Multicenter evaluation of the clinical utility of laparoscopy-assisted ERCP in patients with Roux-en-Y gastric bypass

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Abstract

Background and Aims

The obesity epidemic has led to increased use of Roux-en-Y gastric bypass (RYGB). These patients have an increased incidence of pancreaticobiliary diseases yet standard ERCP is not possible due to surgically altered gastroduodenal anatomy. Laparoscopic-ERCP (LA-ERCP) has been proposed as an option but supporting data are derived from single center small case-series. Therefore, we conducted a large multicenter study to evaluate the feasibility, safety, and outcomes of LA-ERCP.

Methods

This is retrospective cohort study of adult patients with RYGB who underwent LA-ERCP in 34 centers. Data on demographics, indications, procedure success, and adverse events were collected. Procedure success was defined when all of the following were achieved: reaching the papilla, cannulating the desired duct and providing endoscopic therapy as clinically indicated.

Results

A total of 579 patients (median age 51, 84% women) were included. Indication for LA-ERCP was biliary in 89%, pancreatic in 8%, and both in 3%. Procedure success was achieved in 98%. Median total procedure time was 152 minutes (IQR 109-210) with median ERCP time 40 minutes (IQR 28-56). Median hospital stay was 2 days (IQR 1-3). Adverse events were 18% (laparoscopy-related 10%, ERCP-related 7%, both 1%) with the clear majority (92%) classified as mild/moderate whereas 8% were severe and 1 death occurred.

Conclusion

Our large multicenter study indicates that LA-ERCP in patients with RYGB is feasible with a high procedure success rate comparable with that of standard ERCP in patients with normal anatomy. ERCP-related adverse events rate is comparable with conventional ERCP, but the overall adverse event rate was higher due to the added laparoscopy-related events.

Background

The current obesity epidemic has consequently led to an increase in bariatric surgery, with more than 100,000 procedures per year being performed in the United States alone [1]. In recent years, the most common bariatric surgery has been and continues to be Roux-en-Y gastric bypass (RYGB) [1,2]. This operation excludes most of the stomach (ie, remnant stomach) and all of the duodenum making conventional duodenoscopy and per-oral ERCP impossible. Importantly, ERCP is commonly indicated in RYGB patients due to an increased risk of choledocholithiasis and gallstone pancreatitis especially in the setting of rapid weight loss after bariatric surgery [3,4]. Furthermore, several reports have shown increased rate of pancreaticobiliary malignancies in obese patients [5,6].

Various alternative ERCP approaches for patients with RYGB have been described. Per-oral deep enteroscopy techniques such as single-balloon, double-balloon and spiral enteroscopy are minimally invasive but therapeutic success is far lower compared with standard ERCP. This inferiority is due to the inability to reach the papilla secondary to the surgically altered gastroduodenal anatomy, failure to cannulate the desired duct, or failure to provide therapy due

to the change of orientation of the papilla, difficult endoscope position, use of forward optics, lack of elevator, small therapeutic channel and/or limited availability of devices [7-13].

Percutaneous access to the gastric remnant by interventional radiology has been described, but has not gained wide acceptance because it is impractical for urgent cases due to the requirement of serial dilation and track maturation [14-16]. This is further hindered by the inconvenience of needing a gastrostomy tube (G-tube) and the technical difficulties related to the inability to distend the stomach remnant with air [6,17]. EUS-guided transgastric ERCP is another innovative approach [18,19]. However, this methodology has several cited limitations most prominently is the potential for creating a permanent gastro-gastric fistula that compromises the integrity of the RYGB and the need for 2 stage procedure [20-22].

