-procedure was 6 months (range from 1 to 32 months). Among the 163 patients with follow-up information, 99 (61 %) had follow-up > 3 months post-procedure, and 55 (34 %) had follow-up > 6 months post-procedure. The fistula was reassessed post-procedure to check for continued closure in 62 patients (43.6 %), with a mean length of time from LAMS removal to fistula reassessment of 256 days (▶ **Ta-**

▶ **Table 3** Stent migration predictors.

	Stent migration n = 144 (No)	**Stent migration n = 28 (Yes)**	***P* value**
Location			*P* = 0.2408
▪ Pouch	102 (70.8 %)	23 (82 %)	
▪ Blind limb	30 (20.8 %)	5 (18 %)	
▪ Efferent jejunal limb	12 (8.4 %)	0	
Single-session EDGE			*P* = 0.2436
▪ Yes	59 (41 %)	15 (53.6 %)	
▪ No	83 (59 %)	13(46.4 %)	
Axios stent			*P* = 0.3449
▪ 15 mm	25 (17.4 %)	7 (25 %)	
▪ 20 mm	119 (82.6 %)	21 (75 %)	
LAMS balloon dilation after deployment			*P* = 0.9558
▪ (Yes)	124 (86.1 %)	24 (86 %)	
▪ (No)	20 (13.9 %)	4 (14 %)	
LAMS fixated upon placement			*P* = 0.6752
▪ (Yes)	26 (18 %)	6 (21.4 %)	
▪ (No)	118 (82 %)	22 (78.6 %)	
Indwelling duration	71.45 days average (SD 61.8 days)	53.4 days average (SD 38.1 days)	*P* = .09301

EDGE, endoscopic ultrasound-directed transgastric endoscopic retrograde cholangiopancreatography; LAMS, lumen-apposing metal stent; SD, standard deviation.

▶ **Table 4** Fistula outcomes.

Was fistula actively closed at time of LAMS removal?	
▪ Active closure	69 (49 %)
▪ Spontaneous closure	73 (51 %)
Method of fistula reassessment	
▪ Upper gastrointestinal series	31 (50 %)[1]
▪ Repeat endoscopy	29 (47 %)[1]
▪ CT scan	2 (3 %)[1]
Fistula persistence	
▪ Patients with persistent fistula	19 (31 %)[1]
▪ Patients with successful repeat closure	11 (100 %)[2]

LAMS, lumen-apposing metal stent; CT, computed tomography.
[1] Among patients who underwent fistula reassessment (n = 62)
[2] Among patients for which repeat closure was attempted (n = 11)

ble 4). Among those reassessed, 31 patients (50 %) underwent an upper gastrointestinal series, 29 (47 %) underwent endoscopy, and 2 (3 %) underwent a computed tomography scan. Persistence of fistula was observed in 19 patients (31 % among those reassessed).

Among the 62 patients reassessed for fistula closure, characteristics between those with persistent fistula (n = 19) and those without (n = 43) were compared (▶ **Table 5**). The only variable that predicted fistula persistence was total LAMS indwell time. The total duration of time LAMS was in place was 86 days in the persistent group, compared to 50 days in the non-persistent group ($P < 0.004$). Other variables such as location of LAMS deployment, LAMS diameter, attempted endoscopic fistula closure at LAMS removal, APC utilization at fistula closure or performance of single-session vs staged EDGE were not statistically significantly different between the two groups, albeit the small sample was size. A repeat endoscopic procedure to close persistent fistulas was done in 11 of 19 patients, with 100 % technical success using a combination of suturing, APC and OTSCs.

Weight gain

Weight gain was noted in 63 patients (36.6 %) during the time the LAMS was in place (▶ **Table 6**). Average weight gain was 12 lb, with 38 patients (59 % among those with weight gain, 22 % among all patients) gaining < 5 lb. There was no statistically significant predictor of weight gain during the time the LAMS was still in place.

