World Journal of

Gastroenterology

World Journal of Gastroenterology

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AIMS AND SCOPE

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  WJG mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

INDEXING/ABSTRACTING

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Retrospective Study

Operative complications and economic outcomes of cholecystectomy for acute cholecystitis

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Author contributions: Rice CP, Vaishnavi KB, Chao C, Jenson WR, Griffin LW and Mileski WJ contributed to the conception and design of the study; Rice CP, Vaishnavi KB, Chao C and Jenson WR assisted with data acquisition; Rice CP, Chao C, Jupiter D and Mileski WJ analyzed and interpreted the data obtained; Rice CP, Chao C, Schaeffer AB, Jupiter D and Mileski WJ drafted the article and/or made critical revisions related to important intellectual content of the manuscript; all authors contributed to the proof-reading and final approval of the version of the article to be published.

Institutional review board statement: This study was approved by the UTMB Institutional Review Board, No. 18-0042.

Informed consent statement: This manuscript is a retrospective study, therefore, signed informed consent forms are not necessary.

Conflict-of-interest statement: The authors declare no conflicts of

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Abstract

BACKGROUND

Recent management of acute cholecystitis favors same admission (SA) or emergent cholecystectomy based on overall shorter hospital stay and therefore cost savings. We adopted the practice of SA cholecystectomy for the treatment of acute cholecystitis at our tertiary care center and wanted to evaluate the economic benefit of this practice. We hypothesized that the existence of complications, particularly among patients with a higher degree of disease severity, during SA cholecystectomy could negate the cost savings.

AIM

To compare complication rates and hospital costs between SA *vs* delayed cholecystectomy among patients admitted emergently for acute cholecystitis.

METHODS

Under an IRB-approved protocol, complications and charges for were obtained for SA, later after conservative management (Delayed), or elective cholecystectomies over an 8.5-year period. Patients were identified using the acute care surgery registry and billing database. Data was retrieved *via* EMR, operative logs, and Revenue Cycle Operations. The severity of acute cholecystitis was graded according to the Tokyo Guidelines. TG18 categorizes acute cholecystitis by Grades 1, 2, and 3 representing mild, moderate, and severe, respectively. Comparisons were analyzed with χ^2, Fisher's exact test, ANOVA, *t*-tests, and logistic regression; significance was set at $P < 0.05$.

RESULTS

Four hundred eighty-six (87.7%) underwent a SA while 68 patients (12.3%) received Delayed cholecystectomy. Complication rates were increased after SA compared to Delayed cholecystectomy (18.5% *vs* 4.4%, *P* = 0.004). The complication rates of patients undergoing delayed cholecystectomy was similar to the rate for elective cholecystectomy (7.4%, *P* = 0.35). Mortality rates were 0.6% *vs* 0% for SA *vs* Delayed. Patients with moderate disease (Tokyo 2) suffered more complications among SA while none who were delayed experienced a complication (16.1% *vs* 0.0%, *P* < 0.001). Total hospital charges for SA cholecystectomy were increased compared to a Delayed approach ($44500 ± $59000 *vs* $35300 ± $16700, *P* = 0.019). The relative risk of developing a complication was 4.2x [95% confidence interval (CI): 1.4-12.9] in the SA *vs* Delayed groups. Among eight patients (95%CI: 5.0-12.3) with acute cholecystitis undergoing SA cholecystectomy, one patient will suffer a complication.

CONCLUSION

Patients with Tokyo Grade 2 acute cholecystitis had more complications and increased hospital charges when undergoing SA cholecystectomy. This data supports a selective approach to SA cholecystectomy for acute cholecystitis.

Key words: Acute cholecystitis; Tokyo guidelines; Cholecystectomy; Complications; Delayed cholecystectomy

Core tip: Patients presenting with acute cholecystitis (Tokyo Grade 2) have more complications and increased hospital charges when undergoing same admission cholecystectomy. This data supports a selective approach; greater disease severity may have a lower complication rate when surgery is delayed.

INTRODUCTION

Recent recommendations for early or same admission (SA) cholecystectomy[1-8] have become standard practice based mainly on a shorter hospital stay and thus a presumed economic benefit[9]. However, patients who present with acute cholecystitis are a heterogeneous population and for some patients, emergent cholecystectomy may result in complications that might be mitigated if the procedure were delayed. The Tokyo Guidelines (TG) were developed to guide the treatment of acute cholecystitis and to use clinical parameters at presentation to predict risk of complications associated with disease severity. TG defines the criteria for a clinical diagnosis of acute cholecystitis and disease severity grading[10]. The guidelines, first published in 2007, have been revised in 2013 and most recently in 2018. The grading system for TG13 is the same as TG18: Mild cholecystitis (Grade 1) refers to acute cholecystitis in a healthy patient with mild inflammatory changes in the gallbladder, fever and or elevated white blood cell count (WBC), and no organ dysfunction. Moderate cholecystitis (Grade 2) is associated with complaints > 72 h, a WBC ≥ 18K, signs of marked local inflammation (*e.g.*, gangrenous or emphysematous cholecystitis, pericholecystic or hepatic abscess, biliary peritonitis) or a palpable tender mass in the right upper quadrant of the abdomen. Severe cholecystitis (Grade 3) is defined by concurrent organ system dysfunction. TG13/18 severity grading has been shown to correlate with hospital length of stay, conversion to open cholecystectomy, and higher morbidity and mortality[10].

