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Original Article

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Readmissions After Biliary Acute Pancreatitis: Analysis of the Nationwide Readmissions Database

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Abstract

Background: Acute pancreatitis is a common inflammatory condition that involves the pancreas. Gallstones and alcohol are the most common etiologies in the USA. Cholecystectomy is the cornerstone procedure in the management of biliary acute pancreatitis (BAP). In this study, we examined the causes and predictors of readmissions following BAP based on the procedure performed.

Methods: Using the Nationwide Readmissions Database (NRD) and the International Classification of Diseases, Tenth Revision, Clinical Modification/Procedure Coding System (ICD10-CM/PCS), we retrospectively studied BAP hospitalizations (2016 - 2018). The first hospitalization within the year was marked as index hospitalization. Index hospitalizations were categorized based on whether an endoscopic retrograde cholangiopancreatography (ERCP) and/or a cholecystectomy was performed into no procedure group, ERCP group, cholecystectomy group, and both procedures group. We subsequently identified readmissions within 30 days. Using this categorization, we studied reasons, rates, and predictors of readmissions.

Results: A total of 127,318 index hospitalizations were included. The cholecystectomy group constituted the largest share of this cohort (43.5%). Using the no procedure group as a reference, analysis of the outcomes showed that the cholecystectomy group had the lowest inpatient mortality (adjusted odds ratio (aOR): 0.18, P < 0.001), while both procedures group had the highest total hospital charges (adjusted mean difference (aMD): 42,249, P < 0.001). Acute pancreatitis without necrosis or infection was the most frequent principal diagnosis for readmission (18.7%). Analysis of readmission predictors showed that both procedures group had the lowest risk for readmission (adjusted hazard ratio (aHR): 0.40, P < 0.001). Females were less likely to be readmitted compared to males (aHR: 0.82, P < 0.001) and elderly were less likely to be readmitted compared to young adults (aHR: 0.82, P < 0.001). Patients discharged against medical advice were more likely to be readmitted (aHR: 1.76, P < 0.001).

Conclusion: Undergoing both ERCP and cholecystectomy for BAP resulted in significantly higher hospital charges with no additional mortality benefit. However, it decreased the readmission risk significantly. Acute pancreatitis without necrosis or infection was the most frequent reason for readmissions.

Keywords: Biliary acute pancreatitis; Readmission; Nationwide Readmissions Database; ERCP; Cholecystectomy

Introduction

Acute pancreatitis remains one of the most common gastrointestinal diagnoses requiring hospitalization [1, 2]. The estimated global incidence for acute pancreatitis is 33.7 cases per 100,000 person-years with 1.6 deaths per 100,000 person-years [3]. The incidence of acute pancreatitis has been increasing in North America and Europe [4, 5]. Gallstones and alcohol are the most common causes of acute pancreatitis. The proportion of cases attributed to gallstones and alcohol varied among studied countries [4, 6].

The incidence of recurrent biliary acute pancreatitis (BAP) varies widely, from 0% to 57%, depending on the population studied, the initial treatment, and the follow-up time [7]. Current guidelines recommend cholecystectomy during the initial admission in patients with BAP [8, 9]. Unfortunately, many studies showed nonadherence to the current guidelines in the management of these patients [10-13].

In this study, we aimed to provide an additional insight regarding the predictors and causes of readmissions after an initial episode of BAP based on the procedure performed. In addition, we highlight the demographics of patients and treating hospitals for initial hospitalizations and readmissions.

Materials and Methods

Design and data source

This was an observational retrospective study involving hos-

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pitalizations with BAP in the USA from 2016 to 2018. We extracted data from the Nationwide Readmissions Database (NRD) for the years 2016, 2017, and 2018. The NRD is the largest publicly available readmission database in the USA, drawn from the Agency for Healthcare Research and Quality (AHRQ), Healthcare Cost and Utilization Project (HCUP), and State Inpatient Databases (SID) [14]. The NRD is an annual file constructed using one calendar year of discharge data. Discharge weights were calculated using post-stratification on hospital characteristics (census region, urban-rural location, teaching status, bed size, and hospital control) and patient characteristics (sex and five age groups (0, 1 - 17, 18 - 44, 45 - 64, and 65 and older)). The NRD 2018 contains discharge data from 28 geographically dispersed states accounting for 59.7% of the total USA population and 58.7% of all USA hospitalizations. It comprises both patient and hospital-level information. Up to 40 discharge diagnoses and 25 procedures are collected for each patient using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD10-CM/PCS). Diagnoses are classified as a principal diagnosis, which is the reason for hospitalization, and secondary diagnosis which is any other discharge diagnosis. Hospitals are stratified according to ownership control, the number of beds, teaching status, urban/rural location, and geographic region. The NRD allows for weighted analysis to obtain 100% of the USA hospitalizations within a given year [15]. This manuscript conforms with the STROBE statement for reporting observational studies.

