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A comparison of endoscopic and non-endoscopic biliary intervention outcomes in patients with prior bariatric surgery

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ABSTRACT

Background and study aims Endoscopic biliary intervention (BI) is often difficult to perform in patients with prior bariatric surgery (BRS). We sought to analyze outcomes of patients with prior BRS undergoing endoscopic and non-endoscopic BI.

Patients and methods The Nationwide Inpatient Sample (2007 – 2011) was reviewed to identify all adult inpatients (≥ 18 years) with a history of BRS undergoing BI. The clinical outcomes of interest were in-patient mortality, length of stay (LOS), and total hospital charges.

Results There were 7,343 patients with prior BRS who underwent BIs where a majority were endoscopic (4,482 vs. 2,861, $P<0.01$). The mean age was 50±30.8 years and the majority were females (80.5 %). Gallstone-related disease was the most common indication for BI and managed more often with primary endoscopic management (2,146 vs. 1,132, $P<0.01$). Inpatient mortality was not significantly different between patients undergoing primary endoscopic versus non-endoscopic BI (0.2 % vs. 0.7 %, $P=0.2$). Patients with sepsis were significantly more likely to incur failed primary endoscopic BI (OR 2.74, 95 % CI 1.15, 6.53) and were more likely to be managed with non-endoscopic BI (OR 2.13, 95 % CI 1.3, 3.5). Primary non-endoscopic BI and failed endoscopic BI were both associated with longer LOS (by 1.77 days, $P<0.01$ and by 2.17 days, $P<0.01$, respectively) and higher hospitals charges (by $11,400, $P<0.01$ and by $ 14,200, $P<0.01$, respectively).

Conclusion Primary endoscopic management may be a safe and cost-effective approach for patients with prior BRS who need BI. While primary endoscopic biliary intervention is more common, primary non-endoscopic intervention may be used more often for sepsis.

Introduction

Morbid obesity continues to rise significantly in the United States and now effects approximately 1 in 15 adults [1, 2]. Bariatric surgery (BRS) leads to sustained weight loss and improvements in morbidity and mortality [3, 4]. Morbidly obese individuals, especially those with a body mass index (BMI) ≥ 40, have been shown to have an 8-fold higher risk of gallstone formation compared with those with a lower BMI [5]. After BRS, the rapid weight loss often accelerates gallstone formation which may predispose to acute cholecystitis, acute pancreatitis, and ascending cholangitis [6]. Despite this risk, prophylactic concomitant cholecsytectomy is not often performed due to its association with increased BRS complications and only a minority of patients developing symptomatic gallstone disease [7, 8]. Patients with prior BRS often require biliary intervention including endoscopic retrograde cholangio-pancreatography (ERCP) for choledocholithiasis, recurrent pancreatitis, pancreaticobiliary neoplasms, biliary obstruction, and biliary leak [9 – 11].

Roux-en-Y gastric bypass (RYGB) constitutes the vast majority of BRSs, accounting for approximately 60 %-70 % of all BRSs [12]. In patients with prior RYGB BRS that require biliary intervention, alteration of the normal foregut anatomy may make access to the native biliary tree very challenging. Conventional ERCP has a success rate of approximately 50 % in patients with prior Whipple resection, with significant higher success rates (84 %) when used for biliary indications [13]. Transgastric access with laparoscopic methods along with endoscopic single and double balloon enteroscopy, have been described with varying methods of success [9, 14]. In patients with prior RYGB, a laparoscopic-assisted transgastric access with ERCP is recommended for assessment of the duodenum and biliary tree, and evaluation of chronic abdominal pain [15].

To our knowledge, there are no large population-based studies comparing endoscopic (laparoscopic or enteroscopy-assisted ERCP) versus non-endoscopic (percutaneous cholangiography and surgical common bile duct exploration) procedures in patients with prior BRS that require biliary intervention. Thus, our aim was to estimate the prevalence of biliary interventions in patients with prior BRS and to evaluate clinical outcomes comparing endoscopic and non-endoscopic approaches. The clinical outcomes of interest were in-patient mortality, length of stay (LOS), and total hospital charges

Patients and methods

Data source

The Nationwide Inpatient Sample (NIS) Healthcare Cost Utilization Project (HCUP), an administrative claims databank, is the largest all-payer inpatient care database in the US [16]. The NIS is a compilation of more than 8 million inpatient admissions from approximately 1000 hospitals (representing about 85 % of all nonfederal hospitals). It is designed to approximate a 20 % stratified probability sample of patients from all nonfederal acute-care hospitals in the US. Discharge weights are provided, which allows extraction of national level estimates from the unweighted database information [16].

The NIS-HCUP database was queried from 2007 to 2011 using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure for all adult patients (≥ 18 years) with a history of BRS undergoing biliary procedures (ERCP, percutaneous cholangiography (PTC) and surgical common bile duct exploration (CBDE). Due to the limited specificity of ICD-9-CM coding, we were unable to distinguish between laparoscopic, or enteroscopy-assisted ERCP. Therefore, these procedures were grouped into 1 category referred to as endoscopic biliary interventions. Primary endoscopic intervention is defined as the performanance of any endoscopic biliary intervention as the initial procedure for treatment. Primary non-endoscopic intervention is similarly defined as the performance of either PTC or CBDE as the initial therapeutic technique. Failed endoscopic intervention was defined as the performance of a non-endoscopic biliary intervention (PTC or CBDE) within 7 days after a primary endoscopic intervention. A history of prior BRS, etiologic factors for biliary intervention and associated diagnoses, and specific types of biliary intervention were queried by using specific ICD-9-CM codes (**Appendix 1**).

The Ohio State University Data and Specimen Policy and Human Subjects Research Policy does not require Institutional Review Board approval for population-based public data sets. Per 45 Code of Federal Regulations (CFR 46.101), research using certain publicly available data sets does not involve "human subjects."

