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On-site ERCP Availability and Cholangitis Outcomes: A Retrospective Cohort Study

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Abstract:

Introduction: ERCP is important in acute cholangitis (AC) management but is not available at all hospitals. The association between on-site ERCP availability and cholangitis outcomes is unknown.

Methods: We included adults diagnosed with AC at 27 hospitals in Ontario through the GEMINI network. We collected data on demographics, clinical and laboratory values, and interventions. The primary outcome was in-hospital mortality. Secondary outcomes were length of stay, intensive care unit (ICU) admission, readmission rates, and requirement for percutaneous or surgical decompression. We used multivariable regression analyses to assess the impact of on-site ERCP availability on the primary and secondary outcomes with adjustment for relevant variables.

Results: Our cohort included 4492 patients with a median age of 75. Patients at ERCP sites had higher unadjusted rates of undergoing ERCP (55.7% at ERCP sites, 40.8% at non-ERCP sites). Patients at ERCP sites compared to non-ERCP sites did not have significantly different in-hospital mortality (aOR=2.19, 95% CI=0.86-5.55). Compared to non-ERCP sites, patients at ERCP sites with underlying stricturing biliary disease or pancreaticobiliary malignancy (aOR=1.94, 95% CI=1.14-13.58) or severe cholangitis (aOR=2.17, 95% CI=1.17-4.02) had higher odds of in-hospital mortality. In a post-hoc propensity score-based analysis, there was no significant difference between patients at ERCP sites compared to those at non-ERCP sites for in-hospital mortality.

Conclusions: Patients at ERCP sites compared to non-ERCP sites did not have significantly different mortality. The subgroups of patients with underlying stricturing biliary disease or pancreaticobiliary malignancy and severe cholangitis, who have higher mortality at ERCP sites, warrant further study.

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On-site ERCP Availability and Cholangitis Outcomes: A Retrospective Cohort Study

BACKGROUND

Endoscopic retrograde cholangiopancreatography (ERCP) is a crucial component in the management of acute cholangitis (AC) [1], which carries mortality rates of up to 10% and 50% with and without treatment, respectively[2–4]. Meta-analyses and large observational studies support the use of early ERCP for biliary decompression to improve patient outcomes [5–8]. Unlike upper and lower endoscopy, which are widely available at most hospitals, ERCP is offered in certain centers. Patients with AC, however, may present to any hospital. The potential impact of on-site ERCP availability on outcomes in cholangitis is not known.

The limited availability of ERCP is partially due to a lack of personnel, as endoscopists and nurses require specialized training beyond the skills needed for diagnostic endoscopy. Additionally, ERCP is a higher risk procedure with up to 10% of patients experiencing serious adverse events such as pancreatitis, bleeding, infection, or perforation [9]. In Ontario, Canada, ERCP availability is limited to sites where endoscopists perform a larger volume of procedures, a factor associated with fewer AEs and lower procedural failure rates [10,11]. Currently there is no standardized referral stream for ERCP. When patients present to a hospital without ERCP services, they are either managed conservatively with antibiotics and observation, undergo percutaneous drainage locally, or are transferred to an ERCP site.

Given this evidence gap regarding clinical outcomes for AC, we conducted a retrospective cohort study to compare patients admitted with AC to hospitals with ERCP services (henceforth referred to as ERCP sites) with those admitted to hospitals without ERCP services (henceforth referred to as non-ERCP sites).

METHODS

This retrospective cohort study included patients with AC at 27 hospitals in Ontario, Canada that participate in GEMINI[12].

This study received research ethics approval from St. Michael's Hospital on behalf of all participating hospitals through the Clinical Trials Ontario platform, with a waiver of patient consent due to the use of routinely collected data. We reported this study according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [13].

All diagnosis and procedure codes are available in **Supplementary Tables 1, 2, and 3**.

Data source

GEMINI is a hospital research collaborative that collects administrative and clinical data from hospital information systems with 98-100% accuracy of selected data elements when compared to manual chart review [14]. GEMINI includes adult admissions to general internal medicine and subspecialty medical (cardiology, gastroenterology, hematology, medical oncology, respirology) wards. GEMINI also includes all patients who experienced an intensive care unit (ICU)

admission at any point during their hospitalization, including patients who were admitted to surgical wards but required transfer to and/or from an ICU [14].

Patient-level administrative data from individual hospitals are derived from GEMINI as reported to the Canadian Institute for Health Information (CIHI) National Ambulatory Care Reporting System and Discharge Abstract Database [15,16]. These data include patient demographics, admission and discharge diagnoses, interventions (endoscopic, radiological, surgical), mortality. Additionally, laboratory and radiology tests are extracted directly from hospital electronic health record systems into GEMINI. GEMINI data have previously been used to explore the provision of endoscopic procedures for management of gastrointestinal (GI) bleeding during the COVID-19 pandemic [17]. The participating hospitals serve diverse, multiethnic urban and suburban populations through universal single-payer coverage in Ontario [12].