Study population and variables

The study involved hospitalizations with a principal diagnosis of BAP using the ICD-10 code "K85.1x". Hospitalizations involving patients under the age of 18 were excluded. We excluded December hospitalizations for each year due to the lack of an adjoining 30-day period to assess 30-day readmissions. The first hospitalization within the year was marked as the index admission. Using the index admission and unique identifiers available in the NRD, we identified one subsequent hospitalization within 30 days, and this was marked as readmission. Elective and traumatic admissions were excluded.

Index hospitalizations were stratified into four procedural groups as follows. Group 1 included patients who did not have endoscopic retrograde cholangiopancreatography (ERCP) or cholecystectomy (no procedure group), group 2 included patients who had only ERCP (ERCP group), group 3 had only cholecystectomy (cholecystectomy group), and group 4 had both ERCP and cholecystectomy (both procedures group). The procedural codes for ERCP and cholecystectomy were obtained from HCUP validated procedure classes that were refined for the ICD-10-PCS software [16].

The NRD contains variables on patient demographics, including age, sex, median household income (MHOI) by zip code (income quartiles referred to patients as 1 - low income, 2 - middle income, 3 - upper middle income, 4 - high income), and primary payer. It also contains hospital-specific variables including bed size, teaching status, and location. We assessed the comorbidity burden using Sundararajan's adaptation of the modified Deyo's Charlson Comorbidity Index (CCI). The CCI contains a list of comorbidities with a weighted score assigned based on the relative risk of 1-year mortality. Consequently, the sum of the index score is an indicator of disease burden and a good estimator of mortality. Deyo's modification groups CCI into four groups in increasing risk for mortality. It has been adapted to population-based database research [17, 18]. A score of > 3 has about a 25% 10-year mortality, while a score of 2 or 1 has a 10% and 4% 10-year mortality, respectively. This cutoff point was chosen as a mean of assessment of increased risk of mortality [19]. The CCI also predicts healthcare cost utilization [20].

Outcome measures

We compared the demographic data of hospitalizations and readmissions using the no procedure (group 1) as the reference group. Outcomes included the most frequent reasons for readmissions and the rates of readmissions stratified based on procedural group during the index hospitalization. Other outcomes included assessment of index hospitalizations mortality, mean length of hospital stay (LOS), total hospital charges (THC), and independent predictors of readmissions for each procedural group. We adjusted the THC for inflation using the Medical Expenditure Panel Survey index for hospital care, with 2018 as the reference point [21].

Statistical analysis

We analyzed the data using Stata® Version 16 software (StataCorp, Texas, USA). We conducted all the analysis using the weighted samples for national estimates in accordance with HCUP regulations for using the NRD [15]. Age was grouped as 18 - 44 years representing young adults, 45 - 64 years representing middle-aged adults, and above 65 years representing elderly. We calculated comorbidities as proportions of the cohorts and used the Chi-square test to compare characteristics among the procedural groups for both index hospitalizations and readmissions. We used univariable regression to compare readmission mortality, LOS, and THC. We employed a univariable pre-screening model to identify variables associated with readmissions to obtain the independent predictors of 30-day readmissions. We screened age categories, sex, hospital location, hospital teaching status, hospital bed size, MHOI, and the 17 CCI comorbidities. The use of CCI comorbidities is similar to the validated model employed by Moore et al for assessing comorbidity burden in administrative databases [22]. We included those variables having a P-value less than 0.2 in the final multivariable regression analysis. Subsequently, we ran a multivariable Cox regression analysis to identify independent predictors of readmissions with P-values < 0.05 set as the threshold for statistical significance. This model included the procedural group, sex, age categories, discharge against medical advice

status, primary payer, MHOI, hospital teaching status, hospital volume in quintiles, and all the 17 CCI comorbidities excluding mild liver disease.

Ethical considerations

The NRD database lacks patient and hospital level identifiers. This study, therefore, did not require Cook County Health Institutional Review Board approval or informed consents.