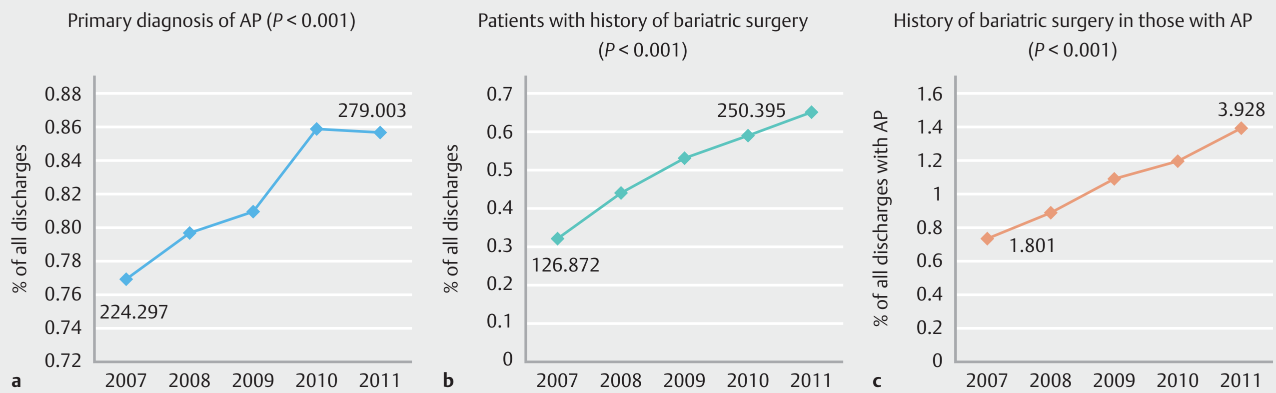
Patients and outcomes

Patient-level variables included age, sex, race, median household income for patient's zip code (quartiles), and insurance status. Race/ethnicity was categorized as White, Black, Hispanic, and others. Insurance status was categorized as Medicare, Medicaid, private insurance, and uninsured/other based on the primary payer listed on the discharge record. Comorbidities for risk adjustment were derived from Agency for Healthcare Research and Quality (AHRQ) comorbidity measures based on the methods by Elixhauser [17]. Patients were given a score of < 3 or ≥ 3 based on the number of comorbidities. Hospital-related potential confounders were hospital location (urban vs. rural), hospital bed size (large, medium, small), and hospital teaching status (teaching vs. nonteaching). Hospital bed size was classified as small, medium, or large based on an algorithm developed by HCUP. Hospital region was classified by the US Census Bureau as Northeast, Midwest, South, or West.

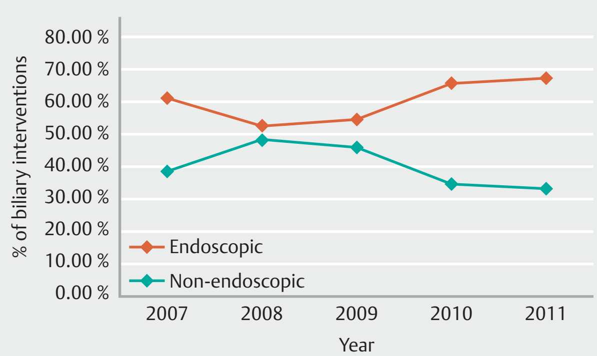
Clinical outcomes of interest were inpatient mortality, LOS, and total hospital charges and we compared these in 2 groups of patients with prior BRS: (a) patients requiring primary endoscopic versus non-endoscopic biliary intervention, and (b) patients undergoing failed versus successful endoscopic biliary interventions. The LOS and total hospital charges were collectively referred to as healthcare resource utilization.

Statistical analysis

Categorical variables and continuous variables were tested for statistical significance with Chi-square tests and *t* tests, respectively. The mean and standard deviation were calculated for all continuous outcomes and frequency counts and percentages were calculated for all categorical outcomes. Temporal trends were assessed using the Cochrane-Armitage trend test. Univariate predictor variables with a *P* value < 0.1 were included in the multivariate analysis. Multivariate linear regression models were fit for continuous outcome variables and multivariate logistic regression models were fit for each dichotomous outcome. All results in the regression model were represented by an odds ratio (OR) and 95 % confidence interval (CI). All regression models were performed separately. Statistical significance



▶ **Fig. 1** Trend analysis of hospitalizations in the Nationwide Inpatient Sample (2007 – 2011). Increasing prevalence of **a** acute pancreatitis, **b** patients with history of bariatric surgery, and **c** history of bariatric surgery in patients admitted with acute pancreatitis.
AP, acute pancreatitis



▶ **Fig. 2** Trends in endoscopic and non-endoscopic biliary interventions among patients with prior bariatric surgery, Nationwide Inpatient Sample, 2007 – 2011.

was defined by $P<0.05$. These analyses were performed on weighted data from the NIS database using SAS 9.3 (SAS Institute, Cary, NC) employing appropriate survey procedures to produce national estimates.

Missing data is enlisted in **Appendix 2**. Race was the variable with the most missing data (9.4 %) since certain states do not document race in discharge information. Other variables had less than 1 % missing data and these were dropped from the final analysis. Imputation was not performed as data was assumed to be missing at random.

Results

Trends in bariatric surgery, cholecystectomy, and biliary drainage procedures

The trends in the different types of bariatric surgeries performed in the United States from 2005 to 2011 are illustrated in **Appendix 3a**. During this time period, the proportion of RYGBs decreased from 81.9 % (97,814 out of 119,382 total BRSs) to 58.3 % (63,178 of 108,354), while the proportion of sleeve gastrectomies and gastric band surgeries increased from 18.1 % to 41.7 %. The proportion of patients undergoing simultaneous cholecystectomies at the time of BRS decreased from 8.3 % in 2005 (9,880 of 119,382) to 3.4 % in 2011 (3,653 of 108,354), $P<0.001$ (**Appendix 3b**). Between 2007 and 2011, there were a total of 988,015 patients discharged with a diagnostic code for history of BRS. The proportion of admissions as well as the total number of patients with prior BRS doubled from 2007 to 2011 (126,872 [0.32 %] to 250,395 [0.65 %], $P<0.001$) (▶ **Fig. 1**).

For patients with a history of BRS, the proportion of primary endoscopic interventions increased (435 [61.3 %] to 1,346 [66.7 %], $P<0.001$) between 2007 and 2011 while the proportion of primary non-endoscopic interventions generally decreased (275 [38.7 %] to 672 [33.3 %], $P<0.001$) (▶ **Fig. 2**).

Patient characteristics and procedure indications

From 2007 to 2011, there were 7,343 (0.74 % of 988,015) patients with a history of BRS who underwent a biliary intervention. The majority of these patients underwent an endoscopic intervention compared to non-endoscopic interventions (4,482 [61 %] vs. 2,861 [39 %] respectively, $P<0.001$) (▶ **Table 1**). Biliary intervention in BRS was more frequent in women and in large urban hospitals. Most procedures (endoscopic or non-endoscopic) were performed within 1 day of hospitalization. A majority of all endoscopic and non-endoscopic interventions were performed for gallstone-related disease (2,146 [47.9 %] and 1,132 [39.6 %] respectively). Among patients that underwent non-endoscopic interventions, more required PTC (1,692 [59 %]) compared to CBDE (1,169 [41 %]) (**Appendix 4**).

Endoscopic versus non-endoscopic biliary intervention

Demographics and hospital variables

Univariate analysis (▶ **Table 1**) revealed that patients who underwent a primary endoscopic biliary intervention were younger, with fewer comorbid conditions, and were treated at teach-

▶ **Table 1** Demographics, etiological associations, and outcomes of patients with a history of bariatric surgery undergoing endoscopic or non-endoscopic biliary intervention: Comparison of endoscopic versus non-endoscopic (PTC/CBDE) in the Nationwide Inpatient Sample from 2007 to 2011.