Cohort

We included adult patients (age \geq 18) admitted to inpatient general internal medicine and subspecialty medical wards or ICUs at 27 hospitals in Ontario, Canada from April 1, 2015 to December 31, 2021 whose most responsible discharge diagnosis was AC based on International Classification of Diseases version 10 (ICD-10) (**supplementary table 1**). For individuals whose most responsible discharge diagnosis was "other and unspecified cholangitis", additional Tokyo criteria [1] for suspected AC were required for inclusion in this study.

We did not include patients with who were admitted with AC to a surgical ward and had no ICU touchpoint during their hospitalization, as these patients are not captured in GEMINI.

Exposure

The primary exposure was on-site ERCP availability. For each individual hospital, we used three independent methods to characterize participating hospitals as ERCP sites or non-ERCP sites. First, study authors (JDM, SCG) who are practicing endoscopists at an ERCP referral centre (St. Michael's Hospital) and who have institutional knowledge of the availability of ERCP across Ontario hospitals. Second, we searched the web pages of individual hospitals' endoscopy units to identify which endoscopic services are provided. Third, we contacted gastroenterology division heads at each participating hospital to confirm ERCP availability or lack thereof.

With the above information, we grouped patients as having been admitted to an ERCP site or non-ERCP site. If there was any conflict between the three different methods above, we used the information from the gastroenterology division head to classify the respective site.

Two hospitals began providing ERCP services during the study period (Toronto General Hospital, Toronto Western Hospital). We classified patients admitted to these hospitals prior to the ERCP start date as admitted to a non-ERCP, and those admitted afterwards as admitted to an ERCP site.

Outcomes

The primary outcome was in-hospital mortality for each episode of care. We defined an episode of care as the initial presentation to a hospital with AC and all subsequent continuous transfers between acute care hospitals. Consistent with CIHI definitions, we defined an inter-facility

transfers as new admissions within 7 hours of discharge, or new admissions within 12 hours of discharge if one hospital had coded the transfer. This unit of analysis captured hospital stays that involve inter-hospital transfers for the provision of ERCP services. Secondary outcomes were length of stay in hospital, 7- and 30-day readmission rates, ICU admission, and requirement for percutaneous or surgical biliary decompression. Intervention codes for ERCP and percutaneous and biliary decompression are available in **supplementary tables 2 and 3**. Readmissions were captured if they were to a medical or ICU service at a GEMINI hospital. Readmissions coded as elective are not counted as readmissions, and episodes of care ending in death are excluded from readmission analyses as they are not eligible for readmission.

We did not include post-ERCP adverse event rates of bleeding, perforation, infection, and pancreatitis. We lacked the granular patient-level data required to adjudicate these outcomes, based on a causal attribution system for post-ERCP adverse events [18], using the administrative data available in GEMINI, and thus excluded them a priori.

Covariates

We included the following patient-level characteristics as covariates: age, sex, Charlson comorbidity index score at admission [19], use of antibiotics, and presence of underlying biliary stricture or pancreaticobiliary malignancy, which included primary sclerosing cholangitis, chronic pancreatitis, and cancer of the ampulla, bile duct, pancreas, and duodenum (**supplementary table 2**). We also included severity of initial presentation based on Tokyo criteria [1] and the provision of antibiotic therapy. We identified antibiotic therapy using an established iterative approach between the GEMINI-RxNorm algorithm and clinical subject matter expert [20]. We considered patients as having severe cholangitis if they had serum creatinine > 176 μ mol/L, international normalized ratio (INR) >1.5, serum platelet count of <120,000/mm³, or requirement of intravenous vasopressors, non-invasive ventilation, or invasive ventilation [1].

Analysis

We summarized patient characteristics descriptively using counts with percentages or medians with interquartile ranges where appropriate.

We used logistic regression to estimate the adjusted association between being an ERCP site (compared to a non-ERCP site) and in-hospital mortality, ICU admission, requirement for intervention, and 7 and 30-day readmission. We used negative binomial regression to estimate the adjusted association between ERCP site and length of in-hospital stay. We presented differences in time-to-ERCP and time-to-death by ERCP site using cumulative incidence curves using the Kaplan-Meier method. We used Cox proportional hazards regression to estimate the adjusted association between admission to an ERCP site and time-to-ERCP. Time-to-event analyses censored patients at discharge or death.