Results

Analysis of demographics

We included a total of 127,318 index hospitalizations with BAP as the primary diagnosis for admission in our study (Table 1). The cholecystectomy group included 55,359 hospitalizations, constituting the largest share of the cohort (43.5%). In contrast, the ERCP group included 13,802 hospitalizations (10.8%). A total of 15,523 hospitalizations (12.2%) included both procedures, while 42,633 hospitalizations had no procedure done (33.5%). In the four groups, most hospitalizations were for females ($P < 0.001$). Analysis of groups' mean age showed that patients in the ERCP group had a mean age of 63.9 (standard deviation (SD): 18.6), which was the highest across the studied groups ($P < 0.001$). In contrast, the cholecystectomy group had a mean age of 53.9 (SD: 19.5), which was the lowest compared to all groups ($P < 0.001$). Consistent across the studied cohort, the highest proportion of patients had a CCI score of 0 ($P < 0.001$). In all four groups, diabetes mellitus (DM) without complications was the most frequent comorbidity ($P < 0.001$). Medicare was the most frequent primary payer for the no procedure group (49.8%), ERCP group (55.4%), and both procedures group (41.6%). However, private insurance was the most frequent primary payer for the cholecystectomy group (40.1%). Analysis of the MHOI showed that most patients were in the lower- and middle-income quartiles ($P < 0.001$). The highest proportion of patients across the studied groups were treated in metropolitan teaching hospitals ($P < 0.001$) with large bed size ($P < 0.001$).

Analysis of outcomes

Among patients in the no procedure group, 1.6% died during the index hospitalization (Table 2). This was higher compared to cholecystectomy group, in which 0.2% died during hospitalization (adjusted odds ratio (aOR): 0.18, $P < 0.001$), both procedures group, in which 0.3% died (aOR: 0.23, $P < 0.001$), and the ERCP group (this finding did not reach statistical significance ($P = 0.123$)). The mean LOS for the no procedure group was 4.7 days (standard error (SE): 0.05), which was lower than all other groups ($P < 0.001$). On average, the ERCP group stayed longer than other groups with a mean LOS of 6.1 days (SE: 0.10, $P < 0.001$). Examination of hospital charges showed that compared to other groups, both procedures group had the highest mean THC at USD83,593 (SE: 1,231.6, $P < 0.001$).

30-day readmission analysis

We included a total of 12,568 readmissions in our study. As shown in Table 3, acute pancreatitis without necrosis or infection was the most frequent principal diagnosis accounting for 18.7% of all readmissions (10.7% were biliary and 8.0% were unspecified), followed by sepsis with unspecified organism (6.2%). As shown in Table 4, the no procedure and the ERCP groups had the highest readmission rates; 15.0% and 13.0% of the index hospitalizations in each group were readmitted, respectively. On the other hand, the cholecystectomy and both procedures groups had the lowest readmission rates (6.5% and 5.8%, respectively). The readmitted cohort in the no procedure group had a mean age of 61.5 (SD: 19.0), which was the highest across all groups ($P < 0.001$). In the ERCP and cholecystectomy groups, DM without complications was the most frequent comorbidity (18.6% and 18.5%, respectively, $P = 0.049$). Renal disease accounted for 20.5% of the studied comorbidities in the no procedure group ($P < 0.001$). Chronic pulmonary disease was the most frequent comorbidity in patients who underwent both procedures; however, this observation did not reach statistical significance ($P = 0.186$). In all four groups, Medicare was the most frequent primary payer ($P < 0.001$). Consistent with the index hospitalizations, readmissions took place most frequently in metropolitan teaching hospitals ($P < 0.001$(, with large bed size ($P = 0.002$). These findings were observed in all groups.

We performed multivariate analysis for predictors of readmission (Table 5). Using the no procedure group as a reference, aHR for readmission in the ERCP group was 0.86 ($P < 0.001$), while the cholecystectomy and both procedures groups had aHR of 0.47 and 0.40, respectively ($P < 0.001$). Females had an aHR of 0.82 for readmission when compared to males ($P < 0.001$). Elderly patients were less likely to be readmitted compared to young adults (aHR: 0.82, $P < 0.001$). Patients who were discharged against medical advised were more likely to be readmitted (aHR: 1.76, $P < 0.001$). Private insurance patients were less likely to be readmitted compared to Medicaid patients (aHR: 0.71, $P < 0.001$). The highest income patients were less likely to be readmitted when compared to the lowest income (aHR: 0.89, $P = 0.006$). Comorbidities that were associated with increased risk for readmission were congestive heart failure (aHR: 1.26, $P < 0.001$), cerebrovascular disease (aHR: 1.27, $P = 0.003$), chronic pulmonary disease (aHR: 1.22, $P < 0.001$), rheumatologic disease (aHR: 1.33, $P < 0.001$), peptic ulcer disease (aHR: 1.51, $P < 0.001$), diabetes without complications (aHR: 1.15, $P < 0.001$), diabetes with complications (aHR: 1.10, $P < 0.001$), renal disease (aHR: 1.18, $P < 0.001$), any malignancy (aHR: 1.22, $P < 0.001$), moderate or severe liver disease (aHR: 1.11, $P < 0.001$), metastatic solid tumor (aHR: 1.12, $P < 0.001$), and human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) (aHR: 1.09, $P = 0.006$).