Total: 7,343	**Endoscopic Intervention n = 4,482 (%)**		**Non-endoscopic Intervention n = 2,861 (%)**		***P* value**
Age (mean, SD)	50.11	30.76	52.14	26.25	0.0039
Gender					0.0003
▪ Male	728	16.25 %	705	24.66 %	
▪ Female	3,754	83.75 %	2,156	75.34 %	
Race					0.1189
▪ White	3,131	76.85 %	2,105	81.48 %	
▪ Black	402	9.86 %	252	9.76 %	
▪ Hispanic	396	9.71 %	167	6.46 %	
▪ Other	146	3.58 %	60	2.31 %	
Income (national quartile)					0.4937
▪ 1	948	21.48 %	561	20.12 %	
▪ 2	1,145	25.95 %	765	27.43 %	
▪ 3	1,131	25.63 %	793	28.41 %	
▪ 4	1,189	26.95 %	671	24.04 %	
Type of insurance					0.2303
▪ Medicare	1,129	25.19 %	833	29.11 %	
▪ Medicaid	297	6.62 %	136	4.74 %	
▪ Private	2,620	58.45 %	1,646	57.53 %	
▪ Other	436	9.74 %	247	8.63 %	
Hospital location					0.0815
▪ Rural	167	3.78 %	163	5.73 %	
▪ Urban	4,243	96.22 %	2,678	94.27 %	
Hospital teaching status					0.0218
▪ Nonteaching	1,835	41.61 %	1,396	49.14 %	
▪ Teaching	2,575	58.39 %	1,445	50.86 %	
Hospital size					0.8159
▪ Small	386	8.75 %	252	8.86 %	
▪ Medium	898	20.36 %	621	21.87 %	
▪ Large	3,126	70.88 %	1,968	69.28 %	
Hospital region					0.0603
▪ Northeast	942	21.02 %	535	18.69 %	
▪ Midwest	1,087	24.25 %	540	18.88 %	
▪ South	1,321	29.48 %	1,057	36.96 %	
▪ West	1,132	25.25 %	729	25.48 %	
Weekend admission					0.4549
▪ No	3,717	82.94 %	2,331	81.46 %	
▪ Yes	765	17.06 %	530	18.54 %	
Elixhauser comorbidity Index					< 0.0001

▶ **Table 1** (Continuation)

Total: 7,343	Endoscopic Intervention n = 4,482 (%)		Non-endoscopic Intervention n = 2,861 (%)		*P* value
▪ <3	2,860	63.82 %	1,508	52.71 %	
▪ ≥ 3	1,622	36.18 %	1,353	47.29 %	
Etiology					
Gallstone related	2,146	47.88 %	1,132	39.57 %	0.0023
Pancreaticobiliary neoplasm	81	1.80 %	197	6.89 %	< 0.0001
Disease of bile duct	223	4.97 %	96	3.34 %	0.1383
Bile leak, bile duct injury, biliary peritonitis	253	5.63 %	309	10.81 %	0.0008
Bile duct obstruction and jaundice NOS	262	5.84 %	186	6.51 %	0.6299
Stent-related (changes, others)	134	2.99 %	53	1.86 %	0.1597
Chronic pancreatitis	54	1.21 %	a	0.00 %	–
Sphincter of oddi dysfunction	22	0.50 %	a	0.11 %	0.1812
Abdominal pain	41	0.92 %	a	0.00 %	–
Time to PTC/CBDE or ERCP					0.2628
▪ < 0 to 1 day	2,294	51.19 %	1,571	54.90 %	
▪ 2 – 4 days	1,593	35.53 %	890	31.11 %	
▪ 5 – 10 days	595	13.27 %	400	13.99 %	
Cholecystectomy	1,697	37.86 %	1,135	39.66 %	0.5294
Associated diagnoses	(DX1-DX25)				
Sepsis	184	4.10 %	303	10.58 %	< 0.0001
Acute pancreatitis	1,146	25.57 %	360	12.57 %	< 0.0001
Cholangitis	532	11.87 %	387	13.54 %	0.3403
Outcome					
Death	a	0.22 %	20	0.69 %	0.2181
Length of stay ≥ 7 days	1,215	27.12 %	1,352	47.25 %	< 0.0001
Length of stay (mean, SD)	5.31	9.46	7.40	11.69	< 0.0001
Total charges (mean, SD)	50,664	92,279	64,349	125,999	< 0.0001

a) The cell's value is not displayed. As per data agreements with AHRQ, researchers cannot report any statistics where the number of observations in any given cell of analyzed data is ≤ 10.
CBDE, common bile duct exploration; ERCP, endoscopy retrograde cholangiopancreatography; PTC, percutaneous transhepatic cholangiography

ing hospitals compared to those requiring primary non-endoscopic interventions. Gallstone-related disease was associated with more frequent primary endoscopic management while pancreaticobiliary neoplasms and bile duct injury were associated with primary non-endoscopic management.

Presence of associated emergent conditions

Acute pancreatitis (AP), as an associated diagnosis, was more frequent in patients requiring an endoscopic approach; however, sepsis, as an associated diagnosis, was more frequent in patients undergoing non-endoscopic biliary interventions (▶ **Table 1**). Multivariate analysis adjusting for demographics, hospital factors, and etiologies confirmed these findings. Sepsis was more than 2 times more likely to be associated with patients requiring non-endoscopic intervention (OR 2.13, 95 % CI 1.30, 3.50, $P = 0.003$). On the contrary, AP was more than 2 times more frequently associated with patients undergoing an endoscopic approach (OR = 2.44, 95 % CI 0.30, 0.56, $P < 0.001$).

Mortality and health care resource utilization

The overall in-hospital mortality rate for patients with prior BRS undergoing biliary intervention was 0.41 % (30 of 7,343 patients). Inpatient mortality was not significantly different between patients undergoing primary endoscopic versus primary non-endoscopic procedures (0.22 % vs. 0.69 %, $P = 0.2$) (▶ **Table 1**). However, non-endoscopic interventions were associated

▶ **Table 2** Multivariate linear regression model for healthcare utilization in patients with a history of bariatric surgery undergoing biliary intervention, Nationwide Inpatient Sample, 2007 – 2011.

