Bile duct clearance and cholecystectomy for choledocholithiasis: Definitive single-stage laparoscopic cholecystectomy with intraoperative endoscopic retrograde cholangiopancreatography versus staged procedures

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BACKGROUND: Clinical equipoise exists regarding optimal sequencing in the definitive management of choledocholithiasis. Our current study compares sequential biliary ductal clearance and cholecystectomy at an interval to simultaneous laparoendoscopic management on index admission in a pragmatic retrospective manner.

METHODS: Records were reviewed for all patients admitted between January 2015 and December 2018 to a Swedish and an Irish university hospital. Both hospitals differ in their practice patterns for definitive management of choledocholithiasis. At the Swedish hospital, patients with choledocholithiasis underwent laparoscopic cholecystectomy with intraoperative rendezvous endoscopic retrograde cholangiopancreatography (ERCP) at index admission (one stage). In contrast, interval day-case laparoscopic cholecystectomy followed index admission ERCP (two stages) at the Irish hospital. Clinical characteristics, postprocedural complications, and inpatient duration were compared between cohorts.

RESULTS: Three hundred fifty-seven patients underwent treatment for choledocholithiasis during the study period, of whom 222 (62.2%) underwent a one-stage procedure in Sweden, while 135 (37.8%) underwent treatment in two stages in Ireland. Patients in both cohorts were closely matched in terms of age, sex, and preoperative serum total bilirubin. Patients in the one-stage group exhibited a greater inflammatory reaction on index admission (peak C-reactive protein, 136 ± 137 vs. 95 ± 102 mg/L; $p = 0.024$), had higher incidence of comorbidities (age-adjusted Charlson Comorbidity Index, ≥3; 37.8% vs. 20.0%; $p = 0.003$), and overall were less fit for surgery (American Society of Anesthesiologists, ≥3; 11.7% vs. 3.7%; $p < 0.001$). Despite this, a significantly shorter mean time to definitive treatment, that is, cholecystectomy (3.1 ± 2.5 vs. 40.3 ± 127 days, $p = 0.017$), without excess morbidity, was seen in the one-stage compared with the two-stage cohort. Patients in the one-stage cohort experienced shorter mean postprocedure length of stay (3.0 ± 4.7 vs. 5.0 ± 4.6 days, $p < 0.001$) and total length of hospital stay (6.5 ± 4.6 vs. 9.0 ± 7.3 days, $p = 0.002$). The only significant difference in postoperative complications between the cohorts was urinary retention, with a higher incidence in the one-stage cohort (19% vs. 1%, $p = 0.004$).

CONCLUSION: Where appropriate expertise and logistics exist within developing models of acute care surgery worldwide, consideration should be given to index-admission laparoscopic cholecystectomy with intraoperative ERCP for the treatment of choledocholithiasis. Our data suggest that this strategy significantly shortens the time to definitive treatment and decreases total hospital stay without any excess in adverse outcomes. (*J Trauma Acute Care Surg.* 2021;90: 240–248. Copyright © 2020 American Association for the Surgery of Trauma.)

LEVEL OF EVIDENCE: Therapeutic/Care Management Level IV.

KEY WORDS: Choledocholithiasis; intraoperative ERCP; laparoscopic cholecystectomy.

Patients with complicated gallstone disease may present with common bile duct (CBD) stones to surgeons and gastroenterologists. The treatment algorithm of resuscitation, endoscopic bile duct clearance with endoscopic retrograde cholangiopancreatography (ERCP), and ultimately definitive day-case or inpatient laparoscopic cholecystectomy is resource intensive, often with a prolonged hospital stay.[1] CBD stones, demonstrated by intraoperative cholangiography, have classically been treated by transcystic CBD stone removal or laparoscopic or open choledochotomy;[2] however, postoperative or intraoperative ERCP has also been shown to be efficacious.[2] The most recent clinical guidelines on the management of CBD stones state that multiple clinical trials have failed to demonstrate a difference in efficacy, mortality, or morbidity between laparoscopic CBD exploration and perioperative ERCP.[3] Outside of a clinical trial setting but rooted in real-world practice, a recent European prospective observational snapshot audit of clinical practice in acute complicated biliary calculous disease across 25 centers in 9 countries reported that endoscopic evaluation and management of the CBD was undertaken in 98 (29%) of the 357 study patients; of these, intraoperative rendezvous ERCP during laparoscopic cholecystectomy was performed in just 11 patients (11.2%) at three centers, while the remaining 87 patients (88.8%) underwent ERCP as a stand-alone procedure (with or without subsequent laparoscopic cholecystectomy).[4]

Significant clinical equipoise exists regarding optimal sequencing in the definitive management of choledocholithiasis.[5–8] Central to this is the migration from sequential biliary ductal clearance and gallstone reservoir management by cholecystectomy (either at index admission or an interval) to simultaneous laparoendoscopic management. While regional and patient heterogeneity may account for some of the variability that could be expected in different clinical practices to treat this condition, local health care center policies and workflows, adherence to consensus guidelines, timely access to endoscopy, and individual surgeon preference might also influence the treatment decisions. This study was undertaken, at least in part, to shine a light on these shortcomings and map a process that might ameliorate them.

