

## ORIGINAL ARTICLE

# Surgical management of chronic pancreatitis: current utilization in the United States

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## Abstract

**Background:** Surgical intervention is uncommon in chronic pancreatitis. Literature largely describes single institution or international experiences. This study describes US-based chronic pancreatitis surgical management.

**Methods:** Retrospective analysis of chronic pancreatitis patients in the Healthcare Cost and Utilization Project Florida State Inpatient Database 2007–2011. Patients with malignancy or congenital abnormalities were excluded. Univariate analysis using the chi-square test. The number of readmissions, inpatient length of stay and cost using Wilcoxon's signed-rank test. Multivariate analysis of surgery by logistic regression.

**Results:** Twenty-one thousand four hundred and forty-five patients with chronic pancreatitis. 10.8% (2 307) underwent surgery including 1652 cholecystectomies, 564 drainage procedures and 498 pancreatectomies. Procedures decreased from 12.1% to 8.3% over time ( $P < 0.001$ ), but intervention within 3 months increased (7.2% to 8.4%;  $P = 0.017$ ). 15.3% (3 278) had pancreatic cysts/pseudocysts and 43.4% (9 312) had diabetes. The median numbers of admissions were 2 [interquartile range (IQR) 1,5] and 3 (IQR 2,7) among non-surgical and surgical patients, respectively ( $P < 0.001$ ). Predictors of surgery were fewer co-morbidities, private insurance, and either diabetes mellitus or pancreatic cyst/pseudocyst.

**Conclusion:** Chronic pancreatitis leads to numerous inpatient readmissions, but surgical intervention only occurs in a minority of cases. Complicated patients are more likely to undergo surgery. The complexities of chronic pancreatitis management warrant early multidisciplinary evaluation and ongoing consideration of surgical and non-surgical options.

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## Background

Chronic pancreatitis is a serious and potentially debilitating condition. Patients may develop complications including chronic pain, weight loss, pancreatic endocrine or exocrine insufficiency, malignancy, intestinal obstruction, haemorrhage

and acute fluid collections.<sup>1–4</sup> The symptoms of chronic pancreatitis, and often its aetiology, can be managed medically, endoscopically and surgically.<sup>5–8</sup>

Previous work has demonstrated that surgical management of chronic pancreatitis, including extensive procedures such as a pancreatectomy, can be performed with an acceptable risk profile. Further, surgery offers more complete pain relief than endoscopic interventions with no negative effect on long-term mortality.<sup>2,9</sup> US-based practice patterns outside of large, academic institutions remain poorly characterized and the

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ongoing impact on inpatient care utilization in chronic pancreatitis patients who do or do not receive surgery is unknown.

This study examined the utilization of surgery in the inpatient management of chronic pancreatitis patients in a US-based population cared for in a broad range of inpatient centres. The timing and nature of surgical interventions, as well as the associated inpatient outcomes, were analysed.

## Patients and methods

### Design

A retrospective review of the Healthcare Cost and Utilization Project (HCUP) Florida State Inpatient Database (SID) was performed. The SID is an administrative all-payer inpatient discharge database assembled by the Agency for Healthcare Research and Quality (AHRQ) HCUP.<sup>10</sup> Patients can be followed across time and institutions through the use of a unique visit link variable. The database includes patient demographics, hospital characteristics, and admission diagnosis codes, procedure codes and charges.

Using ICD-9 diagnosis codes, all discharge records for patients greater than or equal to 18 years of age during 2007 to 2011 with the diagnosis of chronic pancreatitis (ICD-9 577.1) were identified. All subsequent inpatient admissions were linked and analysed. Patients with evidence of anatomic anomalies of the pancreas (751.7) or neoplasms of the pancreas, extrahepatic bile ducts or ampulla (156.1, 156.2, 156.8, 157, 211.6, 235.5, 230.9, 239.0) were excluded from analysis.