Estimates from logistic regression were presented as odds ratios (OR), negative binomial regression as rate ratios (RR), and Cox regression as hazard ratios (HR). All models were adjusted for age, sex, presence of disease/malignancy, requirement for antibiotics, and Charlson comorbidity index score. We reported adjusted estimates and 95% confidence intervals using

hospital-level cluster-robust standard errors to account for the fact that patients are nested within hospitals.

Logistic regression models were fit with the rms package (v6.4-1), negative binomial regressions using the MASS package (v7.3-58.3), cumulative incidence curves using the survminer package (v0.4.9), and Cox regression using the survival package (v3.5-7) [21–24]. All analyses were completed in R version 4.1.2 [25].

We planned three *a priori* subgroup analyses based on clinical factors that could plausibly impact the management and/or outcomes of patients with AC:

- 1. Patients with severe cholangitis, defined using the Tokyo criteria above [1].
- 2. Patients with underlying biliary stricture or pancreaticobiliary malignancy [26].
- 3. Patients admitted to hospital on the weekend (from Friday at 5pm to Monday at 8am) [27].

We performed *post-hoc* analyses, using a propensity score-based method to balance baseline patient covariates to account for potential selection bias with a) the entire cohort, b) only patients who underwent ERCP, and c) only patients admitted to the intensive care unit. The propensity score was calculated using a logistic regression model to calculate the propensity of a patient presenting to a hospital with on-site ERCP, based on the the covariates of age, sex, admission Charlson Comorbidity Index Score, presence of severe AC, and underlying biliary stricture or pancreaticobiliary malignancy. Propensity scores were then balanced across patient exposure groups using overlap weighting. Outcomes were then compared in the weighted populations, including in-hospital mortality, length of stay in hospital, 7- and 30-day readmission rates, and ICU admission. We report the effect of admission to an ERCP site as a risk difference (RD), where a positive RD indicates greater risk for those admitted to an ERCP site. Overlap weight modelling was performed using PSweight package in R (version 1.2.0) [28].

RESULTS

Our cohort included 4492 patients, with 3867 (86.1%) at ERCP sites and 625 (13.9%) at non-ERCP sites. Median age was 75 (interquartile range [IQR] 62-84) and 2084 (46%) of patients were female. Underlying biliary stricture or pancreaticobiliary malignancy was present in 688 (15%) patients, and 822 (18%) had severe AC (**Table 1**).

ERCP was performed for 713 patients (18.4%) at ERCP sites and 23 patients (3.7%) at non-ERCP sites in less than 24h, for 539 patients (13.9%) and 76 patients (12.2%) respectively within 24-48h, and for 903 patients (23.4%) and 156 patients (25.0%) respectively in greater than 48h. ERCP was not performed during the index hospitalization for 1712 (44.3%) patients and 370 patients (59.2%) at ERCP sites and non-ERCP sites respectively (**Table 1, Figure 1**). Patients at ERCP sites were more likely to receive ERCP earlier than patients at non-ERCP sites (adjusted (a) HR = 1.76, 95% CI =1.48-2.10). Cumulative incidence estimates are presented in **Figure 2**.

In-hospital mortality

Overall, 197 (4%) patients died in hospital within the episode of care. Patients at ERCP sites did not have significantly different in-hospital mortality rates than patients at non-ERCP sites

(unadjusted mortality 4% vs. 4%; aOR = 2.19, 95% CI = 0.86-5.55) (**Table 2, Table 3, Figure 3**).

Compared to non-ERCP sites, patients at ERCP sites had higher mortality rates within the subgroups of severe cholangitis (aOR = 2.17, 95% CI = 1.17-4.02) and underlying biliary stricture or pancreaticobiliary malignancy (aOR = 1.94, 95% CI = 1.14-13.58). We observed no difference for in-hospital mortality between ERCP sites and non-ERCP sites within the subgroups of patients admitted on the weekend (**Table 4**).

Length of stay and readmission

We observed no difference between patients at ERCP sites versus non-ERCP sites for hospital LOS (median 5.22 days [IQR 3.31-8.99] vs 6.10 days [IQR 3.87-9.50]; adjusted RR = 0.95, 95% CI = 0.81–1.12), 7-day readmission rates, (4% vs 5%; aOR = 0.77, 95% CI = 0.56–1.08), or 30-day readmission rates (13% vs 13%; aOR = 0.89, 95% CI = 0.59–1.35) (**Table 2, Table 3, Figure 3**).

Patients at ERCP sites with severe cholangitis had shorter LOS (aRR = 0.55, 95% CI = 0.40-0.76), and those with underlying biliary stricture or pancreaticobiliary malignancy had longer LOS (aRR = 1.32, 95% CI = 1.09-1.59). We observed no significant difference between sites for other subgroups for the outcomes of length of stay or 7- or 30-day readmission (**Table 4**).