The World Society of Emergency Surgery (WSES)[1] acknowledges that there are no validated clinical scores to guide clinicians for the evaluation of surgical risk for early operative intervention of acute calculus cholecystitis. For example, one criticism of the

TG is that either drainage or cholecystectomy can be performed for severity Grade 2[11], without specific practice guidelines indicating which therapeutic option is better. Nonetheless, the TG grading correlates with morbidity and mortality[10,12]. Further validating the preoperative value of TG grading, Ambe *et al*[13] demonstrated that increasing severity Tokyo grades significantly correlated worse disease with histologic criteria.

Using the TG severity of the disease grading system, we compared the outcomes of patients operated on during the SA *vs* delayed. Since patients with a higher grade of disease (Grades 2 and 3) are expected to have a greater rate of complications and longer length of hospital stay (compared to Grade 1), we hypothesized that the economic benefit of early cholecystectomy in the setting of complications would be negated.

MATERIALS AND METHODS

Under an Institutional Review Board-approved protocol, we retrospectively reviewed 2118 medical charts of all patients who underwent a cholecystectomy over an 8.5-year period (February 2010 to August 2018) at the University of Texas Medical Branch (UTMB Health) – a tertiary referral center located in Galveston, Texas. Patient information was retrieved using the UTMB Health databases for acute care surgery, billing, and Revenue Cycle Operations. Patient medical charts were reviewed directly from UTMB Health's electronic medical records (EMR, Epic Hyperspace 2017, Epic Systems Corporation). A total of 26 faculty surgeons performed the cholecystectomies during this time period.

Inclusion criteria for each acutely ill patient consisted of a diagnosis of acute cholecystitis upon presentation to any UTMB Health emergency department with admission or direct admit to the hospital. All patients underwent a cholecystectomy performed either during their index admission (*i.e.*, SA) or electively after presenting with acute disease (*i.e.*, delayed cholecystectomy). For comparison only, we also abstracted the charts of all patients who underwent an elective cholecystectomy (non-acute) for a diagnosis of sub-acute conditions (*e.g.*, chronic cholecystitis (biliary colic), cholelithiasis, biliary dyskinesia, porcelain gallbladder, or gallbladder polyp). Exclusion criteria were acutely ill patients without a diagnosis of acute cholecystitis and patients < 18 years of age. We also excluded 27 patients who had a diagnosis of acute cholecystitis but underwent preoperative cholecystotomy tube placement because these patients were deemed to be poor operative candidates initially and were temporized with a drainage procedure first.

We collected information on baseline patient characteristics including demographics, insurance status, comorbidities, diagnoses, health behaviors, dates of presentation, body temperature at presentation, hospital lengths of stay, laboratory values at presentation, complications. Outcome calculations were rates of cholecystectomy on index admission, complication rates, readmission rates, and charges.

We identified data regarding charges incurred for each case from UTMB Health Revenue Cycle Operations using Current Procedural Terminology (CPT) codes, International Classification of Diseases (ICD) codes, medical record numbers of the 1882 patients involved in the study, and the operative dates between April 2013 to August 2018 (hospital charges prior to April 2013 were not activated in our electronic medical record system). The CPT codes used were 47562, 47563, 47600, 47605, 47480, 47564, 47490, and 47570, which represent laparoscopic and open cholecystectomies (with or without an intraoperative cholangiogram), percutaneous or open cholecystostomies (with or without exploration, drainage, or removal of calculus), and cholecystenterostomies, respectively. The ICD-10 included were K81.9, K81.2, K81.1, K81.0, K80.80, K80.60, K80.50, K80.44, K80.20, K80.18, K80.12, K80.10, and K80.00 along with the corresponding ICD-9 (that matched the aforementioned ICD-10) codes. These ICD codes represent combinations of acute and chronic, obstructive and non-obstructive cholecystitis, cholelithiasis, cholangitis, and choledocholithiasis. All charges (which include any admission, clinic visit, urgent care visit, related procedures) were captured for each patient after April 2013 (*i.e.*, we were unable to obtain charge data for 23.5% of the cohort).