	Length of stay			Total charges		
	Days	**95 % CI**	***P* value**	**$**	**95 % CI**	***P* value**
Primary procedure			< 0.0001			< 0.0001
▪ ERCP	Reference			Reference		
▪ CBDE/PTC	1.77	(1.32, 2.21)		11,453	(5,811, 17,095)	
Age	0.01	(-0.01, 0.02)	0.423	-78	(-225, 69)	0.3001
Gender					0.7499	0.0316
▪ Male	Reference			Reference		
▪ Female	-0.09	(-0.61, 0.44)		-6,460	(-12,351, – 569)	
Hospital location			0.0854			< 0.0001
▪ Rural	Reference			Reference		
▪ Urban	0.64	(-0.09, 1.37)		19,625	(12,775, 26,475)	
Hospital teaching status			0.9229			0.7444
▪ Nonteaching	Reference			Reference		
▪ Teaching	0.03	(-0.54, 0.59)		-1,177	(-8,254, 5,901)	
Hospital region			0.9181			0.0001
▪ Northeast	Reference			Reference		
▪ West	-0.16	(-0.92, 0.59)		14,764	(3,652, 25,876)	
▪ South	0.04	(-0.56, 0.64)		-2,088	(-11,703, 7,526)	
▪ Midwest	0.09	(-0.54, 0.72)		-6,548	(-16,804, 3,708)	
Elixhauser comorbidity Index			< 0.0001			< 0.0001
▪ < 3	Reference			Reference		
▪ ≥ 3	1.27	(0.79, 1.75)		10,826	(5,559, 16,092)	
Gallstone related	-0.79	(-1.21, – 0.37)	0.0002	-3,651	(-8,654, 1,351)	0.1525
Pancreaticobiliary neoplasm	1.55	(-0.09, 3.19)	0.0639	3,699	(-9,976, 17,373)	0.5959
Bile leak, bile duct injury, biliary peritonitis	0.79	(-0.37, 1.94)	0.1806	5,833	(-6,525, 18,191)	0.3547
Chronic pancreatitis	-1.35	(-1.89, – 0.80)	< 0.0001	-18,484	(-38,533, 1,565)	0.0707
Time to PTC/CBDE or ERCP			< 0.0001			< 0.0001
▪ < 0 to 1 day	Reference			Reference		
▪ 2 – 4 days	1.72	(1.27, 2.16)		12,004	(7,454, 16,553)	
▪ 5 – 10 days	6.29	(5.45, 7.14)		43,740	(33,291, 54,189)	

CBDE, common bile duct exploration; ERCP, endoscopy retrograde cholangiopancreatography; PTC, percutaneous transhepatic cholangiography;

with a longer length of hospital stay and greater total hospital charges. More specifically, patients with a primary non-endoscopic intervention stayed 1.77 (95 % CI 1.32, 2.21, $P < 0.001$) days longer and were charged $ 11,453 (95 % CI 5,811, 17,095, $P < 0.001$) more than those with a primary endoscopic intervention (▶ **Table 2**). Notably, patients who underwent any biliary intervention within 1 day of hospitalization accounted for significantly lower health care resource utilization (▶ **Table 2**).

Successful versus failed endoscopic interventions

Demographics and hospital variables

A total of 4,482 patients with history of BRS underwent primary endoscopic interventions. Procedure success and failure rates were 88.3 % (n = 3,956) and 11.7 % (n = 526) respectively, $P < 0.001$. Univariate analysis (▶ **Table 3**) revealed that patients who had successful procedures were younger compared to those who had a failed procedure. Failed procedures were associated with more frequent cholecystectomies compared to successful procedures (47.1 % and 36.6 % respectively, $P = 0.04$).

Presence of associated emergent conditions

Acute pancreatitis was an associated diagnosis found more frequently in patients with successful endoscopic interventions while sepsis was an associated diagnosis more frequent in failed interventions (▶ **Table 3**). Specifically, sepsis was more than 2.7 times more likely to be associated with failed endoscopic interventions (OR 2.74, 95 % CI 1.15, 6.53, $P = 0.02$) compared to successful interventions.

Mortality and health care resource utilization

There was no documented death for patients with failed endoscopic interventions and all 10 deaths in the endoscopic intervention group occurred in patients with successful procedures. Failed endoscopic interventions accounted for greater healthcare resource utilization (longer LOS and greater total charges). Specifically, failed endoscopic interventions necessitated 2.17 (95 % CI 1.79, 3.33, $P < 0.001$) additional days of stay and $14,214 (95 % CI 3,749, 24,679, $P = 0.008$) more than successful interventions (▶ **Table 4**). Patients who underwent either successful or failed endoscopic intervention within 1 day of hospitalization accounted for significantly lower health care resource utilization, $P < 0.001$.

Discussion

In this population-based study analysis of all biliary interventions in hospitalized patients with prior BRS from 2007 to 2011, we have demonstrated that gallstone disease is the most common indication for biliary intervention. To our knowledge, this is is the most comprehensive population-based study comparing outcomes of endoscopic versus non-endoscopic interventions in patients with biliary disease and a prior history of BRS. For all patients with BRS needing biliary interventions, a majority underwent endoscopic (ERCP or enteroscopy-assisted or laparscopic-assisted ERCP) guided procedure. Patients with sepsis were significantly more likely to incur failed primary endoscopic BI and were more likely to be managed with non-endoscopic BI. Although there was no difference in inpatient mortality comparing different types of biliary intervention, primary non-endoscopic interventions were associated with increased healthcare resource utilization. Failed endoscopic interventions did not result in greater inpatient mortality but did account for increased healthcare resource utilization.

Our study highlights recent trends in BRS including a steady decrease in RYGBs with a concomittant increase in sleeve gastrectomies; which is consistent with prior studies [18]. Multiple studies have illustrated the increase in prevalence of gallstones with rapid weight loss following BRS, although to varying degrees [5, 19]. Even though the total number of patients with a history of BRS doubled during the study period, the proportion of patients undergoing simultaneous cholecystectomies at the time of BRS decreased by approximately 60 %. Another study analyzing NIS trends during BRS illustrated that the proportion of patients undergoing concomitant cholecystectomy decreased from 26.3 % in 2001 to 3.7 % in 2008 [8]. Concomitant cholecystectomy during gastric bypass surgery is no longer routine practice because operative time, postoperative hospital stay, and postoperative morbidity and mortality are higher with prophylactic cholecystectomy [20]. Several studies have indicated its use only in cases of symptomatic gallbladder disease, particularly cholelithiasis [21].

Among patients who required biliary intervention, the majority underwent primary endoscopic intervention compared to non-endoscopic intervention. The endoscopic intervention failure rate was 12 %. However, the database does not differentiate between the 3 major types of bariatric surgeries and endoscopic biliary intervention is more difficult in patients with RYGB anatomy. Furthermore, prior studies have demonstrated that 60 % to 70 % of all BRS patients had RYGB; thus, we can project that the failure rate of endoscopic biliary intervention in patients with RYGB anatomy would be 17 % to 20 % [18]. This failure rate is comparable to prior literature. With the steady decrease in RYGBs along with an increase in sleeve gastrectomies, the success rate of endoscopic biliary interventions may rise in the future, as the latter procedure, in theory, allows for easier access to the papilla compared to the former. In long limb surgical bypass patients with suspected pancreatobiliary diseases, ERCP was successful in 63 % of patients, and specifically in 88 % when the papilla was reached [22]. Common reasons for ERCP failure include afferent limb entered but papilla not reached, cannulation failure, afferent limb angulation, and jejunojejunostomy not identified [22]. Thus, a safe and effective alternative to these modalities in RYGB patients is laparoscopic transgastric endoscopy [23, 24]. Laparoscopic-assisted ERCP has been shown to be superior than balloon enteroscopy assisted ERCP with a 100 % rate of papilla identification, cannulation rate, and therapeutic success [25]. However, this procedure should be preferred in patients with Roux + biliopancreatic limb (from ligament of Treitz to jejunojejunal anastomosis) of 150 cm or longer while those with a limb length less than 150 cm should be offered deep enteroscopy-assisted ERCP first [25].