Hospital resource utilization

Patients at ERCP sites were more likely to experience an ICU admission (11% *vs* 9%; aOR = 1.96, 95% CI =1.29-2.98). We observed no difference between patients at ERCP sites versus non-ERCP sites for percutaneous intervention rates (7% *vs* 6%; aOR = 1.22, 95% CI =0.53-2.81). For the outcome of surgical intervention, we could not perform an adjusted analysis due to a small number of events. We were not able to perform adjusted for receipt of surgical intervention due to a small number of events. Thirty patients (1%) at ERCP sites and one patient at non-ERCP sites (0.1%) underwent surgical intervention (**Table 2, Table 3, Figure 3**).

Patients at ERCP sites with severe cholangitis (aOR = 3.15, 95% CI = 1.90-5.21), underlying biliary stricture or pancreaticobiliary malignancy, (aOR = 1.79, 95% CI = 1.01-3.16) and those admitted on the weekend (aOR = 3.15, 95% CI = 1.49-6.64) had higher odds of ICU admission. We observed no difference between ERCP sites and non-ERCP sites for receipt of percutaneous intervention among any pre-defined subgroup (**Table 4**).

Propensity score with overlapping weights analysis

The cohorts were perfectly balanced after overlap weighting, by definition (**Supplementary table 4**). There was no significant difference between patients at ERCP sites compared to those at non-ERCP sites for in-hospital mortality (risk difference [RD] = 0.09, 95% CI -0.12-0.03), LOS (RD = 0.4, 95% CI -1.27-2.19), 7-day readmission (RD = -0.02, 95% CI -0.07-0.13), 30-day readmission (RD = -4.76, 95% CI -0.25-0.05), or ICU admission (RD = 3.15, 95% CI -0.06-0.08) (**Supplementary table 5**). When including only patients who underwent ERCP, there were no differences between groups for in-hospital mortality, LOS, 7- and 30-day readmission, or ICU

admission. When including only patients who were admitted to the ICU, there were no differences between groups for in-hospital mortality, LOS, or 7-day readmission. Patients at ERCP-sites had a lower risk of 30-day readmission (RD = 16.09, 95% CI -0.25-0.01), though the event rate for patients at non-ERCP sites was <6 (**Supplementary table 5**).

DISCUSSION

In this retrospective analysis of patients admitted with AC at 27 large urban hospitals, we observed no difference in mortality between patients admitted to ERCP sites compared to non-ERCP sites. Patients at ERCP sites were more likely to experience an ICU admission. Subgroups of patients with underlying biliary stricture or pancreaticobiliary malignancy and severe cholangitis had higher mortality at ERCP sites compared to non-ERCP sites. To our knowledge, this is the first study to examine the effect of on-site ERCP availability on cholangitis outcomes.

Management of cholangitis includes antibiotics, supportive treatment such as fluids or vasopressors, and biliary decompression [2]. While medications and supportive treatment are provided at all hospitals, biliary decompression often requires endoscopic or percutaneous drainage and is not available universally. In Ontario, patients can be transferred between hospitals when they require advanced endoscopic services that are unavailable at their presenting hospital. In our study, patients had higher absolute rates of undergoing ERCP at ERCP sites and were more likely to undergo sooner than patients at non-ERCP sites. Despite this, we found no difference for in-hospital mortality overall.

Several secondary results warrant further discussion. First, we found increased mortality among patients with severe cholangitis and underlying biliary stricture or pancreaticobiliary malignancy at ERCP sites. Though we anticipated that on-site ERCP availability and provider experience with cholangitis at ERCP sites would be associated with improved outcomes, it is possible that there are unmeasured clinical factors that explain higher in-hospital mortality. Indeed, patients at ERCP sites experienced higher rates of ICU admission. There are several possible underlying reasons. There may be more patient complexity and associated morbidity at ERCP sites. Additionally, the provision of an invasive procedure such as ERCP may lead to ICU admission. Patients at ERCP sites may also undergo ICU admission to facilitate emergent ERCP after hours. These potential clinical pathways warrant further study.

Additionally, approximately 44% of patients at ERCP sites and 59% at non-ERCP sites with a diagnosis of AC did not undergo ERCP during the index hospitalization. This is in keeping with other population-based studies of ERCP in cholangitis [27,29]. There are several potential reasons for this finding. First, some patients may respond to antibiotics and supportive care before procedural decompression is performed. If there is adequate clinical response, providers may decide that the risk of an ERCP outweighs the benefit. Additionally, some patients may go on to be discharged and have ERCP at a later time as an outpatient. Third, invasive procedures may not be within certain patients' goals of care. Finally, patients may have been misclassified as having AC and thus would not have warranted biliary drainage. Further work to validate diagnostic codes for cholangitis in administrative data sets are warranted.