### Patient characteristics

Patient demographic information collected from the initial admission with coding of chronic pancreatitis included gender, age, median ZIP code income, insurance type and race. The patient comorbidity burden was calculated as an Elixhauser score, generated using the HCUP Comorbidity Software, Version 3.7.<sup>11</sup> All inpatient admissions were queried to identify chronic pancreatitis-related diagnoses for subset analysis: pancreatic cyst or pseudocyst (577.2), pancreatic steatorrhea (579.4) and diabetes mellitus (249, 250).

### Procedures

Chronic pancreatitis-related surgeries during the index or any subsequent admissions were identified by ICD-9 procedure code. Surgical procedures were divided into pancreatectomies (52.22, 52.51, 52.52, 52.53, 52.59, 52.6, 52.7), drainage procedures (52.3, 52.4, 52.96, 52.01, 52.09), sphincter-related procedures (51.82, 51.83, 81.89) and cholecystectomies (51.21, 51.22, 51.23, 51.25) (Appendix A1). Surgeries performed among all admissions as well as within 1 year of first admission and within 3 months of first admission for patients with at least 1 year of follow-up time were identified. All inpatient endoscopic interventions were identified by ICD-9 procedure codes (51.1, 51.64, 51.84, 51.85, 51.86, 51.87, 51.88, 52.13, 52.21, 52.93, 52.94, 52.97, 52.98).

### Patient outcomes

The primary outcome was the number of inpatient admissions occurring after the diagnosis of chronic pancreatitis, including the first admission. Readmissions were identified using the HCUP Supplemental Variables for revisit analyses. These provide unique visit links to allow patients to be tracked across all inpatient admissions, including those that occur at other institutions in the state.<sup>10</sup>

Other patient outcomes recorded were total inpatient length of stay (LOS) across all admissions after a chronic pancreatitis diagnosis, the number of inpatient admissions prior to any surgical intervention, inpatient death and the total cost of all inpatient care after chronic pancreatitis diagnosis. Further, post-operative complications were identified for any admission with a surgical procedure. Complications were identified using secondary diagnosis codes and included infectious, respiratory, cardiac, wound, thromboembolic and gastrointestinal complications.

### Cost

The charge the hospital billed for each admission was abstracted from the SID. To convert charge information to approximate costs, the supplemental SID HCUP Cost-to-Charge Ratio files were used.<sup>10</sup> The costs for all inpatient hospitalizations after chronic pancreatitis diagnosis were aggregated for each patient.

### Statistical analysis

Race and payer categories with a small number of patients were collapsed into larger categories. Continuous variables, age, median ZIP income and Elixhauser score, were categorized to enhance clinical interpretability. Patient characteristics for those patients with and without chronic pancreatitis-related surgery were compared using chi-square tests. The presence of chronic pancreatitis-related diagnoses and the use of endoscopic interventions in the surgical and non-surgical groups were compared using chi-square tests.

Univariate regression modelling of the likelihood of undergoing chronic pancreatitis-related surgery was performed. A multivariate regression model predicting chronic pancreatitis-related surgery was created using all available patient predictors, including chronic pancreatitis-related diagnoses.

Median values and interquartile ranges (IQRs) were calculated for the total number of inpatient admissions, days to the surgical procedure, inpatient costs, inpatient LOS and the number of endoscopic interventions. Outcomes were compared by surgery status using Wilcoxon's signed-rank test. Surgery and endoscopic intervention rates during each time period were analysed for trends over the course of the study using the Cochran-Armitage trend test.

Owing to the broader range of indications for a cholecystectomy, compared with a pancreatectomy, sphincter-related procedures and drainage procedures, a sensitivity analysis was

performed. The likelihood of undergoing a non-cholecystectomy surgical procedure was assessed using multivariate logistic regression modelling and patient outcomes were analysed as described above.

Statistical analyses were performed using SAS statistical analysis software, version 9.3 (SAS Institute Inc., Cary, NC, USA). A *P*-value of less 0.05 was considered statistically significant for all analyses.