In this study, overall mortality with either endoscopic or non-endoscopic biliary intervention was 0.41 % and there was no difference in mortality between the 2 groups. Notably, primary non-endoscopic and failed endoscopic interventions accounted for increased healthcare resource utilization. A cohort study utilizing administrative data demonstrated that in all patients presenting with biliary emergencies, failed ERCP and open cholecystectomy were associated with increased mortality and increased healthcare resource utilization [26]. Another retrospective analysis showed that failed ERCP prolongs hospital stays and increases costs of hospitalization [27]. The sickest patients in our study (those with sepsis) required primary or secondary non-endoscopic intervention and hence contributed to increased healthcare resource utilization. Failed ERCP may be a marker for sepsis resulting from delayed biliary decompression leading to increased need for hospital-based interventions. This association was demonstrated in this study where patients with sepsis were managed with non-endoscopic

▶ **Table 3** Demographics, etiological associations, and outcomes of patients with a history of bariatric surgery undergoing endoscopic intervention: Comparison of endoscopic intervention success in the Nationwide Inpatient database from 2007 to 2011.

Total: 4,482	Successful endoscopic intervention n = 3,956 (%)		Failed endoscopic intervention n = 526 (%)		*P* value
Age (mean, SD)	49.68	13.69	53.35	14.91	0.0132
Gender					0.6979
▪ Male	650	16.42 %	79	14.97 %	
▪ Female	3,306	83.58 %	447	85.03 %	
Race					0.0901
▪ White	2,744	76.14 %	387	82.26 %	
▪ Black	351	9.75 %	50	10.70 %	
▪ Hispanic	368	10.21 %	28	5.89 %	
▪ Other	140	3.89 %	a	1.15 %	
Income (national quartile)					0.2689
▪ 1	823	21.11 %	125	24.20 %	
▪ 2	984	25.26 %	161	31.12 %	
▪ 3	1,006	25.81 %	125	24.29 %	
▪ 4	1,084	27.82 %	105	20.39 %	
Type of insurance					0.5429
▪ Medicare	967	24.43 %	162	30.85 %	
▪ Medicaid	262	6.61 %	35	6.71 %	
▪ Private	2,342	59.22 %	277	52.71 %	
▪ Other	385	9.74 %	51	9.74 %	
Hospital location					0.7970
▪ Rural	149	3.84 %	18	3.36 %	
▪ Urban	3,740	96.16 %	503	96.64 %	
Hospital teaching status					0.7989
▪ Nonteaching	1,624	41.76 %	211	40.44 %	
▪ Teaching	2,265	58.24 %	310	59.56 %	
Hospital size					0.0486
▪ Small	354	9.10 %	32	6.16 %	
▪ Medium	829	21.31 %	69	13.25 %	
▪ Large	2,706	69.59 %	420	80.59 %	
Hospital region					0.6458
▪ Northeast	851	21.52 %	91	17.28 %	
▪ Midwest	969	24.49 %	118	22.45 %	
▪ South	1,153	29.14 %	168	32.00 %	
▪ West	983	24.85 %	149	28.27 %	
Weekend admission					0.1778
▪ No	3,261	82.43 %	457	86.81 %	
▪ Yes	695	17.57 %	69	13.19 %	

▶ **Table 3** (Continuation)

Total: 4,482	**Successful endoscopic intervention n = 3,956 (%)**		**Failed endoscopic intervention n = 526 (%)**		***P* value**
Elixhauser comorbidity Index					0.2182
▪ < 3	2,553	64.53 %	308	58.48 %	
▪ ≥ 3	1,403	35.47 %	218	41.52 %	
ETIOLOGY					
Gallstone related	1,863	47.11 %	282	53.69 %	0.2901
Pancreaticobiliary neoplasm	76	1.93 %	a	0.86 %	0.2917
Disease of bile duct	207	5.23 %	16	3.02 %	0.2783
Bile leak, bile duct injury, biliary peritonitis	202	5.11 %	50	9.54 %	0.1312
Bile duct obstruction and jaundice NOS	218	5.52 %	43	8.25 %	0.3393
Stent related (changes, others)	125	3.16 %	a	1.72 %	0.2898
Chronic pancreatitis	54	1.38 %	a	0.00 %	–
Sphincter of Oddi dysfunction	22	0.56 %	a	0.00 %	–
Abdominal pain	36	0.91 %	a	0.97 %	0.9534
Time to ERCP					0.4979
▪ < 0 to 1 day	2,029	51.29 %	266	50.46 %	
▪ 2 – 4 days	1,419	35.88 %	173	32.90 %	
▪ 5 – 10 days	507	12.83 %	88	16.63 %	
Cholecystectomy	1,449	36.63 %	248	47.08 %	0.0401
Associated diagnoses	(DX1-DX25)				
Sepsis	130	3.27 %	54	10.30 %	0.0286
Acute pancreatitis	1,047	26.47 %	99	18.79 %	0.0429
Cholangitis	444	11.23 %	88	16.69 %	0.1715
Outcome					
Death	a	0.25 %	a	0.00 %	–
Length of stay ≥ 7 days	964	24.37 %	251	47.80 %	< 0.0001
Length of stay (mean, SD)	5.03	4.03	7.36	5.32	< 0.0001
Total charges (mean, SD)	48,981	41,197	63,200	45,989	0.0040

a) The cell's value is not displayed. As per data agreements with AHRQ, researchers cannot report any statistics where the number of observations in any given cell of analyzed data is ≤ 10.
ERCP, endoscopy retrograde cholangiopancreatography

interventions and more likely to incur failed ERCP. However, difficulties in timing an endoscopic intervention appropriately may explain why patients with sepsis were more often managed with non-endoscopic interventins. A statistically significant mortality difference may have not been seen due to the relatively low death rate and improvements in the management of sepsis [28, 29].

Early biliary intervention in patients with a history of BRS is critical when clinically indicated as patients who underwent biliary intervention within 1 day of hospitalization accounted for significantly lower health care resource utilization. The literature on the timing of endoscopic intervention after hospital admission in patients with BRS remains limited; however, early ERCP has been described in the non-bariatric population. A prospective multicenter study analyzing early ERCP (within 72 hours) versus conservative treatment for acute non-obstructive biliary pancreatitis found that early ERCP was not beneficial in these patients [30]. Other systematic reviews have also found that early ERCP does not effect mortality and complications in patients with acute gallstone pancreatitis compared to conser-

▶ **Table 4** Multivariate linear regression model for healthcare utilization in patients with a history of bariatric surgery undergoing endoscopic biliary intervention, Nationwide Inpatient Sample, 2007 – 2011.