There are several limitations in our present study. First, we did not capture patients that are admitted to surgical services with cholangitis or those from rural hospitals outside the GEMINI network. Second, we did not capture delayed adverse events, such as post-ERCP pancreatitis due to the limitations of administrative data. These adverse events may have contributed to the worse outcomes for patients at ERCP sites for certain subgroups and warrant investigation in a prospective study. Third, accuracy of diagnosis and interventions in an administrative data set are dependent upon the accuracy of initial coding. Fourth, we were unable to capture patients who underwent ERCP as outpatients after their index hospitalization. Fifth, our analyses of time-to-ERCP do not consider the competing risk of in-hospital death; mortality rates in our cohort were very low and this does not meaningfully impact results. Finally, we were unable to account for factors which affect ERCP performance, such as hospital and provider-level volume [10,11]. Our study also has several strengths. We used a comprehensive inpatient medical database that captures variables known to affect cholangitis outcomes. Additionally, we used objective and relevant outcomes such as mortality, intensive care utilization, and readmission.

CONCLUSION

In this cohort study of 4492 patients at 27 large urban hospitals, on-site ERCP availability did not impact in-hospital mortality rates. Compared to non-ERCP sites, patients at ERCP sites with severe cholangitis and underlying biliary stricture or pancreaticobiliary malignancy had higher in-hospital mortality rates, which warrants further study for potential unmeasured variables that are associated with adverse outcomes.

Table 1: Patient characteristics

Variable	Admission to ERCP Centre (N=3867)	Admission to Non- ERCP Centre (N=625)
Median age [Q1 - Q3]	74.0 [61.0 - 84.0]	78.0 [65.0 - 87.0]
Median Charlson comorbidity score [Q1 - Q3]	0 [0 - 2.00]	0 [0 - 2.00]
Female sex, n (%)	1789 (46 %)	295 (47 %)
Severe AC, n (%)	703 (18 %)	119 (19 %)
Weekend admission, n (%)	1090 (28 %)	169 (27 %)
Presence of underlying biliary stricture or pancreaticobiliary malignancy, n (%)	585 (15 %)	103 (16 %)
ERCP performed <24h, n (%)	713 (18.4%)	23 (3.7%)
ERCP performed in 24-48h, n (%)	539 (13.9%)	76 (12.2%)
ERCP performed >48h, n (%)	903 (23.4%)	156 (25.0%)
ERCP not performed, n (%)	1712 (44.3%)	370 (59.2%)

ICU – intensive care unit

Table 2: Unadjusted estimates for primary and secondary outcomes

Outcome	Admission to ERCP Centre (N=3867)	Admission to Non- ERCP Centre (N=625)
In-hospital mortality, n (%)	173 (4 %)	24 (4 %)
ICU admission, n (%)	441 (11 %)	56 (9 %)
7-day readmission, n (%)	164 (4 %)	31 (5 %)
30-day readmission, n (5)	485 (13 %)	84 (13 %)
Median length of stay (days) [Q1 - Q3]	5.22 [3.31 – 8.99]	6.10 [3.87 – 9.50]
Percutaneous Intervention, n (%)	290 (7 %)	35 (6 %)
Surgical Intervention, n (%)	30 (1 %)	1 (0.1%)

ICU – intensive care unit

Table 3: Adjusted primary and secondary outcomes for main and subgroup analyses

Outcome	Unadjusted estimate	Adjusted estimate
In-hospital mortality, aOR (95% CI)	1.17 (0.73-1.8)	2.19 (0.8-5.55)
ICU admission, aOR (95% CI)	1.31 (0.86-1.98)	1.96 (1.29-2.98)*

7-day readmission, aOR (95% CI)	0.83 (0.62-1.10)	0.77 (0.56-1.08)
30-day readmission, aOR (95% CI)	0.90 (0.61-1.32)	0.89 (0.59-1.35)
Median length of stay, aRR (95% CI)	0.82 (0.58-1.15)	0.95 (0.81-1.12)
Percutaneous Intervention, aOR (95% CI)	1.37 (0.58-3.24)	1.22 (0.53-2.81)
Surgical Intervention, aOR (95% CI)	4.71 (0.93-23.84)	-

aOR – adjusted odds ratio, aRR - adjusted rate ratio ICU – intensive care unit

Surgical intervention adjusted estimate not presented as we did not perform adjusted analyses for this outcome