Table 1. Demographics and Hospital Characteristics of Index Hospitalizations

Variable	No procedure	Only ERCP	Only cholecystectomy	ERCP and cholecystectomy	P-value
Number of hospitalizations	42,633 (33.5%)	13,802 (10.8%)	55,359 (43.5%)	15,523 (12.2%)	
Mean age (years ± SD)	60.9 ± 19.9	63.9 ± 18.6	53.9 ± 19.5	56.5 ± 19.7	< 0.001
Age categories (%)					< 0.001
Young adults	21.1	15.9	32.2	28.2	
Middle-aged	32.7	30.7	35.6	32.4	
Elderly	46.2	53.5	32.2	39.4	
Female (%)	55.9	55.8	62.6	58.7	< 0.001
CCI score (%)					< 0.001
0	39.8	39.1	53.1	51.6	
1	25.0	25.7	25.1	24.4	
2	13.8	13.2	10.7	11.3	
≥ 3	21.5	22.0	11.1	12.7	
Mean CCI	1.5	1.5	0.9	1.0	
Primary payer (%)					< 0.001
Medicare	49.8	55.4	35.4	41.6	
Medicaid	15.8	11.8	18.6	17.1	
Private insurance	30.0	29.1	40.1	35.9	
Self-pay	4.4	3.6	6.0	5.5	
MHOI quartile (%)					< 0.001
1	26.5	24.4	28.4	27.4	
2	27.8	29.7	27.8	27.4	
3	25.0	25.7	25.4	25.7	
4	20.6	20.2	18.4	19.5	
Comorbidities (%)					
Myocardial infarction	6.6	6.7	3.6	3.8	< 0.001
Congestive heart failure	12.2	12.8	6.0	7.0	< 0.001
Peripheral vascular disease	6.5	6.8	3.5	3.9	< 0.001
Cerebrovascular disease	2.5	2.3	1.4	1.7	< 0.001
Dementia	5.3	4.9	1.9	2.0	< 0.001
Chronic pulmonary disease	15.9	16.8	13.5	13.0	< 0.001
Rheumatologic disease	2.2	2.1	1.6	2.0	< 0.001
Peptic ulcer disease	1.5	3.6	0.9	2.9	< 0.001
Mild liver disease	11.9	9.9	11.7	11.2	< 0.001
Diabetes without complications	18.4	17.2	15.6	14.6	< 0.001
Diabetes with complications	7.8	8.1	5.1	5.4	< 0.001
Hemiplegia/paraplegia	0.3	0.4	0.3	0.4	0.357
Renal disease	14.0	14.4	7.7	8.9	< 0.001
Any malignancy	2.7	2.7	1.4	1.8	< 0.001
Moderate or severe liver disease	2.0	2.1	0.3	0.6	< 0.001
Metastatic solid tumor	1.0	1.4	0.4	0.4	< 0.001
HIV/AIDS	0.3	0.1	0.2	0.1	0.002
Hospital characteristics					

Table 1. Demographics and Hospital Characteristics of Index Hospitalizations - *(continued)*

Variable	No procedure	Only ERCP	Only cholecystectomy	ERCP and cholecystectomy	P-value
Hospital bed size (%)					< 0.001
Small	21.2	13.7	18.6	13.9	
Medium	29.5	29.3	29.0	28.3	
Large	49.4	57.0	52.4	57.8	
Hospital teaching status and location (%)					< 0.001
Metropolitan non-teaching	26.0	22.7	27.2	25.8	
Metropolitan teaching	63.2	73.8	64.2	70.8	
Non-metropolitan	10.9	3.5	8.6	3.4	

CCI: Charlson comorbidity index; ERCP: endoscopic retrograde cholangiopancreatography; MHOI: median household income for ZIP code; SD: standard deviation from the mean.