Our current study compares these two different approaches in a retrospective, nonrandomized, open-label observational study to clarify if this heterogeneity in practice impacts health care resource exploitation with respect to postprocedural adverse outcomes,

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hospital length of stay (LOS), and unscheduled readmissions. Our hypothesis was that the one-stage approach is safe and that there is a risk of readmission during the waiting period for the scheduled cholecystectomy in the two-staged cohort.

PATIENTS AND METHODS

Participating Centers

The current study is a nonrandomized retrospective cohort study performed according to the guidelines and recommendations from the Strengthening the Reporting of Observational Studies in Epidemiology checklist.[5] Two large, publicly funded European tertiary-referral university hospitals with emergency surgery coverage, Orebro University Hospital (OUH), Sweden, and Tallaght University Hospital (TUH), Ireland, contributed patients to this study. Both centers are located in countries where universal health care is provided for all its citizens and acute care for all patients in need. All emergency surgical care is subsided by the governments.

At OUH, simultaneous index admission laparoscopic cholecystectomy and intraoperative ERCP are performed in all cases where no absolute contraindication to cholecystectomy exists, while in TUH, patients, while admitted under general surgery, undergo ERCP in the endoscopy department during the index admission by a gastroenterologist and, on recovery from their acute illness, are subsequently readmitted for interval day-case laparoscopic cholecystectomy.

Protocol

A retrospective review of hospital inpatient data was performed in two centers. Both centers identified patients, using *International Classification of Diseases, Tenth Revision*, who underwent both ERCP with common bile duct calculus clearance and laparoscopic cholecystectomy in the period 2015 to 2018 (inclusive). Because these anonymized data were retrospective and observational, no change to patient care was made. All data were stored securely on a hospital computer in a locked room, behind a hospital Information Technology (IT) firewall.

Procedures Performed

In OUH, patients suffering from a CBD stone or the consequences of it are subjected to cholecystectomy and intraoperative ERCP by rendezvous technique (as previously described with intraoperative cholangiography).[8] Both procedures are done in the standard operating room with the only addition of a C-arm x-ray, which is used for all cholecystectomies for performing an on-table intraoperative cholangiogram. The ERCP is done by an advanced endoscopy fellowship-trained surgeon. This procedure is initiated with a laparoscopic cholecystectomy; after identification of Calot's triangle in the usual manner, a surgical clip is placed on the cystic duct in proximity to the neck of the gall bladder. A small incision is made into the cystic duct allowing the performance of an intraoperative cholangiogram. Cholangiography is performed in all cholecystectomies at OUH. When a CBD stone is identified, a guidewire is passed through the cystic duct incision into the duodenum through the ampulla of Vater. The pneumoperitoneum is deflated, and endoscopy is performed. The guidewire is looped in a "rendezvous" fashion by the surgeon performing endoscopy. This maneuver is followed by a sphincterotomy and the CBD clearance using a balloon (Boston Scientific, Boston, MA). The entire procedure is performed with the patient in a supine position and under general anesthesia.

TABLE 1. Comparison of Patient Demographics and Comorbidities Between Groups

Variable	Simultaneous Laparoendoscopic (n = 222)	Staged ERCP and Laparoscopic Cholecystectomy (n = 135)	*p*
Clinical characteristics			
Age, mean ± SD; range, y	55 ± 19; 13–91	52 ± 17; 18–87	0.095
Female sex, % (n)	63 (142)	61.5 (83)	0.638
Age-adjusted Charlson Comorbidity Index, median (Q1, Q3)	2 (0, 3)	1 (0, 2)	0.002
ASA classification, % (n)			
I	28.9 (63)	0.0 (0)	<0.001
II	59.2 (129)	83.7 (133)	
III	10.6 (23)	12.6 (17)	
IV	1.4 (3)	3.7 (5.0)	
Comorbidities, % (n)			
Prior myocardial infarction	3.60 (8)	0.74 (1)	0.094
Congestive cardiac failure	3.60 (8)	1.48 (2)	0.239
Chronic obstructive pulmonary disease	1.35 (3)	1.48 (2)	0.919
Prior cerebrovascular accident	7.21 (16)	1.48 (2)	0.017
Peripheral vascular disease	0.90 (2)	0.00 (0)	0.269
Prior peptic ulcer disease	2.70 (6)	1.48 (2)	0.450
Diabetes mellitus	7.21 (16)	2.22 (3)	0.042
Renal impairment	1.35 (3)	2.22 (3)	0.535
Hemiplegia	0.45 (1)	0.00 (0)	0.435
Prior solid organ tumor	4.05 (9)	0.74 (1)	0.082
Hepatic impairment	2.25 (5)	0.00 (0)	0.079