Patients were diagnosed with acute cholecystitis and stratified by severity using the latest TG18 criteria[10]. The diagnosis is based on local signs of inflammation (*e.g.*, Murphy's sign or right upper quadrant mass, pain, or tenderness), systemic signs of inflammation (*e.g.*, fever or elevated WBC), and characteristic imaging findings. TG18 categorizes acute cholecystitis by Grades 1, 2, and 3 representing mild, moderate, and severe, respectively.

Statistical analysis

We conducted our evaluation by means of descriptive statistics using univariate and bivariate analyses of continuous and categorical variables. Bivariate comparison between the groups was analyzed using the Student's *t*-tests, one-way ANOVA, Chi-squared tests, and Fisher's exact tests, where appropriate. We constructed a multivariate model on the covariates potentially predictive of complications with a *P* value on bivariate comparison of ≤ 0.2. A *P* value of < 0.05 was considered statistically significant. Patient data was exported into a comma-separated value format to be imported in to R for analysis; all analyses were executed in the R statistical package (R, Developmental, Core, Team. R: A Language and Environment for Statistical Computing 2015; available at http://www.R-project.org).

RESULTS

Five hundred fifty-four patients met criteria and were included in the study. Four hundred eighty-six (87.7%) underwent an SA cholecystectomy while 68 patients (12.3%) received delayed operative management. Table 1 shows the demographics and patient characteristics of the two groups. Age, gender, race, ethnicity, body mass index, preexisting comorbidities, alcohol use, smoking status, and rates of planned or convert-to-open cholecystectomy were not significantly different between the SA and delayed cholecystectomy groups.

The cohort was stratified by the severity of acute cholecystitis based on the Tokyo grading system (Table 2). There were no differences in severity of disease between the SA and the delayed cholecystectomy groups.

Complication rates were significantly increased for SA compared to Delayed cholecystectomy for a diagnosis of acute cholecystitis (18.5% *vs* 4.4%, respectively, *P* = 0.004; Table 3). Although complications in mild (Grade 1) and severe (Grade 3) acute cholecystitis were not significant, patients with moderate disease (Grade 2) experienced significantly more complications during SA compared to the delayed group (16.1% *vs* 0.0%, *P* < 0.001). When we compared the complication rate of patients undergoing a delayed cholecystectomy, we found that the postoperative complication rate was similar to the rate for elective cholecystectomy for chronic cholecystitis (4.4% *vs* 6.2%, *P* = 0.557). As expected, the overall complication rate of acute cholecystitis (combining both SA and delayed) was significantly greater than that of an elective cholecystectomy (16.8% *vs* 6.2%, *P* < 0.001).

Table 3 also shows the types of complications. A significantly increased rate of subtotal cholecystectomy was performed for the SA patients compared to delayed (7.6% *vs* 0.0%, *P* = 0.016). Since a subtotal cholecystectomy was not the intended operation, we considered the performance of a subtotal cholecystectomy as a complication. Subtotal cholecystectomy, which is essentially a drainage procedure, was only performed in the SA group, suggesting that subtotal cholecystectomy is a surrogate for operative difficulty. A total of 37 patients underwent subtotal cholecystectomies; eight patients were Grade 1, 27 were Grade 2, and two patients were Grade 3. If we excluded subtotal cholecystectomies as a "true" complication, the complication rate was still statistically significant: 13.4% *vs* 4.4% (SA *vs* delayed, respectively, *P* = 0.03). Mortality rates among all patients were 0.6% *vs* 0.0% for SA and delayed, respectively. All three patients who died had cholecystectomy within 24 h of admission from the emergency department. The first death occurred in a 90-year-old with Grade 3 disease. The second patient had Grade 1 disease and a history of congestive heart failure. The third had Grade 2 disease and unrecognized cardiac ischemia postoperatively. Notably, there were no common bile duct injuries in either group (Table 3). All other complication types identified were similar between the groups, including bile leak, retained stone, cholangitis, biliary stenosis, infection, hernia, and complications involving the cardiovascular, respiratory, or gastrointestinal systems.

The time between initial admission and operative intervention for the delayed cholecystectomy group was 48.3 ± 76.3 d (Table 4). Postoperative readmission rates were similar between the groups (22.2% *vs* 21.2%, *P* = 0.854). In comparison to the delayed cases, the SA group had significantly longer total lengths of hospital stay (3.8 ± 5.5 *vs* 1.6 ± 2.0, *P* < 0.001).

SA cholecystectomy hospital charges were higher compared to Delayed intervention for acute cholecystitis ($44500 ± $59000 *vs* $35300 ± $16700, *P* = 0.019, Table 4). Hospital charges for elective cholecystectomies performed on chronic conditions were the lowest at $23000 ± $10300 (*P* < 0.001, 1-way ANOVA comparing all three).