Table 2. Outcomes of Index Hospitalizations

Variable	No procedure	Only ERCP	Only cholecystectomy	ERCP and cholecystectomy
Mortality				
Mortality rate (%)	1.6	1.4	0.2	0.3
aOR (95% CI)	-	0.82 (0.63 - 1.06)	0.18 (0.13 - 0.24)	0.23 (0.15 - 0.36)
P-value	-	0.123	< 0.001	< 0.001
LOS				
Mean LOS in days (SE)	4.7 (0.05)	6.1 (0.10)	5.0 (0.03)	5.9 (0.06)
aMD (95% CI)	-	1.31 (1.10 - 1.52)	0.45 (0.34 - 0.56)	1.31 (1.16 - 1.47)
P-value	-	< 0.001	< 0.001	< 0.001
Hospital charges				
Mean THC in USD (SE)	42,438 (719.2)	69,194 (1,516.4)	61,845 (639.7)	83,593 (1,231.6)
aMD (95% CI)	-	25,999 (23,036 - 28,962)	21,512 (19,981 - 23,043)	42,249 (39,744 - 44,753)
P-value	-	< 0.001	< 0.001	< 0.001

aMD: adjusted mean difference for age categories and sex relative to no procedure group; aOR: adjusted odds ratio for age categories and sex relative no procedure group; CI: confidence interval; ERCP: endoscopic retrograde cholangiopancreatography; LOS: length of hospital stay; SE: standard error; THC: total hospital charge; USD: United States dollar.

Table 3. Most Common Principal Diagnoses for Readmissions

Principal readmission diagnosis	Proportion (%)
Biliary acute pancreatitis without necrosis or infection	10.7
Acute pancreatitis without necrosis or infection, unspecified	8.0
Sepsis, unspecified organism	6.2
Pseudocyst of pancreas	2.8
Calculus of gallbladder with acute cholecystitis without obstruction	2.0
Other postprocedural complications and disorders of the digestive system	1.7
Acute kidney failure, unspecified	1.5
Acute pancreatitis with uninfected necrosis, unspecified	1.5
Biliary acute pancreatitis with uninfected necrosis	1.4
Hypertensive heart and chronic kidney disease with heart failure and stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease	1.0

Table 4. Demographics and Hospital Characteristics of Readmissions

Variable	No procedure	Only ERCP	Only cholecystectomy	ERCP and cholecystectomy	P-value
Readmission[a] (%)	15.0	13.0	6.5	5.8	
Mean age (years ± SD)	61.5 ± 19.0	57.7 ± 19.7	57.8 ± 19.5	57.2 ± 19.7	< 0.001
Age categories (%)					< 0.001
Young adults	19.0	25.9	25.0	27.2	
Middle-aged	33.4	34.1	34.7	31.4	
Elderly	47.6	40.2	40.3	41.4	
Female (%)	51.7	55.5	51.9	52.3	0.355
CCI score (%)					< 0.001
0	31.2	41.7	42.3	46.8	
1	22.1	23.1	24.3	21.9	
2	14.2	12.5	13.5	15.2	
≥ 3	32.5	22.7	20.0	16.1	
Mean CCI	2.0	1.5	1.4	1.2	< 0.001
Primary payer (%)					< 0.001
Medicare	54.3	45.2	46.5	48.6	
Medicaid	16.2	19.8	17.5	17.2	
Private insurance	25.4	31.6	31.1	30.5	
Self-pay	4.1	3.4	4.8	3.8	
MHOI quartile (%)					0.074
1	29.5	27.2	24.0	28.4	
2	28.8	28.0	29.8	30.8	
3	24.4	25.0	25.7	25.1	
4	17.3	19.9	20.5	15.7	
Comorbidities (%)					
Myocardial infarction	8.5	4.9	5.3	6.1	< 0.001
Congestive heart failure	19.4	12.0	11.0	10.1	< 0.001
Peripheral vascular disease	7.0	4.5	5.5	3.5	0.022
Cerebrovascular disease	4.4	1.8	2.4	1.3	< 0.001
Dementia	5.1	3.6	2.5	3.1	0.003
Chronic pulmonary disease	18.8	16.3	17.1	15.2	0.186
Rheumatologic disease	2.5	2.3	2.2	2.8	0.946
Peptic ulcer disease	3.7	4.2	1.5	3.3	0.004
Mild liver disease	7.8	7.5	9.9	10.9	0.109
Diabetes without complications	20.0	18.6	18.5	12.5	0.049
Diabetes with complications	12.2	6.8	7.2	5.2	< 0.001
Hemiplegia/paraplegia	1.0	0.1	0.4	0.8	0.029
Renal disease	20.5	12.4	13.6	11.8	< 0.001
Any malignancy	4.6	6.9	3.7	1.9	0.008
Moderate or severe liver disease	3.1	3.8	1.4	2.2	0.019
Metastatic solid tumor	2.6	1.1	1.3	0.8	0.004
HIV/AIDS	0.5	0.4	0.0	0.3	0.236