ASA, American Society of Anesthesiologists; Q1, first quartile; Q3, third quartile.

TABLE 2. Comparison of Primary Diagnosis and Serum Laboratory Values Between Groups

Variable	All Patients (N = 357)	Simultaneous Laparoendoscopic (n = 222)	Staged ERCP and Laparoscopic Cholecystectomy (n = 135)	*p*
Primary diagnosis, % (n)				0.562
Acute calculous cholecystitis	5.3 (19)	5.9 (13)	4.4 (6)	
Gallstones, uncomplicated	3.9 (14)	5.0 (11)	2.2 (3)	
Choledocholithiasis, uncomplicated	40.1 (143)	41.4 (92)	37.8 (51)	
Acute biliary pancreatitis	18.8 (67)	18.0 (40)	20.0 (27)	
Choledocholithiasis with ascending cholangitis	22.7 (81)	20.3 (45)	26.7 (36)	
Concomitant acute cholecystitis and choledocholithiasis	9.2 (33)	9.5 (21)	8.9 (12)	
Laboratory values, median (Q1, Q3)				
Admission C-reactive protein, mg/L		12.0 (4.3, 42.6)	5.3 (4.9, 9.63)	0.559
Peak C-reactive protein, mg/L		48.0 (13.0, 152.7)	76.1 (19.7, 253.7)	0.023
Leukocyte count, $\times 10^9$/L		8.50 (6.67, 12.50)	10.00 (7.20, 12.72)	0.030
Alanine transferase, U/L		4.65 (1.86, 9.20)	4.00 (1.37, 7.68)	0.132
Alkaline phosphatase, U/L		3.00 (1.90, 4.70)	2.50 (1.50, 4.18)	0.058
Total bilirubin, μmol/L		43.5 (25.0, 78.0)	39.0 (12.03, 64.2)	0.021

Q1, first quartile; Q3, third quartile.

Following ERCP, the duodenum and the stomach are deflated, and the laparoscopic cholecystectomy is completed.

In TUH, patients admitted with clinical, radiologic, and biochemical evidence of choledocholithiasis (with or without complication) proceeded to the endoscopy suite where ERCP, sphincterotomy/sphincteroplasty, and balloon-trawl duct clearance (with or without stent placement) are performed with fluoroscopic guidance, under procedural sedation and analgesia, in the left lateral decubitus position by our gastroenterologists. The patient returns to the inpatient ward, recovers from their acute illness, and is discharged home when clinically well. There is no dedicated emergency operating room access as part of the usual patient flow for these patients, and thus, they are then recalled to the hospital for an elective interval day-case laparoscopic cholecystectomy (in the typical fashion, omitting cystodochotomy and intraoperative cholangiography) to complete their treatment.

Outcome Measures

The primary outcome of interest was the incidence of major 30-day postoperative complications, defined as Clavien-Dindo classification Grades 3 to 5 (reoperation, reintervention, unplanned admission to critical care, organ support requirement, or postoperative mortality).[9] The secondary outcome measures were the postoperative LOS (in whole days), time (in days) to definitive management (i.e., cholecystectomy), and readmission during the interval between ERCP and cholecystectomy.

Statistical Analysis

Descriptive and inferential statistical analyses were performed using the jamovi R graphical user interface 1.2.25 (www.jamovi.com; 2020) running the R statistical programming language 4.0.0 Arbor Day (The R Foundation for Statistical Computing, Vienna, Austria). Measures of central tendency are presented as mean ± SD or median with interquartile range (IQR) values, and comparisons were made with the χ^2 test, Student's *t* test, analysis of variance, or multivariate analysis of covariance, as appropriate.