Laparoscopy-assisted ERCP (LA-ERCP) is accomplished by placing trocar in the remnant stomach under laparoscopic guidance followed by insertion of the conventional duodenoscope through the trocar to reach the ampulla of Vater. ERCP is then carried out in a standard fashion. The main appeal of LA-ERCP is that it is a single-stage procedure and affords the use of standard ERCP equipment including doudenoscope and accessories. This anticipates a very high procedural success, similar to patients with normal upper GI tract anatomy. LA-ERCP was first described in 2002 and since then, only a few small single-center case series have been published showing high success rates and low adverse events rates [6,7,23-25]. Despite these early encouraging results, the role of LA-ERCP has not been well defined due to a lack of high quality data. Therefore, the aim of this study was to evaluate a large multicenter cohort to assess the feasibility, safety and outcomes of LA-ERCP in patients with RYGB.

Methods

This is a retrospective multicenter cohort study that included adult patients with RYGB who underwent LA-ERCP between 2005 and 2016. The study was approved by the institutional review board (IRB) of each of the participating centers, with the University of Florida serving as the central coordinating center. All authors had access to the study data and reviewed and approved the final manuscript.

Procedure

Procedure informed consents for both ERCP and Laparoscopy were obtained from all patients. All procedures were performed in the operating room or designated sterile endoscopy room by both a laparoscopy and endoscopy teams with the patient in supine position under general anesthesia. Percutaneous access with trocar to the remnant stomach was established laparoscopically. Therapeutic duodenoscope was subsequently inserted through the indwelling trocar into the remnant stomach and advanced into the duodenum. ERCP was then carried out in a standard fashion using a conventional duodenoscope and accessories. The gastrostomy and the percutaneous tracts were closed surgically at the end of the procedure or a G-tube is left in place in cases where ERCP might be needed again in the future. All patients were inpatients or were admitted for observation postoperatively.

Data collection

A standardized data entry form was distributed through secured email across all the centers to collect information on baseline characteristics, intra-procedural and follow-up data. Baseline characteristics included patient demographics, American Society of Anesthesiologists (ASA) class, year and type of RYGB surgery (laparoscopic versus open), cholecystectomy status

(before LA-ERCP, at the time of LA-ERCP, after the LA-ERCP), prior failed attempts at pancreatico-biliary interventions, indication and type of LA-ERCP (biliary, pancreatic or both).

Procedure-related data included the use of peri-operative antibiotics, total procedure time, ERCP time, the types of ERCP therapeutic interventions (biliary sphincterotomy, dilation of the papilla, dilation of stricture, biliary or pancreatic stent placement or extraction, stone/sludge removal), need for conversion from laparoscopic to open surgery, G-tube placement, and length of hospital stay (LOS).

Definitions

Procedure success was defined when all of the following were accomplished: reaching the ampulla of Vater, cannulation of the desired duct, and performing the desired therapeutic maneuvers as clinically indicated. Total procedure time was measured from the initial surgical incision to final surgical closure. ERCP time was measured from the scope insertion in the trocar to the scope withdrawal.

Adverse events were classified to either ERCP-related (pancreatitis, cholangitis, sphincterotomy-related perforation, post-sphincterotomy bleeding, stent migration, or others), or laparoscopy-related (bleeding, gastric remnant site entry leak, gastric tube site infection, perforation, cardiovascular, other infection, or others). Severity of adverse events was classified using the American Society for Gastrointestinal Endoscopy lexicon as mild, moderate, severe, and death [26].

Statistical analysis

Data were analyzed using SPSS version 18.0 software (SSPS Inc, Chicago, Ill). Mean, median and interquartile ranges (IQR) were calculated. Categorical data were analyzed using the Fisher

exact and Chi square testing and continuous data were analyzed using t testing for normally distributed variables and Mann–Whitney U test for non-normally distributed variables.

Results

Thirty-four centers participated in this study (31 from the United States, 2 from Brazil, and 1 from Canada, Table 1). A total of 579 patients with RYGB (84% women) with median age of 51 (interquartile range (IQR) 43-61) underwent LA-ERCP during the study period (2005-2016) (Table 2). The number of procedures performed per year increased noticeably after 2011 reflecting increased adoption of this approach (Figure 1).