	Length of stay			Total charges		
	Days	**95 % CI**	***P* value**	**$**	**95 % CI**	***P* value**
Endoscopic intervention			< 0.0001			0.0078
▪ Successful	Reference			Reference		
▪ Failed	2.17	(1.18, 3.16)		14,214	(3,749, 24,679)	
Age	0.01	(–0.01, 0.03)	0.1937	149	(–11, 309)	0.0688
Race			0.7441			0.0834
▪ White	Reference			Reference		
▪ Black	–0.02	(–0.75, 0.72)		4,450	(–5,146, 14,046)	
▪ Hispanic	–0.28	(–0.93, 0.37)		8,751	(1,822, 15,680)	
▪ Other	0.37	(–0.92, 1.65)		–1,142	(–14,208, 11,924)	
Hospital size			0.163			0.4041
▪ Small	Reference			Reference		
▪ Medium	0.14	(–0.46, 0.74)		4,017	(–8,061, 16,096)	
▪ Large	0.49	(–0.06, 1.05)		6,322	(–3,111, 15,756)	
Chronic pancreatitis	–0.18	(–0.86, 0.50)	0.611	–13,961	(–33,873, 5,950)	0.1692
Time to ERCP			< 0.0001			< 0.0001
▪ < 0 to 1 day	Reference			Reference		
▪ 2 – 4 days	1.87	(1.42, 2.33)		14,835	(9,635, 20,034)	
▪ 5 – 10 days	7.16	(6.11, 8.22)		39,107	(28,564, 49,649)	

ERCP, endoscopy retrograde cholangiopancreatography

vative treatment [31, 32]. However, in patients with co-exisiting cholangitis and biliary obstruction, early ERCP significantly reduced mortality and complications [31].

Given changing trends in prevalence of different types of BRS during the study period, we performed a univariate and multivariate sensitivity analysis of the study time period. Specifically, we dichotomized the study period into 2007 – 2008 and 2009 – 2011. Prior studies have demonstrated that gallstone-related problems are typically seen within 1 to 2 years of bariatric surgery [33]. In one study, the mean follow-up time to cholecystectomy for symptomatic gallstone disease after BRS was 21.5 months [33]. Accordingly, we dichotomized the years into these 2 categories as our trend analysis demonstrated that the decrease in RYGB and increase in sleeve gastrectomies was after 2008. Endoscopic biliary intervention was significantly more frequent in the later time period, 2009 – 2011 (62.9 %), compared to 2007 – 2008 (55.7 %) ($P = 0.05$). However, we found that there were higher total charges (by $6,378, $P = 0.03$) in 2009 – 2011 (not adjusted for inflation) and no differences in the length of stay (by 0.07 days, $P = 0.77$) (**Appendix 5**). Moreover, there were no differences between successful and failed interventions during the 2 time periods. While successful endoscopic interventions were more frequent in 2009 – 2011 (89.2 %) compared to 2007 – 2008 (85.1 %), this difference was not statistically significant ($P = 0.13$), and this did not impact health care utilization (**Appendix 6**).

As with all administrative databases, coding errors represent a potential limitation of the present study. In the absence of a national bariatric surgery registry, NIS represents a great data source for different types of BRS given its sophisticated sampling design and large number of observations. However, the code for prior-BRS (v45.86) is a v-code, which unfortunately does not detail the various types of bariatric surgeries. However, based on prior studies, we can project that 60 % to 70 % of all BRS patients had RYGB anatomy [18]. Moreover, the ICD-9 code for BRS has been utilized in other studies in the literature [12, 34]. In addition to the potential for miscoding, some unique features of the NIS database should be recognized. First, this study was unable to differentiate between endoscopic and laparoscopic-guided ERCP due to a lack of specificity in the ICD-9 codes. Second, the presence of an ICD-9 code for gallstones only proves an association but doesn't convey causality. Third, this database is unable to differentiate distinctive patients, and therefore patients with recurrent biliary interventions could be represented multiple times. The influence of this on the current results is uncertain but expected to be of small magnitude considering the statistically large sample size. Lastly, the NIS database cannot account for unobserved characteristics that may influence an intervention, complication, or outcome, so inferring "causality" from observed associations is not valid.

Conclusion

In conclusion, rates of obesity and prevalence of BRS for morbidly obese patients are increasing. In the vast majority of patients with BRS, concurrent prophylactic cholecystectomy is not performed. As a result, the most common indication for biliary intervention in this population is gallbladder-related disease. While primary endoscopic biliary intervention is more common, primary non-endoscopic intervention may be used more often for sepsis. Future research on improving success rates of endoscopic biliary intervention is prudent to reduce healthcare resource utilization.

Competing interests

None

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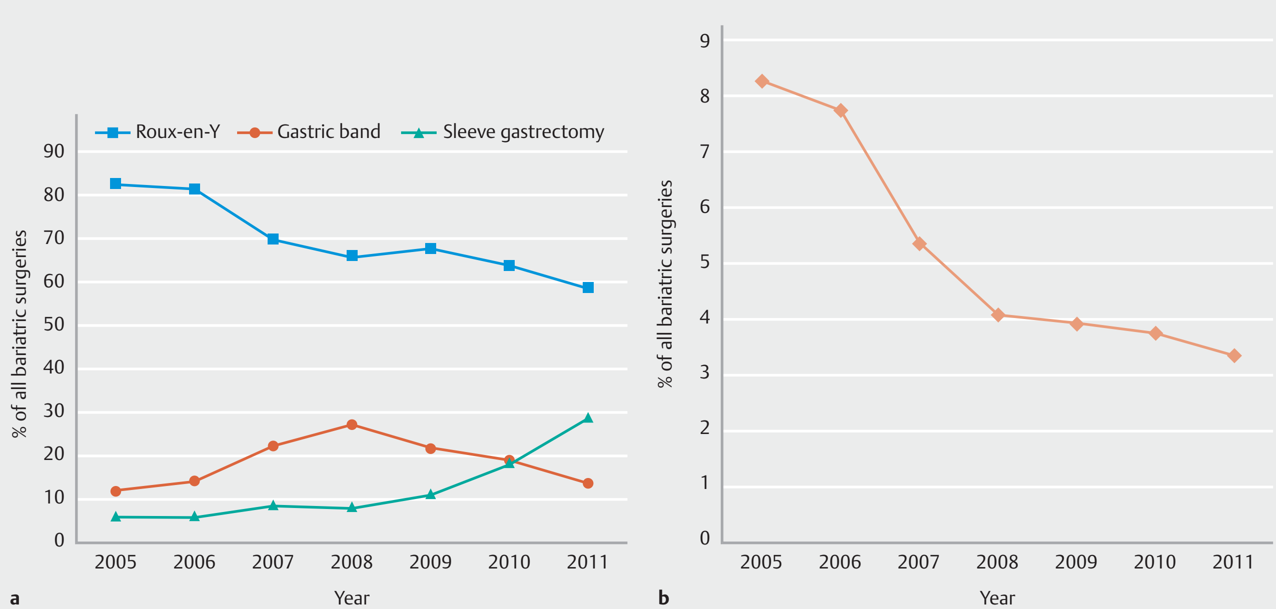
▶ **Appendix 1** ICD-9-CM codes used for data extraction and analysis from the Nationwide Inpatient Sample (2007 – 2011).