Ethical Approval

Approval was received from the Swedish Ethical Review Authority for the Orebro County Region (DNR 2019/04716)

TABLE 3. Comparison of Duration of Operation and Length of Hospital Stay Between Groups

Variable	Simultaneous Laparoendoscopic (n = 222)	Staged ERCP and Laparoscopic Cholecystectomy (n = 135)	*p*
Time to surgery, mean ± SD; range, d*	3.1 ± 2.5; 0–14	40.3 ± 127; 0–809	<0.001
Time under general anesthesia, median (Q1, Q3), min	121 (98, 157)	86 (67, 126)	<0.001
Time to bile duct clearance on index admission, median (Q1, Q3), d	2 (1, 4)	3 (1, 7)	0.017
Postprocedural LOS, median (Q1, Q3), d	2 (1, 3)	3 (2, 6)**	0.001
Total length of hospital stay, median (Q1, Q3), d	6 (4, 8)	7 (4, 11)	0.002

*Note the large right skew of distribution in the two-stage group because of outliers awaiting interval cholecystectomy.
**Post-ERCP LOS.
Q1, first quartile; Q3, third quartile.

and from the Tallaght University Hospital Clinical Audit Registry (September 2019).

RESULTS

Patient Demographics

Three-hundred fifty-seven individual patients admitted to either center between January 1, 2015, and December 31, 2018, were enrolled in the study. Female patients outnumbered males (63% vs. 37%). The mean age at the time of diagnosis was 54 years (mean ± SD, 65 ± 18 years; range, 18–100 years); this did not differ between groups (55 ± 19 in the simultaneous group vs. 52 ± 17 years in the staged group, $p = 0.095$) (Table 1). Age-adjusted Charlson Comorbidity Index[10,11] was significantly greater in patients who underwent simultaneous definitive laparoendoscopic management compared with staged admissions for emergency ERCP and interval laparoscopic cholecystectomy (median [IQR], 2 [0–3] vs. 1 [0–2]; $p = 0.002$) (Table 1).

Diagnosis

All patients had sonographically confirmed gallstones. At the time of laparoscopy, acute calculous cholecystitis was found to be present in 36.1% of the cases, acute biliary pancreatitis in 21.6%, and choledocholithiasis in 63.6%, of whom 18.9% had cholangitis (Table 2). All 135 patients undergoing the two-staged procedure had radiologic evidence of choledocholithiasis, either by Magnetic Resonance Cholangiopancreatography (MRCP) (89.6%) or Computed Tomography (CT) (10.4%). Ultrasonography was never the sole radiologic modality for the diagnosis of choledocholithiasis. In comparison, 77% of patients who underwent the one-stage approach had perioperative radiologic confirmation of choledocholithiasis ($p < 0.001$).

Operative Management

All 357 patients enrolled in the study underwent ERCP and cholecystectomy. All 222 patients admitted to OUH underwent definitive management, that is, cholecystectomy, at index admission. Conversely, just 4.5% patients (n = 6) at TUH underwent cholecystectomy during the index admission, while the remaining 95.5% were reported as having been operated upon electively at an interval after discharge from index admission. This difference in the surgical intervention was statistically significant between the two centers ($p = 0.001$). Median (IQR) time from index admission ERCP to interval cholecystectomy was 136 (64.5–269.5) days. Thirty-one patients (22.9%) not operated during index admission were readmitted while awaiting interval elective laparoscopic cholecystectomy, of whom nine (29%) were readmitted twice and two (9.6%) readmitted three times. Laparoscopic cholecystectomy was completed in 83.4% (n = 353) of the cases. Conversion to open cholecystectomy occurred in 1.1% (n = 4) of cases: two in the one-stage cohort and two in the two-staged cohort. Median (IQR) time under general anesthesia was significantly longer in patients undergoing a one-stage procedure (121 [98–157] minutes) compared with the two-staged cohort (86 [67–125] minutes; $p < 0.001$) (Table 3). The median (IQR) total and postoperative procedure lengths of hospital stay (days) following simultaneous procedures at index admission were statistically significantly shorter than the combined length of hospital stay following ERCP and then interval cholecystectomy in patients undergoing staged procedures over two hospital admissions (total LOS, 6 [4–8] days vs. 7 [4–11] days; $p < 0.001$; postprocedure LOS, 2 [1–3] days vs. 3 [2–6] days; $p < 0.001$) (Table 3).