## Results

### Patient demographics

From 2007 to 2011, 21 445 patients experienced at least one inpatient admission owing to chronic pancreatitis. The overall population was largely white (15 2549, 71.1%), male (11 782, 54.9%), non-elderly (15 152, 70.7%), of lower ZIP-median income quartiles (14 433, 67.3%), and had Elixhauser co-morbidity scores of three or greater (13 089, 61.0%). In total, 2307 (10.8%) patients underwent a chronic pancreatitis-related surgical procedure. Patients undergoing surgery had lower Elixhauser co-morbidity scores ( $P < 0.001$ ), a higher ZIP median income quartile ( $P = 0.004$ ) and higher rates of private insurance ( $P < 0.001$ ). Patient characteristics of patients with and without surgery are included in Table 1.

Among patients without surgery, pancreatic endocrine insufficiency rate was 43.3% (8295 patients), and the rate of cysts or pseudocysts was 12.5% (2 382 patients). 1071 (5.6%) patients had both conditions. Among patients with chronic pancreatitis-related surgery, pancreatic endocrine insufficiency rate was 44.1% (1 017 patients), and the rate of cysts or pseudocysts was 38.8% (896 patients). Four hundred and twenty-three (18.3%) patients had both conditions. Pancreatic exocrine insufficiency was an uncommon inpatient diagnosis (<11 patients).

### Procedures

Two thousand three hundred and seven (10.8%) patients underwent a chronic pancreatitis-related surgical procedure. One thousand six hundred and fifty-two patients (71.6% of the surgery group, 7.7% of overall population) underwent cholecystectomies. Five hundred and sixty-four patients (24.4% of the surgery group, 2.6% of overall population) underwent drainage procedures. Four hundred and ninety-eight patients (21.6% of the surgery group, 2.3% of overall population) underwent pancreatectomies. Thirty-six patients (1.6% of the surgery group, 0.2% of overall population) underwent sphincter procedures. 82.8% of all surgical patients (1911 patients) underwent only one procedure type, whereas 329 patients (14.3%) and 56 (2.4%) underwent two procedure types or three to four procedure types, respectively.

Upon multivariate logistic regression, significant predictors of not receiving surgery were an increasing Elixhauser co-morbidity score and non-private insurance. Patients with diabetes mellitus or pancreatic cyst or pseudocyst were more likely to

**Table 1** Chronic pancreatitis patient characteristics by surgical procedure status

	No surgery n (%)	Surgery n (%)	<i>P</i> -value
Age >65 years	5645 (29.5)	648 (28.9)	0.161
Female	8660 (45.3)	1003 (43.48)	0.106
White	13 584 (71.0)	1665 (72.2)	0.233
Elixhauser			
0	966 (5.1)	225 (9.8)	<b>&lt;0.001</b>
1	2528 (13.2)	373 (16.2)	
2	3772 (19.7)	492 (21.3)	
3+	11 872 (62.0)	1 217 (52.8)	
Income quartile			
Lowest	6661 (34.8)	717 (31.1)	<b>0.004</b>
Lower Middle	6259 (32.7)	796 (34.5)	
Upper Middle	4478 (23.4)	583 (25.7)	
Highest	1740 (9.1)	211 (9.2)	
Insurance			
Medicare	8335 (43.6)	873 (37.8)	<b>&lt;0.001</b>
Medicaid	2547 (13.3)	303 (13.1)	
Private	4033 (21.1)	697 (30.2)	
Missing/Other	4223 (22.1)	434 (18.8)	
Year of first admission			
2007	4497 (23.5)	621 (26.9)	<b>&lt;0.001</b>
2008	3747 (19.6)	462 (20.0)	
2009	3702 (19.3)	475 (20.6)	
2010	3620 (18.9)	424 (18.4)	
2011	3572 (18.7)	325 (14.1)	

Bold values are statistically significant.

receive a surgical intervention. Unadjusted and adjusted odds ratios are presented in Table 2.