Diagnosis	ICD-9-CM codes used	Variable location
Acute pancreatitis	577.0	DX1
History of bariatric surgery	V45.86	DX2-DX25
Morbid obesity	278.01, V85.4, V85.41, V85.42, V85.43, V85.44	DX2-DX25
Cholelithiasis or choledocholithiasis (gallstone related)	574, 574.00, 574.01, 574.10, 574.11, 574.20, 574.21, 574.30, 574.40, 574.41, 574.50, 574.51, 574.60, 574.61, 574.70, 574.71, 574.80, 574.81, 574.90, 574.91	DX2-DX25
Cholangitis	576.1	DX2-DX25
Other diseases and obstruction OF BILE DUCT Adhesions of bile duct [any] Atrophy of bile duct [any] Cyst of bile duct [any] Hypertrophy of bile duct [any] Stasis of bile duct [any] Ulcer of bile duct [any] Bile duct obstruction and jaundice NOS 5762 (bile duct obstruction), 5769 (disease of the bile duct), 7824 (biliary atresia)	576.2, 576.8, 782.4, 576.9	DX2-DX25
Pancreatic neoplasm	156.2, 157, 157.0, 157.1, 157.2, 157.3, 157.8, 157.9	DX2-DX25
Alcohol related	291.0, 291.1, 291.2, 291.3, 291.4, 291.5, 291.81, 291.82, 291.89, 291.9, 303.00, 303.01, 303.02, 303.03, 303.90, 303.91, 303.92, 303.93, 305.00, 305.01, 305.02, 305.03, 760.71, 980.0, 357.5, 425.5, 535.30, 535.31, 571.0, 571.1, 571.2, 571.3	DX2-DX25.
History of chronic pancreatitis	577.1	DX2-DX25
TREATMENT		
Cholecystectomy	51.21, 51.22, 51.23, 51.24	PR1-PR15
Any ERCP	51.83, 51.84, 51.85, 51.86, 51.87, 51.88 – 51.88, 51.10, 51.11, 51.14, 52.13, 52.93, 52.94, 52.98, 97.05	PR1-PR15
Percutaneous biliary procedures	51.01, 51.96, 51.98	PR1-PR15
Open biliary procedures (common bile duct exploration)	51.02, 51.03, 51.04, 51.32, 51.36, 51.37, 51.39, 51.41, 51.43, 51.51, 51.59, 51.63, 51.64, 51.69, 51.71, 51.79	PR1-PR15
Respiratory intubation and mechanical ventilation	93.90, 96.01, 96.02, 96.03, 96.04, 96.05, 96.70, 96.71, 96.72	PR1 to PR15
Alcohol detoxification/rehabilitation	94.61, 94.62, 94.63, 94.64, 94.65, 94.66, 94.67, 94.68, 94.69	PR1-PR15
OUTCOME		
Acute respiratory failure	518.0, 518.81, 518.82, 518.84	DX2-DX25
Acute kidney injury	584.5, 584.6, 584.7, 584.8, 584.9, 586	DX2-DX25
Pancreatectomy	52.01, 52.09, 52.22, 52.51, 52.52, 52.59, 52.6, 52.7, 52.95, 52.96, 52.99	
Roux-en-Y (open and laparoscopic)	4438, 4439, 4431	PR1
Laparascopic gastric band	4495	PR1
Sleeve gastrectomy	4389, 4468, 4382	PR1
Cholecystectomy	5121, 5122, 5123, 5124	PR2-PR15

▶ **Appendix 2** Summary of missing data for demographic and hospital characteristics in the present analysis of Nationwide Inpatient Sample from 2007 – 2011 for 7,343 patients with a history of BRS requiring biliary intervention.

Total: 7,343	**Percent missing**
Gender	0 %
Race	9.36 %
Income	1.87 %
Type of insurance	0 %
Hospital location	1.20 %
Teaching status	1.20 %
Hospital size	1.20 %
Hospital region	0 %
Admission day	0 %



▶ **Appendix 3** Trends in the Type of Bariatric Surgery (**a**) and Frequency of Concomitant Cholecystectomies (**b**) in the Nationwide Inpatient Sample from 2005 – 2011.

▶ **Appendix 4** Demographics, etiological associations, and outcomes of patients with a history of bariatric surgery undergoing endoscopic or non-endoscopic biliary intervention: Comparison of endoscopic versus PTC versus CBDE.

Total: 7,343	**Endoscopic n = 4,482 (%)**		**PTC n = 1,692 (%)**		**CBDE n = 1,169 (%)**	
Age (mean, SD)	50.11	30.76	51.54	27.26	53.01	24.62
Gender						
▪ Male	728	16.25 %	394	23.30 %	311	26.62 %
▪ Female	3,754	83.75 %	1,298	76.70 %	858	73.38 %
Race						
▪ White	3,131	76.85 %	1,225	81.46 %	880	81.50 %
▪ Black	402	9.86 %	147	9.78 %	105	9.72 %
▪ Hispanic	396	9.71 %	102	6.80 %	65	5.98 %
▪ Other	146	3.58 %	29	1.96 %	30	2.80 %
Income (national quartile)						
▪ 1	948	21.48 %	362	22.00 %	199	17.41 %
▪ 2	1,145	25.95 %	480	29.16 %	285	24.94 %
▪ 3	1,131	25.63 %	440	26.73 %	353	30.83 %
▪ 4	1,189	26.95 %	364	22.11 %	307	26.82 %
Type of insurance						
▪ Medicare	1,129	25.19 %	497	29.39 %	336	28.70 %
▪ Medicaid	297	6.62 %	80	4.74 %	55	4.74 %
▪ Private	2,620	58.45 %	974	57.56 %	672	57.49 %
▪ Other	436	9.74 %	141	8.31 %	106	9.07 %
Hospital location						
▪ Rural	167	3.78 %	136	8.15 %	27	2.27 %
▪ Urban	4,243	96.22 %	1,536	91.85 %	1,143	97.73 %
Hospital teaching status						
▪ Nonteaching	1,835	41.61 %	902	53.93 %	495	42.30 %
▪ Teaching	2,575	58.39 %	770	46.07 %	675	57.70 %
Hospital size						
▪ Small	386	8.75 %	169	10.12 %	82	7.05 %
▪ Medium	898	20.36 %	385	23.03 %	236	20.21 %
▪ Large	3,126	70.88 %	1,118	66.85 %	851	72.74 %
Hospital region						
▪ Northeast	942	21.02 %	313	18.48 %	222	18.98 %
▪ Midwest	1,087	24.25 %	324	19.14 %	216	18.50 %
▪ South	1,321	29.48 %	644	38.05 %	414	35.38 %
▪ West	1,132	25.25 %	412	24.33 %	317	27.14 %
Weekend admission						
▪ No	3,717	82.94 %	1,400	82.74 %	931	79.61 %
▪ Yes	765	17.06 %	292	17.26 %	238	20.39 %

▶ **Appendix 4** (Continuation)