There were no differences in complication rates based on insurance status for SA

Table 1 Demographics and patient characteristics

Variable	Same admission cholecystectomy	Delayed cholecystectomy	P value
	(*n* = 486), *n* (%) or mean ± SD	(*n* = 68), *n* (%) or mean ± SD	
Age at surgery	44.7 ± 16.0	45.2 ± 15.7	0.812
Female	280 (64.8)	49 (74.2)	0.132
Race/ethnicity			0.447
White	183 (42.5)	35 (53.0)	
Black	57 (13.2)	7 (10.6)	
Hispanic	185 (42.9)	23 (34.9)	
Other	6 (1.4)	1 (1.5)	
Body mass index	32.2 ± 15.6	32.1 ± 6.4	0.93
Comorbidities			
Coronary artery disease	13 (3.0)	2 (3.0)	1
Myocardial infarction	1 (0.2)	0 (0.0)	1
Diabetes	35 (8.1)	4 (6.1)	0.565
Hypertension	80 (18.5)	18 (27.3)	0.096
Chronic obstructive pulmonary disease	3 (0.7)	1 (1.5)	0.435
Alcohol use	134 (42.8)	27 (46.6)	0.598
Smoking status	100 (26.1)	20 (31.3)	0.39
Open cholecystectomy	8 (1.7)	3 (4.4)	0.142
Convert-to-open cholecystectomy	7 (1.4)	2 (2.9)	0.305

(17.0% insured *vs* 14.1% uninsured, *P* = 0.127) or Delayed cholecystectomy (0.7% insured *vs* 0% uninsured, *P* = 1). As expected, the vast majority of delayed cholecystectomies (97.1%) were insured compared to a lower number for SA patients (71.2%; *P* < 0.001).

A logistic regression analysis was performed to determine if there are any independent variables that can predict a higher risk of complications. We stratified disease severity by TG13/18 and found that complication rates were only significantly different with the Grade 2 subset (Table 5). The odds of any complication occurring was 2.1x greater in patients with Grade 2 disease compared to those with Grade 1 (95%CI: 1.2-3.7, *P* = 0.007, Table 5). The odds of any complication occurring in Grade 2 or 3 was 2.3x greater in males compared to female patients (95%CI: 1.0-5.1, *P* = 0.047).

Risk analysis (Table 6) of developing a complication in the SA *vs* delayed groups demonstrated a relative risk of 4.2x (95%CI: 1.4-12.9) and attributable risk of 14.1% (95%CI: 4.6-23.6). Number needed to harm (NNH) analysis indicated that, among eight patients (95%CI: 5.0-12.3) with acute cholecystitis undergoing SA cholecystectomy, one patient will suffer a complication. Notably, the attributable and NNH for Grades 2 or 3 patients were 28.3% (95%CI: 12.3-44.4) and 4 (95%CI: 2.9-4.6), respectively.

DISCUSSION

Historically, the timing of performing cholecystectomy for a diagnosis of acute cholecystitis has been very controversial. A Cochrane systematic review with meta-analysis of six randomized clinical trials (1998-2003) compared early *vs* delayed laparoscopic cholecystectomy for patients with acute cholecystitis and concluded no significant difference between the groups with regards to immediate postoperative mortality, bile duct injuries, other serious adverse events, or rates of conversion to open cholecystectomy[14]. The only significant clinical outcome in favor of early cholecystectomy was a shorter hospital length of stay by four days. Multiple publications support early (SA) over delayed (interval) cholecystectomy based on equivalent morbidity and mortality, and an overall better economic profile[1-8,15-17]. However, the data from our institution over the past 8.5 years show that for the subset of Grade 2 patients, there is greater risk of morbidity and mortality with SA cholecystectomy. When a complication does occur, we found a concomitant longer length of hospital stay with an associated increase in hospital costs. When Grade 2 patients undergo delayed cholecystectomy, the rate of complications decreases to that

Table 2 Stratification by disease severity using 2013/18 Tokyo guidelines, *n* (%)