Indications for LA-ERCP are outlined in Table 2. Main indications for procedures were: biliary in 89%, pancreatic in 8% and both biliary and pancreatic in 3% of the cases. Approximately half (47%) of all biliary interventions were due to choledocholithiasis whereas acute pancreatitis (93%) was the most common indication for pancreatic intervention. The most common therapeutic interventions were biliary sphincterotomy (96%), stone extraction (44%), and pancreatic stent placement (15%), (Table 3). Eleven patients (26%) among those with pancreatic pre-operative indication had stone extraction. Concomitant laparoscopic cholecystectomy was performed in 21% of the cases and gastric tube was left in place in 17% of the cases for possible subsequent intervention(s).

Overall procedure success was achieved in 98%. The papilla was successful reached in 99% and cannulating the desired duct in 98% of the cases (bile duct cannulation 99%, pancreatic duct cannulation 91%). Success rate in performing the desired intervention was 98% (biliary 99%, pancreatic 89%). Median total procedure time (laparoscopy + ERCP) was 152 minutes (IQR 109-210 minutes) whereas median ERCP time was 40 minutes (IQR 28-56) minutes. Median

total procedure time was significantly longer for patient with history of open versus laparoscopic RYGB (181 versus 147 minutes, p=0.009). Median LOS was 2 (IQR 1-3) days.

Adverse events were reported in 106 out of 579 (18%) patients. Laparoscopy-related adverse events were reported in 10% whereas ERCP-related adverse events were reported in 7% of the patients. One percent of the patients had adverse events related to both laparoscopy and ERCP. The most common laparoscopy associated adverse event was postoperative infections in 24 out of 579 (4.1%), whereas the most common ERCP-related adverse event was acute pancreatitis in 42 out of 579 (7.4%), (Table 4). The rate of pancreatitis varied by the LA-ERCP main indication, among those who had the procedure for biliary indications was 7%. Compared with the rate among those with pancreatic and both (biliary and pancreatic) indications, which was 11% and 13%, respectively (p=0.3). Regarding the severity of these events, 60% were classified as mild and 31% as moderate whereas 8% were classified as severe and one death was reported. In 5% of the cases ERCP was carried out after conversion to open laparotomy to gain access to the remnant stomach.

We explored the factors associated with laparoscopic versus ERCP-related events by series of univariate analysis as presented in Table 5. Longer duration since RYGB showed a trend towards higher laparoscopy-related events (<3 years had 8%, 3-6 years had 10%, 6-9 years had 10%, and those with >10 years since RYGB had 16%, p=0.516). Conversion to open laparotomy was associated with significant increase in the risk of laparoscopy-related events (24% versus 10%, p=0.045). Leaving a G-tube in place at the end of the procedure was also significantly associate with increased risk of adverse events (17% versus 9%, p=0.036). These factors (years since RYGB, conversion to open, and leaving G-tube) did not affect the ERCP-related adverse events.

Most of the patients (85%) received peri-operative antibiotics. Antibiotics use was associated with a numerically higher overall adverse events rate (19% versus 13%, p = 0.198), a numerically higher rate of any infectious adverse events (6.2% versus 3.4%, p = 0.451), and a numerically higher rate of G tube site infection (1.4 % versus 0%, p = 0.603).

Discussion

The feasibility of LA-ERCP has been reported from a few single-center case series, with reported success rate ranging from 80% to 100% and adverse events rate ranging from 0% to 30% [6,7,23-25,27-32]. These reports are limited by small sample size and heterogeneous definitions of procedure success and adverse events. In our large multicenter study, LA-ERCP in patients with RYGB was highly successful with success rates comparable to standard ERCP in patients with normal upper GI tract anatomy [33]. In our study, the overall success rates in reaching the papilla, cannulating the desired duct and performing the indicated therapeutic intervention was 98%. Furthermore, we also demonstrated that LA-ERCP is feasible and efficient. Our total procedure time (laparoscopy + ERCP) was 152 minutes with median length of hospital stay of 2 days.