Discussion

It is evident that currently EDGE is being performed, often as first-line therapy, at many tertiary care centers with therapeutic EUS expertise for the management of pancreaticobiliary disease in patients with RYGB anatomy. Our study reaffirms high technical (99.4 %) and clinical (95 %) success rates for EDGE. These outcomes are comparable to existing published technical success, ranging from 98 % to 100 % and clinical success ranging from 91 % to 100 % [8–23]. The preservation of these high success rates is encouraging as the adoption of EDGE continues to expand globally and in various practice settings.

From a procedural standpoint, one outcome of this study worth mentioning is the higher frequency of use of 20-mm LAMS, which occurred in 81 % of cases. A majority of previous studies utilized 15-mm stents, particularly those completed during the earlier years of EDGE usage when the 20-mm stent was not available. As a result, our findings, which incorporate more recent data, reflect a trend toward the increased use of the new, larger 20-mm LAMS. This transition is not unexpected, due to better ease of duodenoscope advancement through a larger-sized stent, and thus, less risk of AEs such as stent migration [24]. In addition, our mean procedure time was 65 minutes, which falls within the range of previously reported mean procedure times (49–116 minutes) [11, 19, 20].

The most common AE seen in our study was stent migration/dislodgement, reported in 16.3 % of all cases, which is comparable to that previously reported ranging from 15 % to 33 % [9, 10, 12, 18, 21–23]. While only one stent migration required surgical intervention, it highlights the need for more improved strategies to reduce the rate of dislodgement and migration. Our analysis did not show any significant predictors of stent migration, including the primary site of the anastomosis (gastric vs jejunal) or diameter of the LAMS itself (20 vs 15 mm). However, another study by Shinn et al. [24] attempted to identify predictive factors of intraprocedural LAMS migration in single-session EDGE and did suggest that a 20-mm LAMS may be less likely to migrate. They found that the use of a 15-mm-diameter LAMS was the strongest independent predictor of migration (odds ratio 5.36; 95 % confidence interval 1.29–22.24). In addition, dilation after stent deployment and stent fixation may also decrease the risk of migration and improve procedure success [24]. Given the rate of potential migration and resulting complications, further studies are needed that aim to investigate stent migration and how best to mitigate its occurrence.

One major concern with EDGE is the potential risk of non-closure or persistence of the created fistula and the subsequent development of weight gain. Such a consequence could be disconcerting to the patient, as it could effectively reverse the benefit of the original gastric bypass surgery. The data regarding fistula persistence are extremely sparse, and data reporting on weight changes is highly variable with mixed results. One of the first studies to assess fistula status was conducted by James et al. [11] In their study, among 19 EDGE patients, 11 had fistula reassessment with an upper gastrointestinal series, and one of the 11 had a persistent fistula [11]. Other studies have reported rates of fistula persistence among assessed patients ranging from 0.0 % to 8.3 % [10, 22], but these were also smaller studies with a total N ≤ 30 patients. One recent study by Runge et al. [25] reported fistula persistence in 10 % of the 90 of 178 (51 % evaluation rate) patients who underwent follow-up testing. Five of those patients underwent endoscopic closure, which was successful in all cases [25]. In our study, 62 of 142 patients (44 %) who had their LAMS removed underwent specific follow-up studies to assess for possible persistent fistula. Of

▶ **Table 5** Persistent fistula predictors.