Total: 7,343	**Endoscopic n = 4,482 (%)**		**PTC n = 1,692 (%)**		**CBDE n = 1,169 (%)**	
Elixhauser comorbidity Index						
▪ < 3	2,860	63.82 %	994	58.75 %	514	43.96 %
▪ ≥ 3	1,622	36.18 %	698	41.25 %	655	56.04 %
ETIOLOGY						
Gallstone related	2,146	47.88 %	854	50.45 %	279	23.82 %
Pancreaticobiliary Neoplasm	81	1.80 %	72	4.28 %	125	10.67 %
Disease of bile duct	223	4.97 %	40	2.38 %	55	4.74 %
Bile leak, bile duct injury, biliary peritonitis	253	5.63 %	152	9.01 %	157	13.42 %
Bile duct obstruction and jaundice NOS	262	5.84 %	94	5.54 %	93	7.92 %
Stent related (changes, others)	134	2.99 %	21	1.26 %	32	2.74 %
Chronic Pancreatitis	54	1.21 %	a	0.00 %	a	0.00 %
Sphincter of Oddi dysfunction	22	0.50 %	a	0.19 %	a	0.00 %
Abdominal pain	41	0.92 %	a	0.00 %	a	0.00 %
Time to PTC/CBDE or ERCP						
▪ < 0 to 1 day	2,294	51.19 %	1,672	98.81 %	1,165	99.60 %
▪ 2 – 4 days	1,593	35.53 %	a	0.60 %	a	0.40 %
▪ 5 – 10 days	595	13.27 %	a	0.59 %	a	0.00 %
Cholecystectomy	1,697	37.86 %	1,018	60.19 %	116	9.95 %
ASSOCIATED DIAGNOSES	(DX1-DX25)					
Sepsis	184	4.10 %	132	7.80 %	171	14.60 %
Acute Pancreatitis	1,146	25.57 %	198	11.70 %	162	13.84 %
Cholangitis	532	11.87 %	210	12.40 %	178	15.19 %
OUTCOME						
Death	a	0.22 %	a	0.30 %	15	1.26 %
Length of stay ≥ 7 days	1,215	27.12 %	783	46.27 %	569	48.66 %
Length of stay	5.31	9.46	7.11	9.89	7.83	13.89
Total charges	50,664	92,279	66,873	137,658	60,624	106,082

a) The cell's value is not displayed. As per data agreements with AHRQ, researchers cannot report any statistics where the number of observations in any given cell of analyzed data is ≤ 10.

▶ **Appendix 5** Multivariate linear regression model for healthcare utilization in patients with a history of bariatric surgery undergoing biliary intervention with the addition of time period as a variable, Nationwide Inpatient Sample, 2007 – 2011.

	Length of stay			Total charges		
	Days	**95 % CI**	***P*-value**	**$**	**95 % CI**	***P*-value**
Primary procedure			< 0.0001			< 0.0001
▪ ERCP	Reference			Reference		
▪ CBDE/PTC	1.77	(1.32, 2.22)		11,885	(6,462, 17,308)	
Age	0.01	(–0.01, 0.02)	0.4191	–78	(–224, 67)	0.2912
Gender			0.7549			0.0409
▪ Male	Reference			Reference		
▪ Female	–0.08	(–0.60, 0.43)		–6,034	(–11,818, – 251)	
Hospital location			0.0365			< 0.0001
▪ Rural	Reference			Reference		
▪ Urban	0.64	(0.04, 1.23)		19,313	(13,710, 24,917)	
Hospital teaching status			0.9254			0.6763
▪ Nonteaching	Reference			Reference		
▪ Teaching	0.03	(–0.51, 0.56)		–1,409	(–8,035, 5,217)	
Hospital region			0.8802			< 0.0001
▪ Northeast	Reference			Reference		
▪ West	–0.17	(–0.86, 0.53)		14,640	(4,446, 24,834)	
▪ South	0.04	(–0.59, 0.67)		–2,360	(–11,336, 6,615)	
▪ Midwest	0.09	(–0.55, 0.73)		–7,003	(–16,173, 2,167)	
Elixhauser comorbidity Index			< 0.0001			< 0.0001
▪ < 3	Reference			Reference		
▪ ≥ 3	1.27	(0.79, 1.75)		10,306	(5,330, 15,282)	
Gallstone related	–0.79	(–1.22, – 0.36)	0.0004	–3,731	(–8,624, 1,162)	0.1348
Pancreaticobiliary neoplasm	1.55	(0.03, 3.08)	0.0459	4,032	(–7,632, 15,697)	0.4974
Bile leak, bile duct injury, biliary peritonitis	0.79	(–0.38, 1.96)	0.1867	5,770	(–6,532, 18,072)	0.3572
Chronic pancreatitis	–1.34	(–2.29, – 0.38)	0.0064	–17,281	(–35,898, 1,336)	0.0688
Time to PTC/CBDE or ERCP			< 0.0001			< 0.0001
▪ < 0 to 1 day	Reference			Reference		
▪ 2 – 4 days	1.72	(1.29, 2.15)		12,112	(7,779, 16,445)	
▪ 5 – 10 days	6.29	(5.49, 7.09)		43,714	(33,387, 54,040)	
Time period			0.7669			0.0227
▪ 2007 – 2008	Reference					
▪ 2009 – 2011	0.07	(–0.37, 0.50)		6,378	(893, 11,863)	

▶ **Appendix 6** Multivariate linear regression model for healthcare utilization in patients with a history of bariatric surgery undergoing endoscopic biliary intervention with the addition of time period as a variable, Nationwide Inpatient Sample, 2007 – 2011.

	Length of stay			Total charges		
	Days	**95 % CI**	***P*-value**	**$**	**95 % CI**	***P*-value**
Endoscopic intervention			< 0.0001			0.0078
▪ Successful	Reference			Reference		
▪ Failed	2.18	(1.16, 3.19)		14,400	(3,819, 24,981)	
Age	0.01	(–0.01, 0.03)	0.2081	145	(–21, 311)	0.0858
Race			0.7097			0.1255
▪ White	Reference			Reference		
▪ Black	–0.01	(–0.75, 0.73)		4,778	(–4,873, 14,430)	
▪ Hispanic	–0.30	(–0.96, 0.36)		8,178	(1,249, 15,107)	
▪ Other	0.37	(–0.91, 1.66)		–860	(–14,039, 12,319)	
Hospital size			0.1669			0.3426
▪ Small	Reference			Reference		
▪ Medium	0.12	(–0.49, 0.73)		3,299	(–7,999, 14,597)	
▪ Large	0.49	(–0.07, 1.05)		6,217	(–2,439, 14,873)	
Chronic pancreatitis	–0.14	(–0.80, 0.52)	0.6731	–12,795	(–34,539, 8,950)	0.2479
Time to ERCP			< 0.0001			< 0.0001
▪ < 0 to 1 day	Reference			Reference		
▪ 2 – 4 days	1.87	(1.41, 2.33)		14,894	(9,663, 20,124)	
▪ 5 – 10 days	7.16	(6.09, 8.22)		38,859	(28,422, 49,296)	
Time period			0.4483			0.0596
▪ 2007 – 2008	Reference					
▪ 2009 – 2011	0.18	(–0.29, 0.65)		5,950	(–242, 12,142)	