In our series, ERCP-related adverse events rate appear comparable with conventional ERCP, although the overall rate of adverse events was higher due to the addition of those attributed to laparoscopy[33]. Importantly, the clear majority (92%) of the reported adverse events were classified as mild to moderate. Nevertheless, serious adverse events were seen including viscus perforation in 5/579 (0.8%) cases. Two patients had sphincterotomy-related duodenal perforations, whereas the rest were laparoscopy-related (2 colonic and 1 gastric remnant perforation [trocar perforated the posterior stomach wall]). In one of the perforation cases, multi-organ failure occurred and the patient died after a prolonged hospitalization.

Placing an indwelling G-tube and conversion to open laparotomy were factors significantly associated with higher laparoscopy-related adverse events. Patients who had G tube left had higher overall laparoscopy associated adverse events (17% versus 9%, p =0.03). This was attributed to G tube site infection (6%), gastric entry-site leak (4%), and all-causes laparoscopy-associated bleeding (7%). Of note, all patients who had G tube site infection did receive peri-operative antibiotics as part of their care. Based on these data, it seems reasonable to avoid G-tube insertion unless a repeat procedure is definitely indicated, (Table 5).

Most of the patients included in our series (85%) received periprocedural antibiotics. There was no statistically significant difference in infection rate between those who received antibiotics versus those who did not. Nevertheless, we cannot exclude any difference based on our findings due to the very low rate of infections and low statistical power to answer this question. Therefore, our data cannot provide definitive guidance for or against the use of perioperative antibiotics.

Our findings are comparable with the recently published systematic review of 26 studies by Banerjee et al that included 509 laparoscopic and open trans-gastric ERCP cases [34]. The success rate in reaching the papilla, cannulation, and performing therapeutic intervention were 98.9%, 98.5%, and 98.5%, respectively. Adverse events were reported in 14% of cases, with lower G tube site infection (3.7%) and laparoscopy-associated bleeding (0.9%), and no reported death compared with our findings [34].

It is noteworthy that EUS-guided transgastric ERCP is currently an evolving and promising approach that involves deploying lumen-apposing metal stent (LAMS) through the newly formed gastro-gastric fistula[18]. Then the intended ERCP could be performed by passing the endoscope into the remnant stomach through the LAMS [18-20]. This approach can potentially offer great

advantages including the lack of need for surgical team, minimal invasiveness, and the higher success rate and shorter operative time compared with enteroscopy assisted ERCP. However, this methodology has several cited limitations most prominently the potential for creating a permanent fistula that compromises the integrity of the RYGB [20-22], high LAMS dislodgement rate (19%), and the need for multiple sessions in two-thirds of the patients to allow time for track maturation [35]. Nonetheless, this is a promising approach and direct comparison with LA-ERCP is warranted in future research.

The main strengths of our study include (1) large sample size. (2) Diverse patient population from many centers across the United Sates, Brazil, and Canada. This should improve our findings' external validity by providing more generalizable estimates of success and adverse events rates across many levels of endoscopists' and surgeons' experiences. These estimates can serve as reference to physicians when counseling patients. (3) Standardization of definitions for the outcomes and adverse events. (4) Reporting on all cases done in particular institution thus hopefully decreasing the possibility of selection bias. (5) Our findings are congruent with the findings of earlier smaller studies [6,7,23-25,27-32].

Laparoscopy-assisted ERCP has the advantage of using standard side-viewing duodenoscope and the standard ERCP accessories, thus increasing the cannulation and therapeutic intervention success rates. Furthermore, because LA-ERCP is done in conjunction with surgeons in the operating room, concomitant cholecystectomy can be performed if clinically indicated. In our population, concomitant cholecystectomy was performed in 20%. Saleem et al[25] reported performing concomitant cholecystectomy in 20% of the patients. Additionally, laparoscopic approach allows the diagnosis and treatment of internal hernias (reported in 20%-40%) and adhesions (in 20%) of the LA-ERCP procedures [23,25].