	No persistent fistula (N = 43)	Yes persistent fistula (N = 19)	*P* value
Age	60	64 (SD 12.2)	0.7455
Gender	33 females (77 %)	18 females (95 %)	0.3211
ASA score	3	3	0.5521
Inpatient	24/43 (56 %)	13/19 (68 %)	0.7345
Weight at EDGE	194 lb	187 lbs (SD 46.7)	0.7645
Diabetic (No)	25 (65.79 %)	14 (73.68 %)	0.7633
Diabetic (Yes)	13 (34.21 %)	5 (26.32 %)	
Time since RYGB (years)	Mean 10 (SD 6.129)	Mean 13.53 (SD 8.399)	0.1813
Location of proximal flange deployment of LAMS			0.260
▪ Gastric pouch	19 (50.00 %)	13 (68.42 %)	
▪ Jejunal limb	19 (50.00 %)	6 (31.58 %)	
Electrocautery assistance			0.706
▪ No	6 (15.79 %)	2 (10.53 %)	
▪ Yes	32 (84.21 %)	17 (89.47 %)	
Axios size 15 mm	12 (31.58 %)	3 (15.79 %)	0.339
Axios size 20 mm	26 (68.42 %)	16 (84.21 %)	
Was LAMS secured/fixed upon deployment?			0.742
No	30 (78.95 %)	14 (73.68 %)	
Yes	8 (21.05 %)	5 (26.32 %)	
Single-session EDGE vs staged EDGE	13 (35.14 %) 24 (64.86 %)	9 (47.37 %) 10 (52.63 %)	0.401
Total number of days LAMS was in place (days)	Mean 00.973 (SD 30.619)	Mean 85.526 (SD 55.374)	**0.0044**
Was fistula closed at time of LAMS removal?			0.537
▪ No	26 (68.42 %)	15 (78.95 %)	
▪ Yes	12 (31.58 %)	4 (21.05 %)	
Was APC used to ablate rim of fistula at time of LAMS removal?			1
▪ No	9 (45.00 %)	3 (37.50 %)	
▪ Yes	11 (55.00 %)	5 (62.50 %)	

ASA, American Society of Anesthesiologists; RYGH, Roux-en-y gastric bypass; LAMS, lumen-apposing metal stent; EDGE, endoscopic ultrasound-directed transgastric endoscopic retrograde cholangiopancreatography; APC, Argon plasma coagulation.

these 62 patients, 19 (31 %) had persistent fistula, which is higher than the rates (~10 %) reported previously. One possible explanation for this difference is the higher LAMS indwell time in our study (69 days) vs Runge et al. (35 days). Given that our study confirmed that length of LAMS indwell time predicted fistula persistence, this may be a decisive factor. Another smaller study of 22 EDGE patients also found that LAMS indwell time (77 vs 35 days) was predictive of persistent fistula [26]. Also, the rate of attempted endoscopic fistula closure at the time of LAMS removal in our study was 49 %, compared to 80 % in the Runge et al study[25]; however, attempted closure was not shown to be a significant predictor in either study. Also, given the sample size of both studies, it is possible that attempted closure and possible methodology (suturing, APC, OTSC) may affect this outcome if evaluated on a larger scale. It is clear, however, that post-procedure evaluation and management of the EDGE-related fistula is highly variable and inconsistent among centers. The assessment rate alone was only 44 % in our study. Because of this, the true rate of persistent fistula after EDGE is largely unknown, ranging anywhere between 10 % to 31 % depending on the study. Understanding this potentially refractory chronic AE more clearly is paramount to opti-

▶ **Table 6** Weight gain predictors.

	Weight gained n = 63 (Yes)	Weight gained n = 109 (No)	*P* value
Location			*P* = 0.3581
▪ Pouch	44 (81.5 %)	81 (63.2 %)	
▪ Blind limb	16(3.7 %)	19 (21 %)	
▪ Efferent jejunal limb	3 (14.8 %)	9 (15.8 %)	
Single-session EDGE			*P* = 0.5560
▪ Yes	26 (33.3 %)	50 (47.4 %)	
▪ No	37 (66.7 %)	59 (52.6 %)	
Axios stent			*P* = 0.1281
▪ 15 mm	16 (26 %)	16 (31.6 %)	
▪ 20 mm	47 (74 %)	93 (68.4 %)	
LAMS balloon dilation after deployment			*P* = 0.1090
▪ Yes	50 (85.1 %)	98 (63.2 %)	
▪ No	13 (14.9 %)	11 (36.8 %)	
Fistula closure at LAMS removal			*P* = 0.0849
▪ Yes	26 (18.5 %)	60 (21 %)	
▪ No	37 (81.5 %)	49 (79 %)	
Indwelling duration	68.6 days average (SD 45 days)	68.6 days average (SD 66.83 days)	*P* = 0.4980