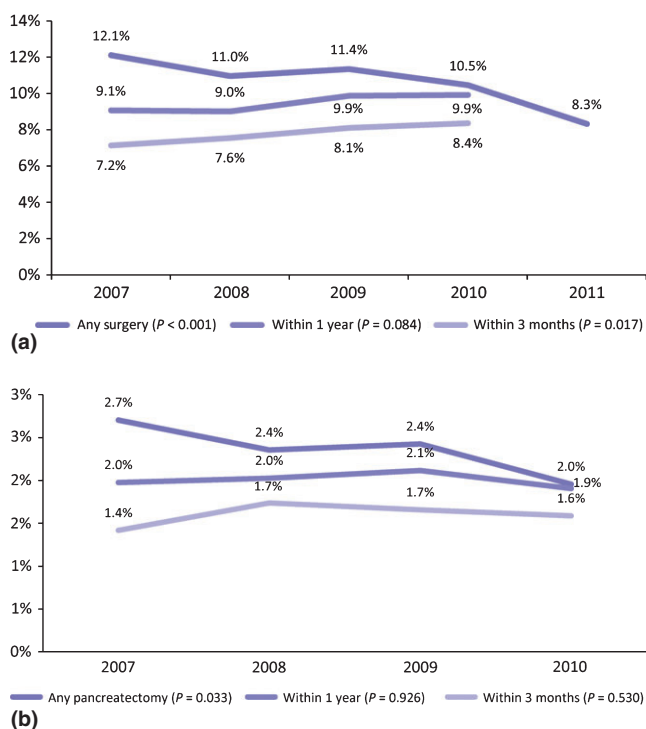
The overall rate of surgery decreased from first admission year of 2007 to 2011 ( $P < 0.001$ ), not adjusting for the length of follow-up. When restricting to surgeries performed within 1 year of first admission among those with at least 1 year follow-up there is no significant trend ( $P = 0.084$ ), but there is an increase in procedures performed within 3 months of the first inpatient admission ( $P = 0.017$ ). Rates of surgery by year of first admission are displayed in Fig. 1a. When examining a pancreatectomy only, the overall rates decreased during the study period ( $P = 0.033$ ) (Fig. 1b).

Two thousand two hundred and fifty-one patients (10.5%) underwent endoscopic interventions. Patients managed with surgery were more likely to undergo at least one endoscopic intervention [29.8% (688 patients) versus 8.2% (1563 patients);  $P < 0.001$ ]. Among those who underwent endoscopic interventions, the median number of endoscopic procedures was 1 [IQR 1,1] and ranged from 1 to more than 6 procedures. Over

**Table 2** Adjusted and unadjusted logistic regression models predicting odds of undergoing surgical procedures for chronic pancreatitis

	Unadjusted			Adjusted		
	Odds Ratio	95% Confidence Interval		Odds Ratio	95% Confidence Interval	
Female (versus male)	0.931	0.853	1.015	1.019	0.930	1.116
Elixhauser Score (versus 0)						
1	<b>0.633</b>	<b>0.528</b>	<b>0.759</b>	<b>0.617</b>	<b>0.511</b>	<b>0.745</b>
2	<b>0.560</b>	<b>0.471</b>	<b>0.666</b>	<b>0.535</b>	<b>0.446</b>	<b>0.642</b>
≥3	<b>0.440</b>	<b>0.376</b>	<b>0.515</b>	<b>0.416</b>	<b>0.351</b>	<b>0.493</b>
Low Income (versus high)	0.917	0.837	1.005	0.987	0.897	1.086
Age (in years)	<b>0.993</b>	<b>0.990</b>	<b>0.996</b>	0.998	0.994	1.001
Insurance (versus Private)						
Medicare	<b>0.606</b>	<b>0.545</b>	<b>0.674</b>	<b>0.799</b>	<b>0.703</b>	<b>0.908</b>
Medicaid	<b>0.688</b>	<b>0.596</b>	<b>0.795</b>	<b>0.786</b>	<b>0.675</b>	<b>0.915</b>
Missing/Other	<b>0.595</b>	<b>0.524</b>	<b>0.675</b>	<b>0.601</b>	<b>0.526</b>	<b>0.687</b>
White Race (versus Non-white)	0.943	0.857	1.038	1.013	0.914	1.122
Pancreatic Cyst or Pseudocyst	<b>4.467</b>	<b>4.066</b>	<b>4.908</b>	<b>4.470</b>	<b>4.060</b>	<b>4.921</b>
Diabetes Mellitus	1.031	0.945	1.124	<b>1.144</b>	<b>1.039</b>	<b>1.259</b>

Bold values are statistically significant.