Table 4. Demographics and Hospital Characteristics of Readmissions - *(continued)*

Variable	No procedure	Only ERCP	Only cholecystectomy	ERCP and cholecystectomy	P-value
Hospital characteristics					
Hospital bed size (%)					0.002
Small	16.5	10.3	17.7	15.6	
Medium	26.8	27.1	28.1	28.7	
Large	56.7	62.7	54.2	55.7	
Hospital teaching status and location (%)					< 0.001
Metropolitan non-teaching	22.8	20.4	24.3	21.2	
Metropolitan teaching	69.3	76.1	68.2	75.1	
Non-metropolitan	7.9	3.5	7.5	3.7	

[a]Percentage of readmissions for each procedural group after index hospitalization. CCI: Charlson Comorbidity Index; ERCP: endoscopic retrograde cholangiopancreatography; MHOI: median household income for ZIP code; SD: standard deviation from the mean; HIV: human immunodeficiency virus; AIDS: acquired immune deficiency syndrome.

Table 5. Predictors of Readmissions

Variable	aHR	95% confidence interval	P-value
ERCP only*[a]	0.86	0.80 - 0.93	< 0.001
Cholecystectomy only[a]	0.47	0.44 - 0.50	< 0.001
ERCP + cholecystectomy[a]	0.40	0.36 - 0.44	< 0.001
Female[b]	0.82	0.78 - 0.87	< 0.001
Middle-aged[c]	1.04	0.96 - 1.12	0.331
Elderly[c]	0.82	0.74 - 0.91	< 0.001
Highest income quartile[d]	0.89	0.82 - 0.97	0.006
Private insurance[e]	0.71	0.65 - 0.78	< 0.001
Myocardial infarction	0.98	0.88 - 1.09	0.683
Congestive heart failure	1.26	1.17 - 1.37	< 0.001
Peripheral vascular disease	1.03	0.92 - 1.14	0.661
Cerebrovascular disease	1.27	1.08 - 1.48	0.003
Dementia	0.92	0.81 - 1.05	0.242
Chronic pulmonary disease	1.22	1.14 - 1.31	< 0.001
Rheumatologic disease	1.33	1.13 - 1.55	< 0.001
Peptic ulcer disease	1.51	1.28 - 1.78	< 0.001
Diabetes without complications	1.15	1.07 - 1.23	< 0.001
Diabetes with complications	1.10	1.05 - 1.15	< 0.001
Hemiplegia/paraplegia	1.15	0.94 - 1.41	0.173
Renal disease	1.18	1.13 - 1.23	< 0.001
Any malignancy	1.22	1.14 - 1.32	< 0.001
Moderate or severe liver disease	1.11	1.05 - 1.18	< 0.001
Metastatic solid tumor	1.12	1.08 - 1.17	< 0.001
HIV/AIDS	1.09	1.03 - 1.64	0.006
Discharge against medical advice	1.76	1.51 - 2.06	< 0.001

[a]Relative to no procedure. [b]Relative to male. [c]Relative to young adults. [d]Relative to lowest income. [e]Relative to Medicare. aHR: adjusted hazard ratio; ERCP: endoscopic retrograde cholangiopancreatography; HIV: human immunodeficiency virus; AIDS: acquired immune deficiency syndrome.