EDGE, endoscopic ultrasound-directed transgastric endoscopic retrograde cholangiopancreatography; LAMS, lumen-apposing metal stent.

mize outcomes of the EDGE technique and reduce the skepticism regarding metabolic and weight gain associated with the procedure. Our study did find a statistically significant predictor of persistent fistula, which is length of LAMS indwell time (86 vs 50 days). This is an important finding as it may influence our clinical algorithm for the timing of procedures associated with EDGE. For example, this may suggest that a shorter interval between staged EDGE procedures or a shift toward single-session EDGE procedures may be beneficial. We believe that all centers performing EDGE should have a standardized protocol to assess their fistula persistence regardless of whether they attempt closure or not, so that more accurate and large-scale data can be reviewed to understand the true risk of persistent fistula after this procedure and the factors that promote it.

Concerning potential weight changes from the EDGE procedure, results from the existing literature are highly variable with extremely mixed results. Data from various studies range from a weight loss of 7.9 lb to a weight gain of 3.7 lb [8, 10, 19, 20, 27–29], likely because of variability and inconsistency of follow-up and recording of weight changes at different centers. In our study, weight gain was noted in 63 patients (36.6 %) during the time the LAMS was in place. The average weight gain was 12 lb, with 38 patients gaining < 5 lb. One possible explanation for the higher-than-average weight gain seen in our study is that the mean LAMS dwell time was 69 days, which is a longer dwell time in comparison to other studies [25]. No predictors of weight gain were discovered in the subgroup analysis, possibly due to the limited number of subjects and follow-up, although there was a trend toward possible weight gain in patients that did not have their fistula closed at the time of LAMS removal. This may suggest that in a large, more complete cohort, persistent fistula could correlate with weight gain. This may be another reason to adjust our timing algorithms for EDGE to keep the LAMS indwell time as short as safely possible. Future prospective studies incorporating dedicated follow-up to ensure fistula closure and assessing weight changes are essential to determine the possible connection between these factors.

Conclusions

In conclusion, the EDGE procedure is an entirely endoscopic, highly efficacious, single-team procedure for performing ERCP in RYGB patients who require pancreaticobiliary interventions and is associated with high clinical success rates and safety profiles. While the technical outcomes of the EDGE procedure are encouraging and reproducible in a variety of endoscopic centers, there is a need for standardization and consistency in follow-up of these patients to evaluate for fistula persistence and weight gain. Data on these two variables are underreported and underassessed in the current standard scope of reported practice, leading to a blind spot in long-term outcomes of the EDGE procedure. Our study showed that rates of fistula persistence

and weight gain may be as high as 31 % and 37 %, respectively, which may be related to LAMS indwell time, which was the only statistically significant predictor of fistula persistence. As EDGE is more widely adopted, it is necessary for performing centers to standardize their post-LAMS removal surveillance of these patients to assess for fistula persistence and weight gain. Understanding the incidence and risk factors for these long-term AEs will allow us to better understand how best to perform the EDGE procedure and answer questions such as: 1) What is the optimal LAMS indwell time? 2) Should single-session EDGE be preferred to staged EDGE? and 3) Should the fistula be endoscopically closed at LAMS removal and by what method? EDGE has changed the landscape of pancreaticobiliary intervention in RYGB patients, but there is still room for refinement and optimization to make it the standard of care.