	Same admission cholecystectomy, *n* = 486	Delayed cholecystectomy, *n* = 68	*P* value
Acute cholecystitis severity			
Tokyo Grade 1	299 (61.5)	36 (52.9)	0.271
Tokyo Grade 2	174 (35.8)	31 (45.6)	
Tokyo Grade 3	13 (2.7)	1 (1.5)	
Tokyo criteria	mean ± SD	mean ± SD	
White blood cell count	11.8 ± 4.5	11.4 ± 3.8	0.605
Duration of complaints	1.9 ± 7.3	1.4 ± 3.2	0.578
Palpable tender mass in RUQ	8 (1.6)	1 (1.5)	1
Marked local inflammation	66 (13.6)	13 (19.1)	0.221
Creatinine	0.9 ± 0.8	0.7 ± 0.2	0.104
International normalized ratio	1.1 ± 0.2	1.4 ± 0.7	0.534
Platelet count	271.9 ± 73.8	282.6 ± 92.0	0.633
Cardiovascular dysfunction	2 (0.41)	0 (0.0)	1
Neurological dysfunction	0 (0.0)	0 (0.0)	1
Respiratory dysfunction	0 (0.0)	0 (0.0)	1
Other vitals and laboratory values			
Temperature (°C)	36.7 ± 0.4	36.6 ± 0.4	0.068
Total bilirubin	1.0 ± 1.4	1.1 ± 1.7	0.852
Direct bilirubin	0.1 ± 0.6	0.5 ± 1.5	0.474
Aspartate aminotransferase	89.5 ± 181.6	64 ± 100.6	0.32
Alanine aminotransferase	94.9 ± 181.8	70.0 ± 96.4	0.32
Alkaline phosphatase	102.3 ± 48.6	111.4 ± 69.6	0.591
Amylase	87.6 ± 235.5	54 ± 5.3	0.112
Lipase	207.6 ± 704.7	477.2 ± 1474.5	0.478

RUQ: Right upper quadrant.

of elective cholecystectomies for subacute diagnoses (*e.g.*, biliary colic, gallbladders polyps). Due to the small sample size in Grade 3 patients, the logistic regression analysis (Table 5) did not identify Grade 3 patients at risk for greater complications and death when comparing operative timing. Although we cannot make definitive statements about Grade 3 patients in our study, multiple investigators with larger sample sizes do validate the highest morbidity and mortality for the highest grade of disease severity[12,18,19].

Hernandez *et al*[18] validated TG13 grading among a cohort of 443 patients at the Mayo Clinic in Rochester, MN. The odds of postoperative complications For TG grade 2 and 3 were 1.8 times and 4.9 times the risk compared to grade 1 patients. Their finding for Grade 2 patients is similar to our study where Grade 2 patients had an odds ratio of 2.1 for complications compared to Grade 1 patients. Cheng *et al*[20] compared complication rates between 103 patients with acute cholecystitis of either Tokyo Grades 1, 2, or 3. Similar to our work, they noticed an increased surgical complication rate in Grade 2 (25.0%) compared to Grades 1 (5.6%) and 3 (0.0%). The low complication rate for Grade 3 patients in both Chen and our data are due to low sample size. Also in agreement with our findings, the literature has demonstrated an excess risk of complications in males undergoing cholecystectomy for acute cholecystitis[21-23] although the reason for the association between gender and complication risk with cholecystectomy remains unclear.

In our study, among the SA cholecystectomy patients, the mean time from admission to operation was 2.2 ± 14.2 d, with an overall mortality rate of 0.6%. In a recent population-based study the 30-d operative mortality for all cholecystectomies (elective and emergent) performed for gallstone disease was 0.15% (72 deaths out of *n* = 47912 patients)[24]. They report that the risk of death for "acute" surgery compared with "planned" surgery was 10-fold higher (95%CI: 2.41-41.95). Patients with perioperative complications were 3.3-fold higher (95%CI: 1.74-6.15) for risk of death. Furthermore, patients between ages 50-70 and > 70 had a 2.12 (95%CI: 0.67-6.74) and a 7.04 (95%CI: 2.23-22.26) fold increase risk of death compared to patients < age 50, respectively. Among the three patients in our study who died postoperatively, two

Table 3 Complication rates and types, *n* (%)