Endoscopic Management and Complications

Endoscopic retrograde cholangiopancreatography, sphincterotomy/sphincteroplasty, and balloon-trawl CBD clearance were performed in all 357 patients in this study. The time from admission to bile duct clearance during the index admission was significantly shorter for patients admitted to OUH compared with those admitted to TUH (median [IQR], 2 [1–4] vs. 3 [1–7]; $p = 0.017$). Post-ERCP pancreatitis was seen in 4.2% (n = 15) of patients: 12 (5.4%) who underwent one-stage procedure versus 3 (2%) in the two-staged cohort ($p = 0.146$) (Table 3). Postsphincterotomy bleed occurred in eight patients (0.2%): seven (3.2%) one-stage and one (0.7%) two-staged cohort, respectively ($p = 0.135$) (Table 4). Two patients (0.9%) in the one-stage group sustained a duodenal injury with retroperitoneal perforation following ERCP, while none were seen following index ERCP in the staged group ($p = 0.269$); both of these patients were managed nonoperatively and recovered fully.

Postoperative Complications

Eighty-nine complications, including 16 severe (Clavien-Dindo Grade 3 or above), were recorded in 73 of the 357 studied patients; no significant difference was seen between simultaneous

TABLE 4. Comparison of Postprocedure Complications per Group

Variable	All Patients (N = 357)	Simultaneous Laparoendoscopic (n = 222)	Staged ERCP and Laparoscopic Cholecystectomy (n = 135)	*p*
Complication, % (n)				
Wound infection	3.1 (11)	3.6 (8)	2.2 (3)	0.677
Pulmonary embolism	3.6 (13)	3.2 (7)	4.4 (6)	0.528
Pneumonia	3.4 (12)	2.3 (5)	5.2 (7)	0.136
Urinary retention	5.6 (20)	8.6 (19)	0.7 (1)	0.004
Postsphincterotomy bleeding	2.2 (8)	3.2 (7)	0.7 (1)	0.261
Post-ERCP pancreatitis	4.2 (15)	5.4 (12)	2.2 (3)	0.237
Endoscopic duodenal injury	0.6 (2)	0.9 (2)	0.0 (0)	0.708
Bile duct leak (Strasberg A)	2.8 (10)	2.7 (6)	3.0 (4)	1.000
Clavien-Dindo Grade 3 or 4	4.5 (16)	4.9 (11)	3.7 (5)	0.658
Mortality	0 (0)	0 (0)	0 (0)	1.000

and staged procedures in terms of Clavien-Dindo Grade 3 or 4 complications (Table 4). Multivariate analysis of covariance revealed that postoperative complications were more common in male patients ($p = 0.010$), and those older than 65 years ($p = 0.025$) but did not differ based on admitting diagnosis ($p = 0.070$) or procedure sequence ($p = 0.658$). Pulmonary embolism was seen in 13 patients (3.6%): 7 (3.2%) in the one-stage and 6 (4.4%) in patients undergoing two-staged procedures ($p = 0.528$). Pneumonia was seen in 12 patients (3.4%): 5 (2.3%) in the one-stage and 7 (5.2%) in patients undergoing two-staged procedures ($p = 0.136$). Urinary retention following general anesthesia was seen in 20 patients (5.6%): 19 (8.6%) in one-stage versus 1 (0.7%) in the two-stage cohort ($p = 0.002$). Postoperative wound infection was seen in 11 patients: 8 (3.6%) undergoing simultaneous procedures versus 3 (2.2%) undergoing staged procedures ($p = 0.464$). Strasberg grade A (injury to small ducts in continuity with the biliary system, with a leak in the duct of Luschka or the cystic duct) bile leak was seen in 10 patients, 6 (2.7%) in patients subjected to simultaneous procedures, and 4 (3.0%) in those who had an interval laparoscopic cholecystectomy ($p = 0.885$); all patients were treated with ERCP and stenting of CBD and recovered well without the need for further surgical intervention.

DISCUSSION

The current study, comparing two well-matched patient populations in differing health care systems, shows that a significantly decreased time to definitive treatment, shorter length of hospital stay, and decreased readmission can be achieved without excess morbidity in patients suffering from choledocholithiasis who are subjected to one-stage cholecystectomy and ERCP assisted CBD clearance.

Biliary calculi may produce acute complications requiring urgent hospital presentation for surgical care; these complications may be morbid and are complex to manage. Choledocholithiasis, a serious sequel of gallstone disease, which may be further complicated by cholangitis or biliary pancreatitis, is seen in approximately 10% to 15% of Western patients with gallstones.[10] While open and laparoscopic bile-duct exploration strategies do exist, minimally invasive endoscopic duct clearance is the mainstay of treatment, most commonly followed by definitive management of the stone reservoir by cholecystectomy. Despite the frequency of presentation of these patients, there remains some clinical equipoise around the optimal timing of diagnostic investigations and the timing of surgical, endoscopic, or percutaneous interventional radiologic therapies.