Table 4: Adjusted estimates for primary and secondary outcomes among subgroups

Outcome	Severe	Weekend	Underlying biliary
	cholangitis	admission	stricture or
			pancreaticobiliary
			malignancy
In-hospital mortality, aOR (95% CI)	2.17 (1.17-	6.51 (0.60-	3.94 (1.14-
	4.02)*	70.19)	13.58)*
ICU admission, aOR (95% CI)	3.15 (1.90-	3.15 (1.49-	1.79 (1.01-3.16)*
ICO dullission, aor (95% CI)	5.21)*	6.64)*	
7 days readmission, aOD (000/ CI)	0.74 (0.42-	0.66 (0.38-	0.89 (0.57-1.37)
7-day readmission, aOR (95% CI)	1.30)	1.13)	
30-day readmission, aOR (95% CI)	0.67 (0.35-	1.07 (0.67-	0.88 (0.55-1.41)
50-day readiffission, aOR (95% CI)	1.29)	1.72)	
Madian langth of stay, aDD (000/CI)	0.55 (0.40-	1.15 (0.98-	1.32 (1.09-1.59)*
Median length of stay, aRR (95% CI)	0.76)*	1.36)	
Percutaneous Intervention, aOR (95%	1.23 (0.58-	3.11 (0.58-	0.82 (0.37-1.80)
CI)	2.61)	16.63)	

aOR – adjusted odds ratio, aRR - adjusted rate ratio ICU – intensive care unit

Surgical intervention estimates not presented as we did not perform adjusted analyses for this outcome

^{*} significant at *p*<0.05

^{*} significant at p < 0.05

FIGURE LEGENDS

Figure 1: Percentage of patients undergoing ERCP prior to 24 hours, within 24 hours to 48 hours, after 48 hours, and not at all.

Figure 2: Cumulative incidence curves of time-to-ERCP (solid lines) and time-to-death (dashed lines) using the Kaplan-Meier method, with 0 = non-ERCP sites and 1 = ERCP sites. These time-to event analyses censored patients at discharge or death

Figure 3: Forest plot of adjusted estimates for primary and secondary outcomes.



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Supplementary Documents

Supplementary table 1: Diagnostic codes for acute cholangitis

Code	Definition
K8302	Ascending cholangitis
K8031	Calculus of bile duct with cholangitis with
	obstruction
K8030	Calculus of bile duct with cholangitis without
	obstruction
K830	Cholangitis
K8308	Other and unspecified cholangitis (these
	patients also were required to meet Tokyo
	criteria for study inclusion)

Supplementary table 2: Diagnostic codes for underlying hepatopancreaticobiliary disease

Code	Short description	Long-form
C25.0-C25.3, C25.7-9	Malignant neoplasm of	Head of pancreas – C25.0
	pancreas	Body of pancreas – C25.1
		Tail of pancreas – C25.2
		Duct of pancreas – C25.3
		Other – C25.7 or C25.8
		Unspecified – C25.9
C17.0	Malignant neoplasm of small	N/A
	intestine - duodenum	
C22.1	Intrahepatic bile duct	N/A
	carcinoma	
C24.0, C24.1, C24.8, C24.9	Malignant neoplasm of other	C24.0 Malignant neoplasm of
	and unspecified parts of	extrahepatic bile duct
	biliary tract	C24.1 Malignant neoplasm of ampulla of Vater
		C24.8 Malignant neoplasm of
		overlapping sites of biliary
		tract
		C24.9 Malignant neoplasm of
		biliary tract, unspecified
K83.01	Primary sclerosing	
	cholangitis	
K86.0, K86.1	Chronic pancreatitis	K86.0 – alcohol-induced
		chronic pancreatitis
		K86.1 – other chronic
		pancreatitis