Discussion

In our analysis, the largest share of index hospitalizations underwent cholecystectomy, accounting for 43.5% of the cohort. On the other hand, only a minority of them underwent both procedures (12.2%). The American Gastroenterological Association (AGA) and American College of Gastroenterology (ACG) guidelines strongly recommend cholecystectomy during the initial admission in patients with BAP. In addition, both guidelines recommend against the use of ERCP in the absence of cholangitis and biliary obstruction; however, these recommendations are based on low quality of evidence [8, 9]. The International Association of Pancreatology/American Pancreatic Association (IAP/APA) guidelines also recommend against ERCP in patients without cholangitis and biliary obstruction [23]. In a systematic review of eight randomized controlled trials, Vege et al found that mortality, multiorgan failure, single organ failure (respiratory, renal, circulatory), infected (peri) pancreatic necrosis, and total necrotizing pancreatitis were no different between patients randomized to the urgent ERCP or the conservative management groups [24]. Despite the fact that included trials attempted to exclude patients with cholangitis, marked clinical heterogeneity in adopted selection criteria/definitions limited the interpretation of these findings. Similarly, Tse et al found no evidence that early routine ERCP significantly affects mortality or local or systemic complications of pancreatitis, regardless of predicted severity [25]. Another metanalysis that involved 11 randomized controlled trials showed that the overall complications were significantly reduced in the ERCP group in severe pancreatitis patients; however, there was no statistically significant difference in mild pancreatitis group [26]. Unfortunately, many studies showed poor adherence to recommended guidelines resulting in higher mortality and costs [10-13]. In addition, there was a trend of decreasing procedures for BAP between 2010 and 2014 [27].

Gallstones are more common in females [28-31], which likely reflects the lithogenic effect of estrogen as it promotes cholesterol crystallization [32, 33]. As expected, most hospitalizations in the four studied groups were for females. Patients in the cholecystectomy and both procedures group were younger compared to the other groups. Elderly patients are at higher risk of morbidity and mortality from cholecystectomy when compared to younger patients, and they also have longer hospital stays and higher costs [34-37]. As a result, they have lower rates of laparoscopic cholecystectomy when compared to nonelderly patients [37-39].

Many studies have shown increased risk of gallstones in diabetic patients [40-44]. Possible explanations include the secretion of supersaturated bile [45] and poor gallbladder contractility [46, 47]. Interestingly, Maringhini et al found that gallbladder motility is needed to promote the expulsion of biliary sludge and stones to trigger and develop acute pancreatitis [48-50]. In our study, DM was the most frequent comorbidity in all four groups. Management of hospitalized patients can be affected by insurance and socioeconomic status, and this applies to BAP as well [51]. We found that Medicare was the primary payer for the largest proportion of hospitalizations except for the cholecystectomy group. According to the HCUP, Medicare had the largest share of total readmissions in the USA (55.9%) [52]. Private insurance was the most frequent primary payer for the cholecystectomy group. Janeway et al found that privately insured patients had higher rates of cholecystectomy compared to all other insurance types [53]. Similarly, Shmelev et al found that same-admission cholecystectomy in biliary pancreatitis was higher in privately insured patients [11].

Analysis of index hospitalizations' outcomes showed that the cholecystectomy group had the lowest mortality rates among the four groups. Previous studies showed that cholecystectomy was associated with decreased mortality in patients with BAP [10, 54]. Both procedures group had also a comparable low mortality rate, and this was consistent with the available evidence of no additional mortality benefit when ERCP was performed along with cholecystectomy as discussed above. Given the high costs of such procedures, both procedures group had the highest hospital charges, and the no procedure group had the lowest charges during index hospitalizations.

Our study showed that acute pancreatitis without necrosis or infection was the most common reason for readmission. Krishna et al found that 50% of readmissions in BAP patients were related to recurrences or acute pancreatitis-related complications [55]. Similarly, Garg et al found that recurrent acute pancreatitis was the most common reason for readmission (41.5%) in patients with acute pancreatitis [56]. These readmissions are thought to be related to exacerbation of smoldering symptoms, progression of local complications, or recurrent attacks likely related to persistence of risk factors for the index admissions [57].

Analysis of predictors of readmissions showed that undergoing both procedures carried the lowest risk for readmission compared to the other groups, a finding that is consistent with the available data [7, 58]. This observation might be related to residual stones in the biliary tree in patients who undergo cholecystectomy alone. Van Geenen et al found that intraoperative choledocholithiasis was present in 13-24% of those undergoing cholecystectomy [7]. Stone migration from the gallbladder into the common bile duct (CBD) after initial stone clearance increases the risk of recurrent pancreatitis in those who did not undergo cholecystectomy. Moreau et al found that regardless of whether patients with gallstones have had a prior attack of pancreatitis, cholecystectomy reduces the risk of acute pancreatitis to almost the same level of the general population [59].