**Figure 1** Rates of (a) any surgical procedure and (b) pancreatotomy for chronic pancreatitis at any time, within 1 year of first inpatient admission and within 3 months of first inpatient admission

the course of the study, the rates of endoscopic intervention decreased from 12.8% (657 patients) in 2007 to 7.8% (305 patients) in 2011 ( $P < 0.001$ ).

## Outcomes

The receipt of surgery was associated with a greater total number of admissions, a higher total inpatient LOS and a larger total inpatient cost of care (all  $P < 0.001$ ; Table 3). Prior to surgical intervention, those patients undergoing a pancreatectomy had a median number of inpatient admissions of 1 [IQR 0,2] whereas the median for those undergoing drainage procedures, cholecystectomies and sphincter-related procedures were 1 [0,3], 0 [0,2] and 2 [0,4], respectively.

Overall inpatient mortality rates were lower among those undergoing chronic pancreatitis-related surgery [6.6% (152 patients) versus 8.7% (1 670 patients),  $P = 0.0001$ ]. Inpatient mortality rates and the proportion of deaths occurring during first chronic pancreatitis-related admission are displayed in Fig. 2. Among those who underwent surgical intervention, the complication rate was 29.8% (688 patients). Complication rates were 46.4% (231 patients) for a pancreatectomy, 34.9% (197 patients) for drainage procedures, 30.6% (11 patients) for sphincter procedures and 26.7% (441 patients) for a cholecystectomy. The complication rate for those undergoing endoscopic interventions was 10.0% (224 patients). Over time, the rates of post-operative complications remained stable ( $P = 0.651$ ).

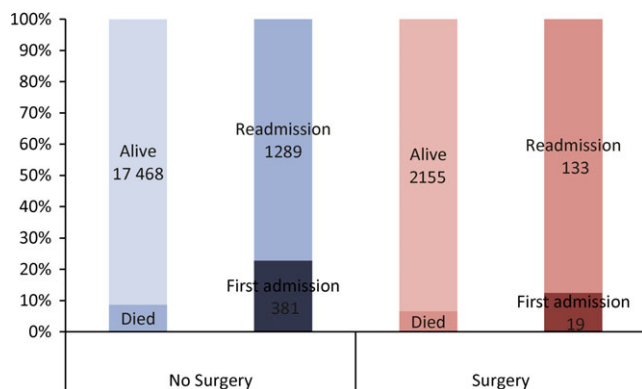
## Sensitivity analysis

With the exclusion of cholecystectomy, the overall rate of surgical procedures decreased to 4.6% (975 patients). Among this population, 93.0% (907 patients) had at least one chronic pancreatitis-related diagnosis, including 709 (72.7%) with a pancreatic cyst or pseudocyst. The majority (74.6%) of cases were performed emergently and the overall rate of surgeries

**Table 3** Admission patterns and outcomes for chronic pancreatitis patients undergoing and not undergoing surgery

	No Surgery		Surgery		P-value
	Median	[IQR]	Median	[IQR]	
Inpatient Admissions	2	[1, 5]	3	[2, 7]	<0.001
Total Inpatient LOS (days)	13	[5, 30]	24	[10, 52]	<0.001
Total Inpatient Cost (US\$)	\$20 694	[\$8849, \$49 653]	\$45 072	[\$20 700, \$90 965]	<0.001

IQR, interquartile range; LOS, length of stay.