Competing interests

Amy Tyberg: Consultant for Ninepoint Medical, Endogastric Solutions, and Obalon Therapeutics. Avik Sarkar has done consulting work for US Endoscopy and Obalon Therapeutics. Haroon Shahid. has done consulting work for US Endoscopy. Michel Kahaleh has received grants support from Boston Scientific, Fujinon, W.L. Gore, Apollo Endosurgery, Cook Endoscopy, GI Dynamics, Merit Medical, Interscope Med, Olympus, ERBE, and MI Tech. He is a consultant for Boston Scientific and Laboratories Inc. and AbbVie. Monica Gaidhane has done consulting work for 3D Matrix. Prashant Kedia has done consulting work for Boston Scientific. None of those funding was related to this paper. All other authors declare that they have no conflicts of interest.

Clinical trial

ClinicalTrials.gov (http://www.clinicaltrials.gov/)
NCT05051358
TRIAL REGISTRATION: Multi-center retrospective study
NCT05051358 at ClinicalTrials.gov (http://www.clinicaltrials.gov/)

References

[1] Hales CM, Carroll MD, Fryar CD et al. Prevalence of obesity and severe obesity among adults: United States, 2017-2018. NCHS Data Brief 2020; 360: 1–8

[2] English WJ, DeMaria EJ, Hutter MM et al. American Society for Metabolic and Bariatric Surgery 2018 estimate of metabolic and bariatric procedures performed in the United States. Surg Obes Relat Dis 2020; 16: 457–463

[3] Shiffman ML, Sugerman HJ, Kellum JM et al. Changes in gallbladder bile composition following gallstone formation and weight reduction. Gastroenterology 1992; 103: 214–221

[4] Nagem RG, Lázaro-da-Silva A, de Oliveira RM et al. Gallstone-related complications after Roux-en-Y gastric bypass: a prospective study. Hepatobiliary Pancreat Dis Int 2012; 11: 630–635

[5] Uy MC, Talingdan-Te MC, Espinosa WZ et al. Ursodeoxycholic acid in the prevention of gallstone formation after bariatric surgery: a meta-analysis. Obes Surg 2008; 18: 1532–1538

[6] Miller K, Hell E, Lang B et al. Gallstone formation prophylaxis after gastric restrictive procedures for weight loss: a randomized double-blind placebo-controlled trial. Ann Surg 2003; 238: 697–702

[7] Kedia P, Sharaiha RZ, Kumta NA et al. Internal EUS-directed transgastric ERCP (EDGE): game over. Gastroenterology 2014; 147: 566–568

[8] Runge TM, Kowalski TE, Baron TH et al. 1026 Living on the edge - success, long-term complications, and implications following EUS-directed transgastric ERCP: a multicenter study. Gastrointest Endosc 2019; 89: AB131

[9] Tyberg A, Nieto J, Salgado S et al. Endoscopic ultrasound (EUS)-directed transgastric endoscopic retrograde cholangiopancreatography or EUS: Mid-term analysis of an emerging procedure. Clin Endosc 2017; 50: 185–190

[10] Ngamruengphong S, Nieto J, Kunda R et al. Endoscopic ultrasound-guided creation of a transgastric fistula for the management of hepatobiliary disease in patients with Roux-en-Y gastric bypass. Endoscopy 2017; 49: 549–552

[11] James TW, Baron TH. Endoscopic ultrasound-directed transgastric ERCP (EDGE): a single-center US experience with follow-up data on fistula closure. Obes Surg 2019; 29: 451–456

[12] Wang TJ, Thompson CC, Ryou M. Gastric access temporary for endoscopy (GATE): a proposed algorithm for EUS-directed transgastric ERCP in gastric bypass patients. Surg Endosc 2019; 33: 2024–2033

[13] Cotton PB, Eisen GM, Aabakken L et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. Gastrointest Endosc 2010; 71: 446–454

[14] Hintze RE, Adler A, Veltzke W et al. Endoscopic access to the papilla of Vater for endoscopic retrograde cholangiopancreatography in patients with billroth II or Roux-en-Y gastrojejunostomy. Endoscopy 1997; 29: 69–73