Surprisingly, older age was associated with lower rates of readmission in our analysis, which comes consistent with the available data [56, 57, 60]. Higher mortality in elderly might have removed them from the readmission cohort. In addition, interventions in elderly might result in different outcomes when compared to the general population [61, 62]. Welbourn et al found that endoscopic sphincterotomy alone was an acceptable alternative to cholecystectomy in the prevention of further attacks of BAP in the elderly [62]. Females were less likely to be readmitted compared to males in our analysis, consistent with the available evidence [56, 57]. Studies have found that women were more likely to undergo cholecystectomy for BAP and were subsequently less likely to be readmitted for any cause [27, 63]. Yol et al found that in the context of symp-

tomatic gallbladder stones, inflammation and fibrosis are more extensive in men than in women. In addition, conversion to open surgery was higher in men than in women [64]. Private insurance and higher income were associated with lower readmission rates in our analysis. As discussed above, privately insured patients were more likely to undergo cholecystectomy. Nguyen et al found that lower income was associated with disproportionately admitted to hospitals with lower cholecystectomy volumes [13]. Discharge against medical advice is associated with over twice the odds of all-cause unplanned 30-day readmission compared with routine discharge [65]. Our analysis showed higher rates of readmission in patients left against medical advice. These patients likely were discharged before completion of guideline-directed therapy for BAP which makes them more likely to be readmitted for recurrent BAP or complications associated with BAP. Analysis of comorbidities showed that the presence of any of them was associated with higher risk of readmission (except for dementia and myocardial infarction which were associated with decreased risk; however, these were statistically insignificant). Previous studies showed that patients with fewer comorbidities were more likely to undergo early cholecystectomy [11, 66]. Tabak et al found that higher comorbidity index was associated with more adverse events during ERCP [67].

More than 12% of the patients did not have any procedure performed in our study. Studies showed variable rates for cholecystectomy and ERCP in patients with BAP. This variation is likely multifactorial; as race, severity of disease, presence of comorbidities, hospital location, availability of specialists, and income play a role in the decision to perform procedures. Nguyen et al found that cholecystectomy and ERCP rates were lower among African Americans and Asians compared to Whites [12]. Toh et al found that in mild cases of BAP, only one-third of patients had definitive treatment within 4 weeks [68]. Kamal et al found that patients who underwent cholecystectomy for BAP had fewer comorbidities [66]. In addition, patients from rural areas and with lower income were disproportionately admitted to hospitals with lower cholecystectomy volumes [13]. Aly et al found that implementation of national guidelines for the management of acute pancreatitis was greater in the practice of hepatobiliary and pancreatic specialists than non-specialists [69].

We found that undergoing both procedures (ERCP and cholecystectomy) decreased the risk of readmission; however, it did not improve mortality and was associated with significantly higher hospital charges. Acute pancreatitis without infection or necrosis was the most common reason for readmission. Females, elderly, and privately insured were less likely to be readmitted. Our study has some important limitation. The NRD reports information on hospitalizations rather than individual patients, as a result, one patient can be included more than one time in the analysis. The study used ICD codes; therefore, it may contain errors related to miscoding. The severity of pancreatitis, medications given, radiologic and laboratory investigations cannot be determined from the data provided in NRD. This study did not assess other surgical or procedural interventions that can be performed in these patients including percutaneous drainage. Lastly, patients were not stratified based on the presence of ascending cholangitis in our analysis, a complication that might impact the outcomes and procedures performed.

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Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Informed Consent

Not applicable.

Author Contributions

Dr. Attar supervised the entire study including the design and the analysis. Dr. Laswi and Dr. Shaka designed the study, performed data analysis, and reviewed the final manuscript. Dr. Kwei, Dr. Ishaya, Dr. Ojemolon, Dr. Natour, and Dr. Darweesh wrote the manuscript in consultation with Dr. Laswi.

Data Availability

The Nationwide Readmissions Database is publicly available as stated in the methods. Any inquiries regarding supporting data of this study should be directed to the corresponding author.

Abbreviations

ACG: American College of Gastroenterology; AGA: American Gastroenterological Association; AHRQ: Agency for Healthcare Research and Quality; aMD: adjusted mean difference; aOR: adjusted odds ratio; APA: American Pancreatic Association; BAP: biliary acute pancreatitis; CBD: common bile duct; CCI: Charlson Comorbidity Index; CI: confidence interval; ERCP: endoscopic retrograde cholangiopancreatography; IAP: International Association of Pancreatology; ICD10-CM/PCS: International Classification of DiseasesTenth Revision, Clinical Modification/Procedure Coding System; LOS: length of hospital stay; MHOI: median household income; NRD: Nationwide Readmissions Database; SD: standard deviation; SE:

standard error; SID: State Inpatient Databases; THC: total hospital charges; USD: United States dollar

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