**Figure 2** Inpatient mortality among all inpatient admissions and during the first inpatient admission for chronic pancreatitis patients who did and did not undergo surgery

decreased over the study period from 4.9% (253 patients) in 2007 to 3.8% (146 patients) in 2011 ( $P = 0.005$ ). Upon multivariate modelling, significant predictors of undergoing a surgery other than a cholecystectomy were the presence of a pancreatic cyst or pseudocyst [odds ratio (OR) 18.229; 95% confidence interval (CI) 15.705, 21.159] and the presence of diabetes mellitus (OR 1.314; 95% CI 1.135, 1.523). Higher Elixhauser co-morbidity scores and increasing age were associated with a decreased likelihood of undergoing surgery. The median total LOS was 32 days (IQR 16, 59) and the median total cost of care was \$59 947 (IQR \$33 980, \$105 543). Seventy-two patients (7.4%) died during the study period.

## Discussion

This study determined that in a large, diverse US state the minority of chronic pancreatitis patients undergo surgery. Those who receive surgery are more likely also to be diagnosed with diabetes mellitus and have an ICD-9 diagnosis code of either pancreatic cysts or pseudocysts. When excluding cholecystectomy, pancreatic cyst or pseudocyst is an extremely strong predictor of surgical management. Patients with a large number of co-morbid conditions and non-private insurance are less likely to undergo surgery. Those patients who undergo surgery have higher admission rates, longer total inpatient LOSs and higher total inpatient costs of care, but similar

mortality rates compared with those patients who do not undergo surgery. While the overall use of surgery has decreased across the study period, the rate of early surgery, performed within 3 months of first inpatient chronic pancreatitis admission, has increased. The use of endoscopic interventions has decreased over time but is more common in patients who receive surgery.

Surgical management for chronic pancreatitis can produce sustained relief of pain and restore quality of life. The poor health of many chronic pancreatitis patients suggests operative intervention may only be appropriate in a highly select population.<sup>2,12–15</sup> However, in-hospital mortality rates are significantly lower for patients undergoing resection for pancreatitis compared with malignant neoplasm, suggesting pancreatectomy for chronic pancreatitis is an acceptably safe procedure.<sup>16</sup> Similarly, post-operative morbidity rates are acceptable given the extensive nature of these procedures.<sup>17</sup> Surgical management offers more definitive relief of pain and resolution of biliary obstruction than endoscopic management.<sup>7,9,18,19</sup> Further, surgical management of pancreatic pseudocysts may reduce inpatient morbidity compared with percutaneous management and may reduce the risk of pancreatic cancer development.<sup>20,21</sup>

The timing of the operative management of chronic pancreatitis remains controversial.<sup>22</sup> Multiple studies suggest that surgical intervention before the start of opioid dependence may be beneficial.<sup>23,24</sup> While the ESCAPE trial aims to address definitively the choice between a step-up approach versus early surgery, recent retrospective analyses suggest earlier surgical intervention improves patient symptoms.<sup>22,25</sup> In our recent systematic review and meta-analysis, patients who received early surgery had an increased likelihood of complete post-operative pain relief and a reduced risk of pancreatic insufficiency when compared with those undergoing late surgery.<sup>26</sup>

The vast majority of studies addressing the use of surgery in chronic pancreatitis compare patients treated at high-volume, academic centres. In this study, it is demonstrated that at a population level surgery is uncommonly deployed in the management of chronic pancreatitis. Those who undergo surgery place a greater burden on the inpatient care system, although it is not clear whether this reflects a higher severity of disease in this population or adverse effects of large operative interventions. Surgical intervention is not evenly deployed across all

patient populations as patients with private insurance are more likely to receive surgical management.