Variable	Same admission cholecystectomy (*n* = 486)	Delayed cholecystectomy (*n* = 68)	*P* value
Total patients with at least 1 complication	90 (18.5)	3 (4.4)	0.004[a]
Tokyo Grade 1	37 (12.4)	3 (8.3)	0.480
Tokyo Grade 2	46 (26.4)	0 (0.0)	< 0.001[a]
Tokyo Grade 3	7 (53.8)	0 (0.0)	1
Subtotal cholecystectomy	37 (7.6)	0 (0.0)	0.016[a]
Death	3 (0.6)	0 (0.0)	1
Hepatobiliary			
Common bile duct injury	0 (0.0)	0 (0.0)	–
Bile leak	9 (1.9)	0 (0.0)	0.610
Retained stone	12 (2.5)	0 (0.0)	0.377
Cholangitis	2 (0.4)	0 (0.0)	1
Biliary stenosis	3 (0.6)	0 (0.0)	1
Infection			
Wound infection	10 (2.1)	0 (0.0)	0.620
Abscess	2 (0.4)	0 (0.0)	1
Sepsis	1 (0.2)	1 (1.5)	0.231
Clostridium difficile colitis	3 (0.6)	0 (0.0)	1
Intravenous catheter infection	1 (0.2)	0 (0.0)	1
Cardiovascular			
Hemorrhage	4 (0.8)	1 (1.5)	0.482
Hemorrhagic shock	1 (0.2)	0 (0.0)	1
Cardiogenic shock	1 (0.2)	0 (0.0)	1
Congestive heart failure exacerbation	3 (0.6)	0 (0.0)	1
Chest pain	1 (0.2)	0 (0.0)	1
Respiratory			
Pneumonia	4 (0.8)	1 (1.5)	0.482
Respiratory failure	2 (0.4)	0 (0.0)	1
Pulmonary embolism	1 (0.2)	0 (0.0)	1
Pulmonary edema	1 (0.2)	0 (0.0)	1
Pleural effusion	1 (0.2)	0 (0.0)	1
Gastrointestinal			
Pancreatitis	6 (1.2)	0 (0.0)	1
Gastroenteritis	1 (0.2)	0 (0.0)	1
Small bowel injury	1 (0.2)	0 (0.0)	1
Ileus	2 (0.4)	0 (0.0)	1
Hernia			
Ventral hernia	1 (0.2)	0 (0.0)	1
Incisional hernia	2 (0.4)	1 (1.5)	0.325
Other			
Seizure	1 (0.2)	0 (0.0)	1
Wound dehiscence	2 (0.4)	0 (0.0)	1
Reactive hydrocele	1 (0.2)	0 (0.0)	1

Level of significance was
[a]*P* < 0.05.

were in their 5th decade of life and one patient was in the 9th decade of life.

In a study by Zafar *et al*[25] using Nationwide Inpatient Sample data from 2005-2009, a multivariate analysis demonstrated that the odds of complications and death increased when cholecystectomy was performed between days 2-5 [mortality OR 1.26 (95%CI: 1.00-1.58)] and 6-10 d [mortality OR = 1.93 (1.38-2.69)] after admission, compared to days 0-1 (OR = 1). Based on this large dataset of with *n* > 95500 patients, the authors determined that the optimal time to perform cholecystectomy was less than 48 h, and that if the timing exceeds 48 h, the delay would result in higher

Table 4 Hospital length of stay, postoperative readmissions, and charges

Variable	Same admission cholecystectomy, (*n* = 486), *n* (%) or mean ± SD	Delayed cholecystectomy, (*n* = 68), *n* (%) or mean ± SD	*P* value
Time to surgical admission (d)		48.3 ± 76.3	
Surgical admission length of stay (d)	3.4 ± 5.3	0.4 ± 1.0	< 0.001[a]
Preoperative (d)	2.2 ± 14.2	0.0 ± 0.2	< 0.001[a]
Postoperative (d)	1.2 ± 14.8	0.4 ± 0.9	0.204
Readmissions after cholecystectomy			
Patients with at least 1 readmission	96 (22.2)	14 (21.2)	0.854
Mean number of readmissions Among those readmitted	1.8 ± 1.5	1.4 ± 0.6	0.074
Total length of stay[1] (d)	3.8 ± 5.5	1.6 ± 2.0	< 0.001[a]
Total hospital charges (× $1000)[2]	44.5 ± 59.0	35.3 ± 16.7	0.019[a]

[1]Total length of stay includes index admission, elective operative admission for delayed cases, and all postoperative complication-related readmissions.
[2]Hospital charges for April 2013-August 2018 only. Level of significance was
[a]$P < 0.05$.

morbidity and mortality. Gutt *et al*[16] found that cholecystectomy within 24 h (mean 0.6 d) of admission had the lowest morbidity compared to delayed cholecystectomy 7-45 d (mean 25 d) after presentation; mortality was equivalent with one death in each group (0.33%). However, Brooks *et al*[26] did not find an association between the timing of SA operation (0 d, 1 d, 2 d, 3 d and ≥ 4 d from admission) with 30-d morbidity and mortality after risk adjustment when analyzing data from the American College of Surgeons National Surgical Quality Improvement Program database; this result may be due to a smaller sample size compared with Zafar's dataset. Although our cohort of patients generally underwent cholecystectomy close to the 48-h time-frame, it is noteworthy that all three deaths were operated on within 24 hours of admission. The mortality rates in Zafar's study were 0.2%, 0.6% and 1.7% for 0-1 d, 2-5 d and 6-10 d, respectively. Interestingly, while Zafar *et al*[25] advocate early cholecystectomy within 48 hours of admission, they note that the mortality rate for day 0 was higher at 0.42%; they hypothesized that some patients may be under-resuscitated at day 0 and therefore at higher risk for death.