Nonetheless, there are several challenging aspects of LA-ERCP that must be addressed before adoption of this procedure by a medical center. The center must have expertise in bariatric surgery as well as advanced endoscopy. Secondly, maintaining sterility, the lay out of the OR, and its equipment are different from what the endoscopy team is accustomed to in the usual endoscopy suites [25]. Thus, a special protocol has to be devised and taught to the endoscopy team [25]. In addition, a great deal of schedule coordination is required to ensure that the endoscopist and the surgeon along with their teams are present in the OR at the same time to avoid delays[25]. At the University of Florida and The Cleveland Clinic, the LA-ERCPs are typically scheduled as the first cases of the day to ensure that the 2 teams are available and there would be no interference with the rest of the OR and endoscopy schedules.

Our study has the typical limitations inherent to retrospective design related to potential for patient selection bias, and measurement bias particularly the under-reporting of adverse events. We anticipate that underreporting was minimized in our cohort because all of our patients were inpatients or were admitted to the hospital after surgery, making detection and reporting of adverse events more likely. In addition, for clarity of reporting we divided adverse events into ERCP or laparoscopy-related categories. Such a distinction may be straightforward for most adverse events such as post-ERCP pancreatitis but could be arbitrary for others such as cardiovascular compromise. Nevertheless, the reported overall adverse event rate should provide an accurate estimate to use as a guide for physicians and patients.

Our large multicenter study indicates that LA-ERCP in patients with RYGB is highly successful, with success rates comparable to standard ERCP in patients with normal upper GI tract anatomy. ERCP-related adverse event rates also appear comparable with those expected of conventional ERCP, but the overall adverse events rate was higher due to the addition of laparoscopy- related

events. Although the majority of such events were mild to moderate, rare severe adverse events are possible. Given the exceptionally high technical success rate and acceptable safety profile, LA-ERCP can be considered as one of the first-line approaches in patients with RYGB who require ERCP. Comparative studies with alternative procedures such as EUS-guided gastro-gastrostomy may further refine our approach in this very challenging patient population.

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Table 1: Participating Centers

Center name	City	State	Country	Patients
Cirurgia Digestiva e Obesidade	Salvador	Bahia	Brazil	26
Cleveland Clinic	Cleveland	OH	USA	52
Dartmouth-Hitchcock Medical Center	Lebanon	NH	USA	14
Duke University	Durham	NC	USA	28
Fox Chase Cancer Center	Philadelphia	PA	USA	6
Geisinger Medical Center	Danville	PA	USA	49
Indiana University	Indianapolis	IN	USA	24
Mayo Clinic Scottsdale	Scottsdale	AZ	USA	7
Medical College of Wisconsin	Milwaukee	WI	USA	11
Medical University of South Carolina	Charleston	SC	USA	12
Methodist Dallas Medical Center	Dallas	TX	USA	23
Northwestern University	Chicago	IL	USA	6
Oregon Health & Science University	Portland	OR	USA	17
Poudre Valley Hospital	Fort Collins	CO	USA	10
Stony Brook University School of Medicine	Stony Brook	NY	USA	5
The University of Ottawa	Ottawa	ON	CA	3
Thomas Jefferson University	Philadelphia	PA	USA	8
University Hospitals Case Medical Center	Cleveland	OH	USA	8
University of California Los Angeles (UCLA)	Santa Monica	CA	USA	16
University of Colorado, Denver	Denver	CO	USA	36
University of Florida	Gainesville	FL	USA	20
University of Maryland School of Medicine	Baltimore	MD	USA	30
University of Massachusetts	Worcester	MA	USA	28
University of Michigan	Ann Arbor	MI	USA	14
University of Rochester Medical Center	Rochester	NY	USA	8
University of São Paulo Medical School & Gastro-Obeso-Center Institute	São Paulo	São Paulo	Brazil	14
University of South Alabama	Mobile	AL	USA	2
University of South Florida	Tampa	FL	USA	8
University of Virginia	Charlottesville	VA	USA	10
University of Washington	Seattle	WA	USA	17
Virginia Mason Medical Center	Seattle	WA	USA	28
Virginia Tech Carilion School of Medicine	Roanoke	VA	USA	9
Wake Forest Baptist Medical Center	Winston Salem	NC	USA	16
Yale School of Medicine	New Haven	CT	USA	14