Our analysis is a retrospective review, so the use of surgery is not random. The sickest patients may not survive to surgery, whereas patients with a more severe disease requiring more frequent, lengthy inpatient hospitalizations may be more likely to receive surgery. Further, the utilization of an administrative database presents several limitations. Clinical information, including pain scores and disease severity, is lacking, and data are subject to miscoding. The single ICD-9 diagnosis of code for both pancreatic cysts and pseudocysts prevents identification of resections performed for potential neoplasms compared with those performed for other CP-related indications. Additionally, some clinical diagnoses, such as steatorrhea, may be unreported in the inpatient setting. Physician identity and specialty cannot be established using the SID, so we are unable to assess the role of multidisciplinary care teams or how physician specialty influences time to receipt of surgery. Finally, the SID only captures inpatient care, so outpatient procedures, particularly endoscopy, are not reflected in the present results.

Despite these limitations, this study represents the largest population-based analysis of surgical practices in the setting of chronic pancreatitis. It provides longitudinal data about a large group of subjects who receive care at non-academic medical centres and possibly multiple facilities. Additionally, this population-level data will provide a broader context for the pending ESCAPE trial findings, given the study enrollment limitations of randomized controlled trials.<sup>22</sup>

Chronic pancreatitis can lead to persistent pain and pancreatic insufficiency among other devastating outcomes. Surgical management is an infrequently utilized, viable management strategy that can be associated with improved long-term outcomes. While surgically managed patients have an increased burden on the inpatient care system, this may reflect the current selection of patients with severe disease. Literature suggests that earlier surgical intervention may reduce the need for prolonged opioid pain management and our findings suggest a shift towards earlier surgical intervention over time. Additional prospective studies of the surgical management of chronic pancreatitis are needed to determine optimal timing and patient selection to improve patient outcomes and reduce utilization of inpatient healthcare services.

#### Author contributions

Study design: Bliss, Yang, Eskander, deGeus, Callery, Kent, Moser, Freedman, Tseng. Data acquisition and analysis: Bliss, Yang, Eskander, Tseng. Critical review of manuscript: Bliss, Eskander, deGeus, Callery, Kent, Moser, Freedman, Tseng.

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#### Conflicts of interest

None declared.

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## Appendix A1

Category	ICD-9 Procedure Code	Procedure
Cholecystectomies	51.21	Other partial cholecystectomy
	51.22	Cholecystectomy
	51.23	Laparoscopic cholecystectomy
	51.25	Laparoscopic partial cholecystectomy
Drainage Procedures	43.0	Gastrostomy
	43.19	Other gastrostomy
	46.32	Percutaneous jejunostomy
	46.39	Other enterostomy
	52.01	Drainage of pancreatic cyst by catheter
	52.09	Other pancreatotomy
	52.3	Marsupialization of pancreatic cyst
	52.4	Internal drainage of pancreatic cyst
52.96	Anastomosis of pancreas	

## Appendix Continued

Category	ICD-9 Procedure Code	Procedure
Endoscopic Procedures	51.1	Endoscopic retrograde cholangiopancreatography (ERCP)
	51.64	Endoscopic excision or destruction of lesion of biliary ducts or sphincter of Oddi
	51.84	Endoscopic dilation of ampulla and biliary duct
	51.85	Endoscopic sphincterotomy and papillotomy
	51.86	Endoscopic insertion of nasobiliary drainage tube
	51.87	Endoscopic insertion of stent (tube) into bile duct
	51.88	Endoscopic removal of stone(s) from biliary tract
	52.13	Endoscopic retrograde pancreatography (ERP)
	52.21	Endoscopic excision or destruction of lesion or tissue of pancreatic duct
	52.93	Endoscopic insertion of stent (tube) into pancreatic duct
	52.94	Endoscopic removal of stone(s) from pancreatic duct
	52.97	Endoscopic insertion of nasopancreatic drainage tube
	52.98	Endoscopic dilation of pancreatic duct
	Pancreatectomies	52.22
52.51		Proximal pancreatectomy
52.52		Distal pancreatectomy
52.53		Radical subtotal pancreatectomy
52.59		Other partial pancreatectomy
52.6		Total pancreatectomy
52.7		Radical pancreaticoduodenectomy
Sphincter-related procedures	51.82	Pancreatic sphincterotomy
	51.83	Pancreatic sphincteroplasty
	81.89	Other operations on sphincter of Oddi