[15] Shah RJ, Smolkin M, Yen R et al. A multicenter, U.S. experience of single-balloon, double-balloon, and rotational overtube-assisted enteroscopy ERCP in patients with surgically altered pancreaticobiliary anatomy (with video). Gastrointest Endosc 2013; 77: 593–600

[16] Banerjee N, Parepally M, Byrne TK et al. Systematic review of transgastric ERCP in Roux-en-Y gastric bypass patients. Surg Obes Relat Dis 2017; 13: 1236–1242

[17] Baron TH, Song LM, Ferreira LE et al. Novel approach to therapeutic ERCP after long-limb Roux-en-Y gastric bypass surgery using transgastric self-expandable metal stents: experimental outcomes and first human case study (with videos). Gastrointest Endosc 2012; 75: 1258–1263

[18] Prakash S, Elmunzer BJ, Forster EM et al. Endoscopic ultrasound-directed transgastric ERCP (EDGE): a systematic review describing the outcomes, adverse events, and knowledge gaps. Endoscopy 2022; 54: 52–61

[19] Bukhari M, Kowalski T, Nieto J et al. An international, multicenter, comparative trial of EUS-guided gastrogastrostomy-assisted ERCP versus enteroscopy-assisted ERCP in patients with Roux-en-Y gastric bypass anatomy. Gastrointest Endosc 2018; 88: 486–494

[20] Kedia P, Tarnasky PR, Nieto J et al. EUS-directed transgastric ERCP (EDGE) versus laparoscopy-assisted ERCP (LA-ERCP) for Roux-en-Y gastric bypass (RYGB) anatomy: a multicenter early comparative experience of clinical outcomes. J Clin Gastroenterol 2019; 53: 304–308

[21] Kedia P, Tyberg A, Kumta NA et al. EUS-directed transgastric ERCP for Roux-en-Y gastric bypass anatomy: a minimally invasive approach. Gastrointest Endosc 2015; 82: 560–565

[22] Krafft MR, Hsueh W, James TW et al. The EDGI new take on EDGE: EUS-directed transgastric intervention (EDGI), other than ERCP, for Roux-en-Y gastric bypass anatomy: a multicenter study. Endosc Int Open 2019; 7: E1231–E1240

[23] Nylund K, Hausken T, Ødegaard S et al. Gastrointestinal wall thickness measured with transabdominal ultrasonography and its relationship to demographic factors in healthy subjects. Ultraschall Med 2012; 33: E225–E232 doi:10.1055/s-0031-1299329

[24] Shinn B, Boortalary T, Raijman I et al. Maximizing success in single-session EUS-directed transgastric ERCP: a retrospective cohort study to identify predictive factors of stent migration. Gastrointest Endosc 2021; 94: 727–732

[25] Runge TM, Chiang AL, Kowalski TE et al. Endoscopic ultrasound-directed transgastric ERCP (EDGE): a retrospective multicenter study. Endoscopy 2021; 53: 611–618

[26] Krafft MR, Lorenze A, Croglio MP et al. "Innocent as a LAMS": Does spontaneous fistula closure (secondary intention), after EUS-directed transgastric ERCP (EDGE) via 20-mm lumen-apposing metal stent, confer an increased risk of persistent fistula and unintentional weight gain? Dig Dis Sci 2022; 67: 2337–2346

[27] Fernandez-Esparrach G, Lautz DB, Thompson CC. Endoscopic repair of gastrogastric fistula after Roux-en-Y gastric bypass: a less-invasive approach. Surg Obes Relat Dis 2010; 6: 282–288

[28] Mukewar S, Kumar N, Catalano M et al. Safety and efficacy of fistula closure by endoscopic suturing: a multi-center study. Endoscopy 2016; 48: 1023–1028

[29] Parvataneni S, Kumar V, Confer B et al. EUS-directed transgastric ERCP (EDGE) versus laparoscopy-assisted ERCP (LAERCP) for Roux-en-Y gastric bypass (RYGB): A single center experience: 917. Am J Gastroenterol 2019; 114: S536