In a large retrospective study from Japan and Taiwan, the 30-d mortality rate for among 2947 patients undergoing primary cholecystectomy for TG grades 1, 2, and 3 of acute cholecystitis were 0.3%, 0.4%, and 4.1%, respectively[19]. Joseph *et al*[27] presented contemporary data (*n* = 857) from a single institution and noted no mortality in Tokyo Grade 1 patients, 8 (0.5%) deaths in Grade 2 patients and 6 (1.8%) deaths in Grade 3 patients. Their patient population is a heterogeneous mix, with only 51% who had an elevated WBC and 45% with no ultrasonographic signs of acute cholecystitis. They included a significant number of patients categorized as having "acute on chronic" disease, who do not meet the TG clinical criteria for acute cholecystitis. Although their thesis was that the Tokyo criteria were not sensitive for acute cholecystitis, the inclusion a significant number of patients with normal WBC implies that they had a larger denominator in their reported mortality rate. The mortality rate would be higher with a smaller denominator (if only patients who meet the TG criteria for acute cholecystitis were included). The increase in death rate among the SA group in our study was not statistically significant when compared to the delayed group due to our small sample size; however, postoperative death for a benign condition concerns us sufficiently to revisit the optimal timing of surgical intervention for acute cholecystitis.

To manage "difficult" gallbladders, the WSES recommends subtotal cholecystectomy especially in the acute setting or a delayed cholecystectomy 45 d from symptom onset. We defined a delayed cholecystectomy for acute cholecystitis as a procedure occurring after discharge electively after stabilization of acute disease. However, the literature does not have an agreed upon definition of a "delayed" cholecystectomy and ranges from 1 d to 6 wk after symptom onset, diagnosis, or index presentation. On average, patients in this study received a delayed, elective cholecystectomy 48.3 d from index presentation of acute disease. Our work supports the 2016 WSES recommendations for subtotal cholecystectomies and delayed time frame[1].

A limitation of this study is the retrospective nature of our data; there is selection

Table 5 Logistic regression analysis

Variable	OR	95%CI	P value
Occurrence of any complication - all patients			
Same admission cholecystectomy	0.7	0.1-7.7	0.759
Grade 2	2.1	1.2-3.7	0.007[a]
Grade 3	2.0	0.4-10.2	0.404
Male	1.4	0.8-2.5	0.262
Diabetes	1.2	0.5-3.1	0.722
Hypertension	1.1	0.5-2.4	0.773
Open cholecystectomy	1.1	0.2-5.4	0.863
Insurance status	0.6	0.3-1.2	0.180
Age	1.0	1.0-1.0	0.919
Creatinine	0.9	0.7-1.4	0.780
Occurrence of any complication - Grade 1 patients			
Same admission cholecystectomy	0.2	0.0-1.3	0.094
Diabetes	2.5	0.7-9.0	0.157
Insurance status	0.3	0.1-1.0	0.052
Body mass index	1.1	1.0-1.1	0.048[a]
Occurrence of any complication - Grade 2 patients			
Male	1.9	0.7-5.4	0.238
Smoking status	2.1	0.8-5.7	0.156
Open cholecystectomy	2.1	0.1-31.8	0.598
Age	1.0	1.0-1.0	0.975
Body mass index	1.0	1.0-1.1	0.277
Postoperative length of stay	1.4	1.0-2.1	0.056
Aspartate aminotransferase	1.0	1.0-1.0	0.848
Alanine aminotransferase	1.0	1.0-1.0	0.481
Lipase	1.0	1.0-1.0	0.482
Creatinine	2.8	0.3-30.7	0.402
Occurrence of any complication - Grade 2 or 3 patients			
Male	2.3	1.0-5.1	0.047[a]
Open cholecystectomy	1.3	0.2-9.5	0.767
Age	1.0	1.0-1.0	0.326
Body mass index	1.0	1.0-1.0	0.565
Preoperative length of stay	0.8	0.6-1.0	0.061
Creatinine	1.0	0.7-1.4	0.919

Level of significance was

[a]$P < 0.05$. OR: Odds ratio; CI: Confidence interval.

bias especially for Grade 3 patients, where the small sample size precluded definitive conclusions. Since we did not include preoperative percutaneous cholecystostomy tubes, we likely excluded a significant number of Grade 3 patients from this study. Additionally, hospital charge data for the SA and delayed represent 78.4% and 69.1% of the total patients, respectively. Financial comparisons were made on the majority of patients, but would be more reliable if we could obtain all of the data. Finally, this study represents the experience at one academic, teaching institution with 26 faculty members performing the cholecystectomies. The faculty members are board-certified general surgeons with competency for laparoscopic and open cholecystectomy; only a few self-identify as having specific hepatobiliary or advanced laparoscopic expertise. We have a general surgery training program and all surgeons and surgical residents on these cases have earned Fundamentals of Laparoscopic Surgery-certification. The applicability of this study may not be generalizable in all practice settings.