Supplementary table 3: Intervention codes

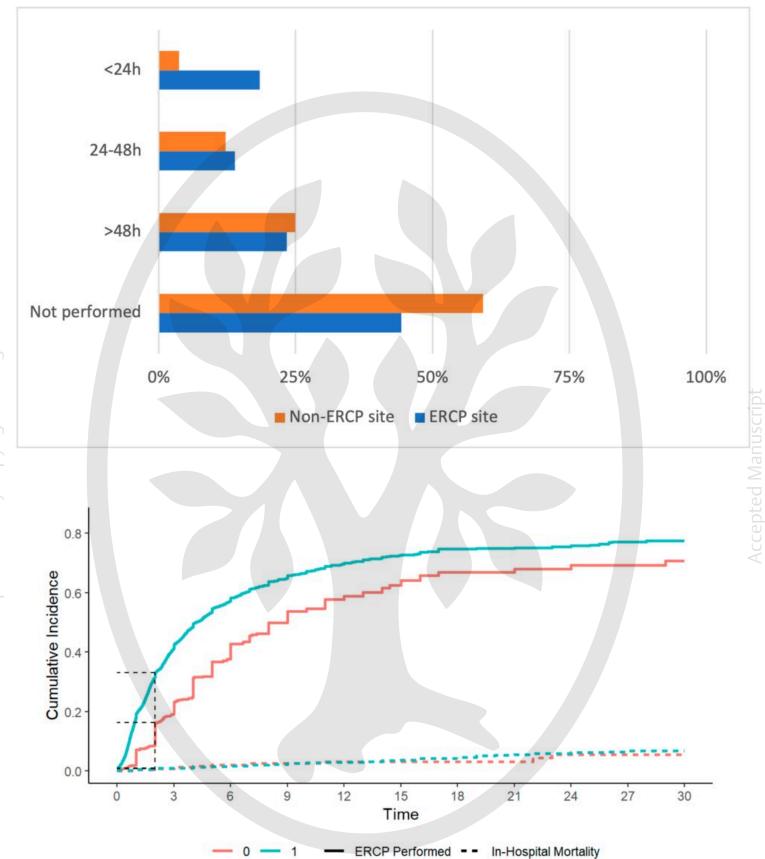
Code	Short description	Long-form
ERCP codes	Short description	
Error codes		Control of bleeding, bile
		ducts using endoscopic per
	Contr bleed bile dct EPO	orifice approach and cardiac
10E13BAE3	&card stimul	stimulant (e.g. epinephrine)
TOLIOBILLO	Geard Stiffer	Control of bleeding, bile
	Contr bleed bile dct EPO &	ducts using endoscopic per
1OE13BAFF	clips	orifice approach and clips
1021021111	enpe	Pharmacotherapy (local), bile
		ducts using endoscopic per
	Pharm tx bile dct EPO retro	orifice approach and
10E35BAZ9	agnt NEC	chemical agent NEC
1020021120	ught 1.25	Dilation, bile ducts
		endoscopic [retrograde] per
		orifice approach [ERC] using
10E50BA	Dilate bile dct EPO	incision alone
		Dilation, bile ducts
		endoscopic [retrograde] per
		orifice approach [e.g. ERC]
	Dilate bile dct EPO retro	using laser [with or without
1OE50BAAG	&lasr	stent]
		Dilation, bile ducts
		endoscopic [retrograde] per
		orifice approach [e.g. ERC]
	Dilate bile dct EPO retro	using balloon dilator [with or
1OE50BABD	&mech balloon dilat	without stent]
		Dilation, bile ducts
		endoscopic [retrograde] per
	Dilate bile dct EPO retro	orifice approach [e.g. ERC]
1OE50BANR	&stent	using rigid dilator [e.g. stent]
		Drainage, bile ducts using
		endoscopic [retrograde] per
		orifice approach [e.g. ERC or
	Drain bile dct EPO &tube	ERCP] leaving catheter (tube)
10E52BATS	NOS	in situ
		Management of internal
		device, bile ducts of drainage
		device using endoscopic
	Manage int dev bile dct EPO	[retrograde] per orifice [e.g.
10E54BATS	&tube	ERC or ERCP] approach
		Removal of device, bile ducts
	Remove dev bile dct EPO &	of stent using endoscopic per
10E55BANR	stent	orifice approach
1OE55BATS	Remove dev bile dct EPO	Removal of device, bile ducts
	&tube	of drainage device [e.g. tube,

		catheter, T-tube] using endoscopic per orifice
		approach
		Removal of device, bile ducts
	Remove dev bile dct PO	of radioactive implant using
1OE55CAEB	&interst radioact imp	per orifice approach
		Extraction, bile ducts
	T I II . I . IIIO	endoscopic [retrograde]per
100570 4 4 4 4	Extract bile dct EPO retro	orifice approach [ERC] using
10E57BAAM	&basket	basket [dormia] device
		Extraction, bile ducts
	Extract bile dct retro EPO &	endoscopic [retrograde]per
10E57BABD	balloon	orifice approach [ERC] using balloon device
TOE3/BABD	Dalloon	Extraction, bile ducts
		endoscopic [retrograde]per
		orifice approach [ERC] using
	Extract bile dct retro EPO &	other device NEC [e.g.
10E57BAGX	dev	forceps, meatome]
1020/211011		Destruction, bile ducts using
		endoscopic [retrograde
		cholangiography] per orifice
1OE59BAAG	Destruct bile dct EPO & lasr	approach [ERC] laser
		Destruction, bile ducts using
		endoscopic [retrograde
		cholangiography] per orifice
		approach [ERC]
	Destruct bile dct EPO &	electrohydraulic device
1OE59BAAS	electhydrlc	[probe]
		Destruction, bile ducts using
		endoscopic [retrograde
	Destroyet hile det EDO 9 11/2	cholangiography] per orifice
10FE0D A A 7	Destruct bile dct EPO & u/s	approach [ERC] ultrasonic
10E59BAAZ	dev	device [probe] Excision partial, bile ducts
		using endoscopic [retrograde:
10E87BA	Excise prt bile dct EPO	ERC] per orifice approach
TOLO/ D/1	Excise pit blie det Li O	Drainage, pancreas without
		leaving drainage tube in situ
		using endoscopic per orifice
10J52BA	Drain pancreas EPO	[e.g. ERCP] approach
		Drainage, pancreas leaving
		drainage tube in situ using
	Drain pancreas EPO &tube	endoscopic per orifice [e.g.
1OJ52BATS	NOS	ERCP] approach
2OE70BA	Inspect bile dct EPO app	Inspection, bile ducts using