Table 2: Demographics and other clinical factors of the included population

		No.	%
Age quartile	**<42**	144	25%
	42-51	148	26%
	52-61	157	27%
	>61	130	22%
Gender	**Female**	488	84%
	Male	91	16%
ASA class	**1**	4	1%
	2	242	44%
	3	291	53%
	4	14	3%
Type bariatric surgery	**Laparoscopic Roux-en-Y gastric bypass**	340	68%
	Open Roux-en-Y gastric bypass	160	32%
Years since RYGB, quartiles	**<3**	146	30%
	3-6	106	22%
	7-10	125	25%
	>10	116	24%
Cholecystectomy	**Before ERCP**	423	78%
	At the time of ERCP	114	21%
	After ERCP	6	1%
Prior failed attempts of pancreaticobiliary interventions	**No prior attempt reported**	438	76%
	Enteroscopy ERCP	109	19%
	PTC	26	4%
	Laparoscopic bile duct exploration	5	1%
	Open bile duct exploration	1	0%
Main Indication	**Biliary**	518	89%
	Pancreatic	45	8%
	Both	16	3%
Biliary indication	**Biliary stone**	254	47%
	Suspected papillary stenosis	102	19%
	Dilated duct	75	14%
	Abnormal LFTs	46	9%
	Bile duct stricture	20	4%
	Post cholecystectomy pain	10	2%
	Others/abdominal pain	9	2%
	Bile leak	7	1%
	Ampullary lesion	7	1%
	Biliary stent removal	3	1%
	Abnormal intraoperative cholangiogram	2	0%
Pancreatic Indications	**Pancreatitis**	56	93%
	Dilated pancreatic duct	3	5%
	Pancreatic duct stone	1	2%
Peri-operative antibiotics	**No**	89	15%
	Yes	489	85%
LA-ERCP goal	**Therapeutic**	574	99%
	Diagnostic	5	1%

Notes, LA-ERCP: Laparoscopy assisted ERCP.

Table 3: Interventions performed during LA-ERCP.

	No.	%
Biliary sphincterotomy	550	96%
Stone/sludge/cast extraction	253	44%
Pancreatic duct stent placement	88	15%
Dilation of the papilla	82	14%
Dilation of the ampullary orifice with large balloon (≥ 12 mm)	48	8%
Plastic biliary stent placement	32	6%
Pancreatic stent extraction	10	2%
Biliary stent extraction	20	3%
Dilation of a stricture	17	3%
Metal biliary stent placement	6	1%