Disease recidivism is a significant concern in the traditional staged management of choledocholithiasis.[12–14] Analysis of our data must recognize unscheduled readmission of 22.9% of these patients as an unacceptably high failure rate for this strategy. These data are not outliers, however, and readmission during the interval before cholecystectomy has been reported in the range 17% to 33%.[13,15,16] Proponents of the staged management approach cite the REWO Study,[17] which demonstrates excess morbidity (RR, 2.12) and a 3.9% mortality associated with early versus delayed cholecystectomy. However, multiple other groups have shown the safety of index admission cholecystectomy[18] and have established a higher risk of disease-related complications, recurrent hospital admission due to biliary calculus related complications, and ultimately greater morbidity following cholecystectomy at the interval operation.[19–21] A recent analysis of a retrospective Canadian administrative data set has demonstrated a 38% pooled overall relative risk reduction in the development of complications among those receiving index admission cholecystectomy compared with patients receiving the same procedure at an interval under a general surgery "on-call" model of unscheduled care (RR, 0.62; 95% confidence interval, 0.41–0.94).[22]

Index admission lap cholecystectomy, while proven to be preferable, is by no means the ubiquitous approach, in the United States or elsewhere. Many US surgeons and centers report a preference for performing two-stage ERCP and cholecystectomy at index admission, while this is likely to be much more common than in Europe (where index cholecystectomy hovers around 50%), there is a danger in conflating preference and performance.[23] Indeed contemporary data from very large administrative data sets demonstrate that the practice of index admission cholecystectomy is far from ubiquitous in the United States; by way of illustration, safety-net hospitals in the northeast were 26% less likely to perform index admission cholecystectomy than a non–safety-net hospital in their region and were almost twice as likely (OR, 1.89) to defer cholecystectomy than hospitals in the south and east of the country.[24]

This study design is retrospective and is subject to recall bias and uncontrolled heterogeneity in patient populations. It is not a prospective randomized controlled trial; we present retrospective purely observational data from two different health care systems, both tertiary-referral, publicly funded hospitals with valid but diametrically opposed models of surgical care for a relatively common disease. One limitation of the study is the intention-to-treat inclusion of patients in the simultaneous arm without preoperative radiologic confirmation of CBD stones; while this policy is not without precedent in the literature,[11] it may be argued that some of these patients accrued the potential morbidity of intraoperative cholangiography via cystodochotomy (cystic duct leak, duodenal perforation, pancreatitis) without benefit.

The slightly higher incidence of complications in the simultaneous group is not statistically significant and is likely related to the small sample size. A systemic review and network meta-analysis conducted by Ricci et al.[25] found that the combination of laparoscopic cholecystectomy with intraoperative ERCP enjoyed the best safety profile and appeared to be the most successful for stone removal, compared with laparoscopic cholecystectomy and CBD exploration or ERCP followed by interval cholecystectomy. They also recommended that ERCP plus laparoscopic cholecystectomy, that is, two-staged procedure, as presently described, was indisputably the worst choice in terms of acute pancreatitis. This finding has been shown previously and has been attributed to the fact that the rendezvous technique does protect against accidental cannulation of the pancreatic duct, which can happen when ERCP is conducted without the guidance of a guidewire.[1,26] In the current study, no difference between the two approaches in regard to post-ERCP pancreatitis could be measured. An explanation for this result could be the retrospective design or a type-2 statistical error because of sample size.

Learnings from our present comparison, coupled with lessons from the literature,[27,28] suggest that there may also be

financial and workflow advantages associated with index-admission definitive treatment. A recent meta-analysis by Lin et al.,[28] including a total of 1,061 patients, showed that the one-step rendezvous approach is equivalent to traditional two-stage procedures in terms of CBD stone clearance and conversion, with less pancreatitis, lower overall morbidity, and shorter hospital stay but longer operation time. Estimates from the Activity-Based Funding Price List 2019 (Healthcare Pricing Office of the Health Service Executive, Ireland), which applies a weighted multiplier to the base cost of inpatient admission based on the LOS and the complexity of the disease process and interventions required, suggest a mean cost of €12,302.54 (US $14,399.07) per patient undergoing the staged procedure pathway in Ireland. This may be compared with a projected mean cost of €9,379.02 (US $10,981.06) per patient for the same 135 patients if treated with simultaneous laparoscopic cholecystectomy and ERCP on index admission, generating a potential cost saving of €394,674.93 (US $462,089.85) and 135 fewer day-case bed days. Our findings are congruent with a small pilot study of 20 patients from Las Vegas, NV, in 2013, which compared index admission ERCP followed by cholecystectomy with simultaneous ERCP and cholecystectomy, noting a statistically significant difference existed between hospital charges for one-step (US $58,145.30; SD, US $17,963.09) and two-step (US $78,895.53; SD, US $21,954.78) procedures ($p = 0.033$).[29] Decreasing the incidence of unplanned readmission has significant financial implications. Not only does the overall lower length of hospital stay result in a decrease in direct costs related to medical care, but there is also a significant saving in indirect cost, which is much harder to objectively measure. Indirect cost savings include a faster return to work/lesser need to take time off from work and lesser demand for childcare/homecare services resulting from the unexpected absence or prolonged hospitalization. While these calculations provide an extremely crude retrospective financial estimate, they provide an argument for future work in the form of a time-driven activity-based costing exercise to truly map cost to the patient pathway and to inform process improvement.[30]