		endoscopic per orifice
		approach
		Inspection, bile ducts using
	I III I EDO O I	endoscopic per orifice
20E70DN	Inspect bile dct EPO & lsr	approach and laser assisted
2OE70BN	assist optic bx	optical ""biopsy""
		Biopsy, bile ducts using
2OE71BA	Biopsy bile dct EPO app	endoscopic per orifice
ZOE/IBA	Biopsy blie dct EPO app	(retrograde)[ERC] approach Xray, bile ducts following
	Xray bile dct after endo	endoscopic (retrograde)
3OE10WZ	retrograde injet contr	injection of contrast
SOETOWZ	retrograde injet conti	Xray, biliary ducts with
		pancreas following
	Xray b dct w pancr w endo	endoscopic (retrograde)
3OG10WZ	retrograde injet contr	injection of contrast [ERCP]
Percutaneous intervention co		injection of condust [Effer]
10E50HAAG	Dilate bile dct perc app &lasr	Dilation, bile ducts
10200111110	Share one act percupp shaor	percutaneous [transhepatic]
		transluminal approach using
		laser [with or without stent]
1OE50HABD	Dilate bile dct perc app	Dilation, bile ducts
	&mech balloon dilat	percutaneous [transhepatic]
		transluminal approach using
		balloon dilator [with or
		without stent]
1OE50HANR	Dilate bile dct perc app	Dilation, bile ducts
	&stent	percutaneous [transhepatic]
		transluminal approach using
		rigid dilator [e.g. stent]
1OE52GPTS	Drain bile dct PTA &tube	Drainage, bile ducts using
	NOS	percutaneous transluminal
		approach [e.g. transhepatic]
400000114	7	leaving catheter (tube) in situ
1OE57HAAM	Extract bile dct perc app	Extraction, bile ducts
	&basket	percutaneous trans- hepatic
		approach [PTC] using basket
1000711400	Estable det and 0	[dormia] device
1OE57HABD	Extract bile dct perc app &	Extraction, bile ducts
	balloon	percutaneous trans- hepatic
		approach [PTC] using balloon
10EE7HACV	Extract hile det neve ann 0	device
1OE57HAGX	Extract bile dct perc app &	Extraction, bile ducts
	dev	percutaneous trans- hepatic approach [PTC] using other
		device NEC [e.g. forceps,
		device INDO [e.g. iorceps,

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		device
10E57DAGX	Extract bile dct EA & dev	Extraction, bile ducts endoscopic (laparoscopic) approach using other device
		NEC [e.g. forceps, meatome]
1OE57LAAM	Extract bile dct OA &basket	Extraction, bile ducts open approach using basket [dormia] device
1OE57LABD	Extract bile dct OA &mech balloon dilat	Extraction, bile ducts open approach using balloon device
1OE57LAGX	Extract bile dct OA &dev NEC	Extraction, bile ducts open approach using other device NEC [e.g. forceps, meatome]
2OE70DA	Inspect bile dct endo app	Inspection, bile ducts using endoscopic (laparoscopic) approach
2OE70LA	Inspect bile dct OA	Inspection, bile ducts using open approach
1OE55LAEB	Remove dev bile dct OA &interst radioact imp	Removal of device, bile ducts of radioactive implant using open approach
1OE59DAAG	Destruct bile dct EA & lasr	Destruction, bile ducts using endoscopic [laparoscopic] approach laser
10E59DAAS	Destruct bile dct EA & electhydrlc	Destruction, bile ducts using endoscopic [laparoscopic] approach electrohydraulic device [probe]
1OE59DAAZ	Destruct bile dct EA & u/s dev	Destruction, bile ducts using endoscopic [laparoscopic] approach ultrasonic device [probe]
1OE59LAAG	Destruct bile dct OA & lasr	Destruction, bile ducts using open approach laser
1OE59LAAS	Destruct bile dct OA & electhydrlc	Destruction, bile ducts using open approach electrohydraulic device [probe]
1OE59LAAZ	Destruct bile dct OA & u/s dev	Destruction, bile ducts using open approach ultrasonic device [probe]



p-value

0.10

0.00

0.64

0.13

0.58

0.54