Our work supports the 2018 TG for the management of Grades 1 and 2 acute cholecystitis[10]. Specifically, if a patient has significant co-morbidities and/or is a high-risk surgical candidate, conservative management with antibiotics, fluid resuscitation, and pain control should be followed by elective cholecystectomy. If the

Table 6 Relative risk, attributable risk, and number needed to harm analysis		
Variable	**Risk**	**95%CI**
All, SA *vs* delayed		
Relative risk	4.2x	1.4 to 12.9[a]
Attributable risk	14.1%	4.6 to 23.6[a]
Number needed to harm	8	5.0 to 12.3[a]
Grade 1, SA *vs* delayed		
Relative risk	1.7x	0.5 to 5.1[a]
Attributable risk	4.9%	-5.7 to 15.5
Number needed to harm	21	-7.2 to 24.4
Grade 2, SA *vs* delayed		
Relative risk[1]	–	–
Attributable risk	26.4%	13.2 to 39.7[a]
Number needed to harm	4	3.0 to 5.0[a]
Grade 2 or 3[2], SA *vs* delayed		
Relative risk[1]	–	–
Attributable risk	28.3%	12.3 to 44.4[a]
Number needed to harm	4	2.9 to 4.6[a]

[1]Relative risk analysis could not be performed in Grades 2 or 3 due to zero complications in the delayed group.
[2]Due to a small sample size of the rarer Grade 3 disease, combined analysis of Grades 2 and 3 was performed to represent all moderate and severe cases.
[a]Statistically significant. CI: Confidence Interval; SA: Same admission.

patient does not improve clinically with conservative management, percutaneous cholecystotomy can be performed to drain the septic source. In this study, we have compared the clinical and economic outcomes of SA cholecystectomy with delayed cholecystectomy for acute cholecystitis. Early cholecystectomy for Tokyo Grades 2 and 3 patients should be considered with care. The risks of complications are higher in these patient groups, leading to greater cost. Future studies are needed to confirm our findings and also should focus on strategies to avoid mortality in these high-risk groups.

In conclusion, patients presenting with acute cholecystitis Tokyo Grade 2 developed more complications and incur increased charges when undergoing SA cholecystectomy compared to a delayed approach. This data supports a selective approach to surgery for patients with acute cholecystitis; Tokyo Grade 2 patients have a lower complication rate when cholecystectomy is delayed.

ARTICLE HIGHLIGHTS

Research background
The timeframe of when to perform cholecystectomy for acute cholecystitis has been controversial for years. Most recently, clinical practice has favored operative intervention during the same admission (SA) (early cholecystectomy). We present a comparison of complications between SA *vs* interval (delayed) cholecystectomy.

Research motivation
Recent enthusiasm for SA cholecystectomy is based on projected economic advantage. We hypothesized that the economic advantage may be lost if complication rates are higher than expected.

Research objectives
We compared the complication rates and hospital charges between SA *vs* delayed cholecystectomy patients. Patients were stratified by Tokyo Grade.

Research methods
We performed a retrospective chart review of all patients at a single institution who presented for cholecystectomy due to acute cholecystitis between February 2010 through August 2018. Hospital charges were also obtained when available. Descriptive statistics were used to compare the groups; a multivariate model on the covariates predicting complications was also performed.

Research results

SA cholecystectomy patients had an overall complication rate of 18.5% compared to Delayed cholecystectomy patients with a complication rate of 4.4% (P = 0.004). For the Tokyo Grade 2 patients (moderate disease), SA and delayed cholecystectomy complication rates were 16% *vs* 0%, respectively (P < 0.001). SA cholecystectomy hospital charges were higher compared to Delayed cholecystectomy (P = 0.019) due to an increase in cost from the management of complications. There were no significant differences in clinical outcomes for Tokyo Grade 1 patients (mild disease). We did not have sufficient numbers of patients with Tokyo Grade 3 (severe disease) for meaningful comparisons.

Research conclusions

Our study demonstrates that SA cholecystectomy patients have higher complication rates with associated higher costs. The data supports a selective approach to operative intervention for acute cholecystitis; Tokyo Grade 2 patients have a lower complication rate when cholecystectomy is Delayed. Risk factors for complications include Tokyo Grade 2 severity of disease. In a risk analysis, among eight patients with acute cholecystitis undergoing SA cholecystectomy, one patient will suffer a complication.

Research perspectives

This study suggests that SA cholecystectomy does not always afford an economic advantage, especially if there are complications. Future studies are needed to confirm our findings since this study is limited because the data was collected retrospectively from a single institution.

ACKNOWLEDGEMENTS

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