The management of choledocholithiasis is costly and resource intensive.[14,31–33] Ultimately, these current data show that simultaneous ERCP and laparoscopic cholecystectomy offer many benefits for patients and, once a protocol is established and adequately resourced, improve efficiency in patient flow and provide cost savings for the health care system by decreasing bed occupancy through the shorter LOS and fewer readmissions. It may also be time to explore closer ties with endoscopy during the evolution of acute care surgical services, as well as the possibility of endoscopic fellowship for surgeons as an additional competency. There are convincing data that services with workflows that facilitate access to a dedicated emergency operating room and to emergency complex endoscopy have better adherence to practice guidelines and perform index admission cholecystectomy more frequently.[4,9] The exclusive use of a single management strategy (simultaneous index admission laparoscopic cholecystectomy and ERCP in Sweden and staged index admission ERCP and interval cholecystectomy in TUH) is a potential confounder, as some differences between groups could conceivably have arisen from center-specific idiosyncracies rather than differences in the management strategy. It is not possible to control for these unknown variables in a retrospective observational study of this type. These current data suggest that deferring patients with CBD stones to later surgical intervention should be considered a less attractive approach.

CONCLUSIONS

Where appropriate expertise exists and where logistically feasible within developing European and US models of Acute Care Surgery, consideration should be given to a single-stage approach of index-admission laparoscopic cholecystectomy with intraoperative ERCP for the treatment of choledocholithiasis. Our data suggest that this strategy significantly shortens time to definitive treatment, decreases total hospital stay without any excess in adverse outcomes, accrues cost savings for the health care system, and could potentially increase patient satisfaction.

AUTHORSHIP

S.M. and G.A.B. conceived the idea for the study. A.P., M.D., S.F., C.M., and R.A. collected the data. G.A.B. and Y.C. analyzed the data. G.A.B., S.M., A.E.G., B.S., R.A., and D.M. wrote the article, and the final version was reviewed and approved by all authors.

DISCLOSURE

The authors declare no conflicts of interest.

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DISCUSSION

CAROLINE REINKE, M.D. (Charlotte, North Carolina): Good morning, Dr. Kim and members and guests. Thank you to the AAST Program Committee for the opportunity to review this study.

Congratulations to Dr. Bass and colleagues who have undertaken an analysis of patients undergoing treatment of choledocholithiasis at two hospitals with very different management practices.

The primary focus of this study was to compare outcomes and resource utilization between the simultaneous ERCP and cholecystectomy versus the ERCP with an interval cholecystectomy.

As a single-stage procedure is not something that I have experienced in the hospitals I have worked at, I appreciated his description of the procedure.

Overall, the authors found that while patients were similar in many ways, the simultaneous cohort, not surprisingly, had a shorter total length of stay and time to definitive treatment.

It was a little bit surprising that the staged group had a longer time to ERCP and that the simultaneous group had a zero percent readmission rate.

This topic remains important because there are a variety of management options available to surgeons within their toolkit to manage choledocholithiasis.

There remains significant variation in management and understanding the benefits of the different options is important to improve value in surgical care.

I believe your study reinforces the benefits of patient-focused care design and compares two management options that are probably relatively rare in the United States: the laparoscopic cholecystectomy with the intraoperative rendezvous ERCP versus ERCP with discharge and subsequent outpatient cholecystectomy.

I have a few questions for you this morning.

Your comparison groups did have some notable differences, including the comorbidity index, the ASA score, and inflammatory indices. Additionally, the simultaneous arm has an intention to treat component. Only if a CCBD stone was seen on the intraoperative cholangiogram was the ERCP actually performed.

I would be interested to know what percent of those patients received the rendezvous ERCP and what impact that you think that may have had on your findings.

I think the most compelling findings of this study surround total health care utilization. While the median total hospital length of stay is six versus seven days, again, the time to definitive management and readmissions were quite substantial.