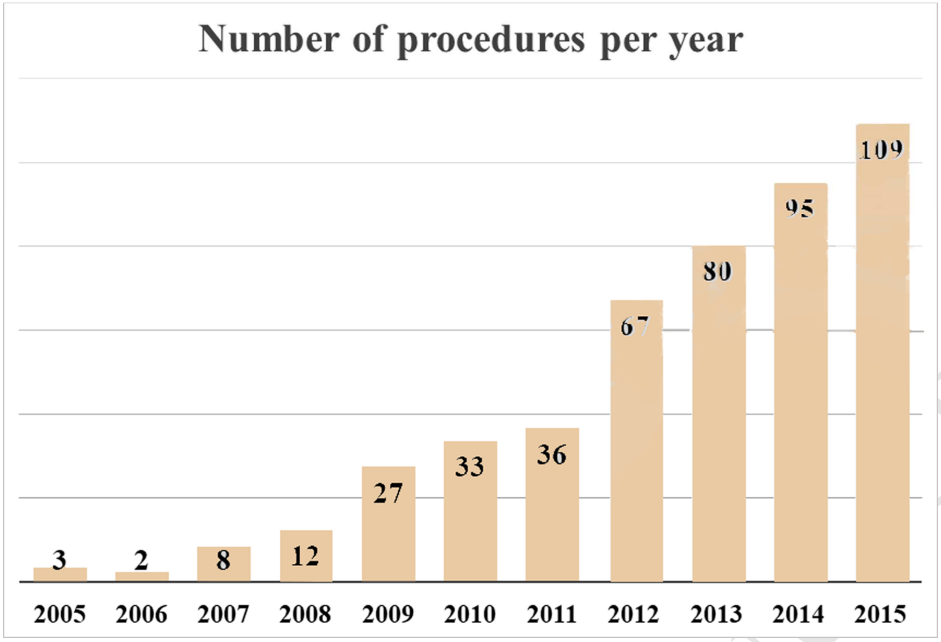
Table 4: Adverse events

Laparoscopy related		
Other postoperative infections	24/579	4.1%
Laparoscopy-related bleeding	10/579	1.7%
Gastric site leak	7/579	1.2%
Gastric tube site infection	7/579	1.2%
Postoperative respiratory adverse events	6/579	1.0%
Postoperative cardiovascular adverse events	4/579	0.7%
Laparoscopy related perforation	3/579	0.5%
Other laparoscopic related adverse event	11/579	1.9%
ERCP-related		
Pancreatitis	43/579	7.4%
Cholangitis	6/579	1.0%
ERCP-related bleeding	3/579	0.5%
ERCP-related perforation	2/579	0.3%
Stent migration	1/579	0.2%

Table 5: Subgroup analyses of adverse events

		Adverse Events						
		Non		ERCP-Related		Laparoscopy-Related		
		No.	%	No.	%	No.	%	*P* value
Age quartile	**<42**	121	86%	11	8%	9	6%	0.448
	42-51	122	82%	13	9%	13	9%	
	52-61	124	81%	10	7%	19	12%	
	>61	107	83%	6	5%	16	12%	
Gender	**Female**	395	82%	37	8%	50	10%	0.237
	Male	79	89%	3	3%	7	8%	
ASA class	**1**	4	100%	0	0%	0	0%	0.225
	2	198	83%	23	10%	18	8%	
	3	235	82%	15	5%	37	13%	
	4	11	79%	1	7%	2	14%	
Type Bariatric Surgery	**Lap RYGB**	285	85%	20	6%	30	9%	0.180
	Open RYGB	123	78%	14	9%	20	13%	
Cholecystectomy	**Before the ERCP**	341	82%	34	8%	41	10%	0.135
	At the time of ERCP	99	88%	2	2%	12	11%	
	After ERCP	6	100%	0	0%	0	0%	
Main Indication	**Biliary**	428	84%	34	7%	50	10%	0.029
	Pancreatic	36	84%	5	12%	2	5%	
	Both	10	63%	1	6%	5	31%	
Years since RYGB, quartiles	**<3**	123	85%	10	7%	11	8%	0.516
	3-6	86	82%	8	8%	11	10%	
	6-10	102	82%	9	7%	13	10%	
	>10	85	75%	10	9%	18	16%	
Conversion to open	**No**	432	83%	36	7%	50	10%	0.045
	Yes	20	69%	2	7%	7	24%	
G tube left in place	**No**	384	84%	30	7%	41	9%	0.036
	Yes	68	74%	8	9%	16	17%	

Note: patients who had both ERCP and laparoscopy related adverse events were excluded from this analysis (8 patients). *P* values are derived from comparing the distribution of adverse event across all the groups within the same variable.



LA-ERCP = Laparoscopy-Assisted Endoscopic Retrograde Cholangiopancreatography

RYGB = Patients with Roux-en-Y Gastric Bypass

G-tube = gastrostomy tube

IRB = institutional review board

LOS = length of hospital stay

IQR = interquartile ranges