It appears that a lot of the factors that contribute to the overall length of stay were affected by the longer time to

ERCP on the index admission. What are some factors you think affected that? And what are some solutions that might impact that difference?

There was a higher rate of some significant complications, although not statistically different. Additionally, there was shorter post-procedural length of stay in the simultaneous group. Do you think that there are hospital or cultural differences that led to this post-procedural length of stay that were independent of the actual procedural outcomes?

And then assuming that process changes could be made to allow interval cholecystectomies to be performed in a shorter timeframe than what was seen in this study, resulting in a significant reduction in the unplanned readmission rate, do you think the benefits would be as pronounced?

Ultimately, at the end of the day I think this study leads us all to wonder more about how we determine within our individual hospital and the resources available what is the best option for patients in management of this disease.

Thank you, again, for the opportunity to discuss this paper.

GARY BASS, M.D., M.S., M.B.A. (Philadelphia, Pennsylvania): Thank you very much for the many interesting questions; In particular thank you very much, Dr. Reinke, for taking the time and effort to go through the manuscript as thoroughly as you did.

If I may take Dr. Reinke's questions together as they're largely on a similar topic, I think they allude greatly to a culture difference between the two studied institutions, and, indeed, between those two institutions and what is perceived to be the normal practice in the United States.

The two-stage procedure, where patients are admitted, have an ERCP, and then are scheduled for an interval cholecystectomy is a practice pattern that remains extremely common across Europe; indeed, when we polled 25 centers in nine European countries we found that at least 50 percent of them practiced this pattern. An outlier in that study was my colleagues in Orebro who, with the benefit of an acute care surgery model, seemed able to put all the "ducks in a row" to allow them to perform this intraoperative simultaneous procedure. This was a driver to directly compare the 2 models.

In terms of the demographics of the patients, the patients who went for a single-stage index admission procedure were older with higher baseline comorbidities. They were biochemically and, indeed, clinically sicker. Despite this, they had no statistically significant difference in the complication rate.

Our study is not a randomized controlled trial, nor do we pretend that it is. It is very much retrospective observational data with all the limitations that are attendant to that. What we set out to achieve was to demonstrate that this single-stage approach was safe, with potential trickle-down benefits in terms of resource utilization and finances, et cetera.

The median time for the single stage procedure was 120 mins, compared with 86 mins for the interval lap chole alone, about 30 minutes or 40% longer. While we did not capture the duration of the ERCP in the interval cholecystectomy group, we imagine it was approximately 30 mins in length, and that there is no real difference in time. We agree with Dr Martin that a single GA, of equivalent length to 2 separate encounters, must be better for the patient, and is likely more cost effective.

In terms of the intention to treat, by virtue of the fact that they don't necessarily all have pre-OR imaging and have intraoperative intraoperative cholangiography, as is the practice in Sweden, just under 10 percent of patients who had intraoperative cholangiography did not have stones and then do not go on to ERCP, whereas, in the other side of the study all patients had choledocholithiasis, underwent duct clearance, and then cholecystectomy without any intraoperative cholangiography.

The longer time to ERCP eminates from hospital cultural differences. In the Swedish center, an ERCP-facile second surgeon comes into the operating room and provides the ERCP clearance during the cholecystectomy. The patient flow pathway in Dublin, is that the patient is admitted to a surgery service who then consult a gastroenterology service for free slots on an endoscopy list when that arises within the working week and within hours. So patients coming on Friday, unless they are in extremis, tended to not to have an ERCP, for example, over the weekend period. And so there is that lag that is demonstrated in the time to duct clearance. A practice pattern of general surgery with an elective interest providing on-call, rather than there being an acute care service line with dedicated OR time has evolved a preference for treating the choledocholithiasis stones and then booking the patients to an elective cholecystectomy to take care of the stone reservoir. Our experience with this study has allowed us in Dublin to see the huge process advantages across the board, both in an ACS model and, indeed, in changing our process flow to the extent that our endoscopists are now onboard with piloting this single-stage approach because we've demonstrated that significant cost savings of approximately $15,000 per patient could have been achieved by changing our process flows to a single-stage or, indeed, an all-index admission approach.

Finally, then, it has been suggested that the common approach in the United States is to have index admission ERCP and then, perhaps, the next day to return to the OR for laparoscopic cholecystectomy. Examining the literature, however, there seems to be very significant geographic differences across the United States, with safety net hospitals being shown to be 26 percent less likely than community hospitals to offer this. So there still is a rumbling undercurrent of interval cholecystectomy in the US, and I suppose it remains really important not to conflate preference with performance. Many thanks again for the opportunity to share this work and to address your questions.