The American Journal of Surgery 218 (2019) 1084–1089

Contents lists available at ScienceDirect

The American Journal of Surgery

journal homepage: www.americanjournalofsurgery.com

Ideal timing of early cholecystectomy for acute cholecystitis: An ACS-NSQIP review

Elizabeth A. Alore, Jeremy L. Ward, S. Rob Todd, Chad T. Wilson, Stephanie D. Gordy, Marcus K. Hoffman, James W. Suliburk*

Michael E. DeBakey Department of Surgery, Baylor College of Medicine, One Baylor Plaza MS390, Houston, TX, USA

ARTICLE INFO

Article history:
Received 15 March 2019
Received in revised form
9 July 2019
Accepted 10 August 2019

Keywords:
Acute cholecystitis
Cholecystectomy
ACS-NSQIP
Timing of operation
Surgical outcomes

ABSTRACT

Background: Current guidelines fail to specify optimal timing of early cholecystectomy for acute cholecystitis. We hypothesized delaying operation past hospital day (HD) 2 would result in increased 30-day morbidity and mortality.

Methods: The ACS-NSQIP database was queried from 2012 to 2015 for all cholecystectomies for acute cholecystitis from HD 1-7.

Results: Delay in cholecystectomy to HD 3-7 was observed in 30% of patients with acute cholecystitis. Patients undergoing operation on HD 3-7 were older with higher rates of comorbidities (median 58yrs; 66%) than HD 1 (48yrs; 51%) or HD 2 (51yrs, $p < 0.001$; 55%, $p < 0.001$). Operations on HD 3-7 had increased 30-day mortality (1.0%) and morbidity (12%) in comparison to HD 1 (0.3%, 7%) or HD 2 (0.5%, $p < 0.001$; 8%, $p < 0.001$). On multivariable analysis, HD was an independent predictor of mortality (OR 1.15, 95% CI [1.04–1.26]).

Conclusions: Acute cholecystitis should be treated with an urgent operation within 2 days of admission due to increased morbidity and mortality when delayed past HD 2.

Introduction

Over 400,000 cholecystectomies are performed in the United states each year with acute calculous cholecystitis representing over 70% of cases.[1,2] Early operative intervention during the index admission has become the standard of care over classic teachings that dictated a delay in surgery of 4–6 weeks from initial presentation.[3] However, timing of early cholecystectomy is poorly defined, with some authors defining early operation anywhere between 24 h and 7 days from admission.[4–6] Current consensus guidelines remain ambiguous and inconsistent regarding the ideal timing of early cholecystectomy.[3,7,8]

We aimed to determine national trends in operative intervention for acute cholecystitis and evaluate 30-day outcomes following cholecystectomy using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database. We hypothesized that a delay in operation past hospital day 2 for acute cholecystitis would be associated with increased 30-day morbidity and mortality.

Material and methods

Data source

The ACS-NSQIP database comprises 30-day surgical outcomes from a random sample of patients from participating institutions, including 183 institutions in 2007 to 603 institutions in 2015.[9] A systematic sampling process with an 8-day cycle was utilized by ACS-NSQIP. The database limits reporting to the first three operations performed for each 8-day cycle for common surgical procedures, including laparoscopic cholecystectomy.[10] Quality of data was ensured by requiring each participating site to maintain a 30-day follow-up rate of >80% and inter-rater reliability disagreement rate of <5%.[10]

The ACS-NSQIP database was queried from 2007 to 2015 for all patients undergoing cholecystectomy by Current Procedural Terminology (CPT) code with a post-operative diagnosis of acute cholecystitis by International Classification of Diseases (ICD) code, 9th or 10th edition (Supplemental Table 1). Patients were excluded

* Corresponding author. Baylor College of Medicine, One Baylor Plaza BCM 390, Houston, TX, 77030, USA.
E-mail address: suliburk@bcm.edu (J.W. Suliburk).

https://doi.org/10.1016/j.amjsurg.2019.08.008
0002-9610/

if hospital day (HD) of operation was not reported or if surgery was delayed past HD 7. Within the ACS-NSQIP database, HD is reported as calendar days and does not necessarily represent a 24-h period.[10] The cohort was divided based on HD of operation into HD 1, HD 2, and HD 3–7.

Temporal trends in cholecystectomy

Data from 2007 to 2015 was utilized to examine temporal trends in operations performed for acute cholecystitis. Cholangiogram and common bile duct (CBD) exploration were based on CPT code. Both operations initially listed as open and operations converted from laparoscopic to open were considered open procedures based on CPT codes.

Baseline characteristics and 30-day outcomes

For the analysis of baseline characteristics and 30-day outcomes, the cohort was limited to non-elective operations. This variable was introduced within the database in 2012, and as such, the remainder of the analysis was limited to 2012–2015.

Baseline characteristics including demographics, baseline health status as defined by American Society of Anesthesiology Physical Status (ASA-PS) classification, type of operation performed, comorbid conditions, and clinical risk factors at time of operation were compared between groups. Presence of bile duct stones by post-operative ICD code was used to determine whether presence of concurrent choledocholithiasis may have played a role in delay in surgical intervention (Supplemental Table 1).

Our primary outcome was 30-day major morbidity or mortality. Major complications included acute renal failure, cardiac arrest, cerebrovascular accident or stroke, deep venous thrombosis, myocardial infarction, organ/space surgical site infection (SSI), pneumonia, pulmonary embolism, reintubation, and reoperation related to the initial surgery. Secondary outcomes included minor complications (superficial or deep SSI, prolonged mechanical ventilation, unplanned readmission, red blood cell transfusion intra-operatively or 72 h post-operatively, renal insufficiency, sepsis, septic shock, urinary tract infection, or wound dehiscence) and hospital length of hospital (LOS).

Statistical analyses

Univariate analyses were performed using Pearson's Chi square for categorical variables and Kruskal-Wallis test for continuous variables. Reverse stepwise logistic regression using $p > 0.2$ for removal from the model was performed to determine significant predictors of 30-day morbidity and mortality while controlling for age, sex, race/ethnicity, BMI, ASA-PS class, open procedures, intra-operative cholangiogram or common bile duct (CBD) exploration, number of comorbid conditions, preoperative sepsis, acute renal failure, ventilator dependence, transfusion, presence of concurrent choledocholithiasis, and hospital day of operation.

Number and severity of comorbid conditions is often viewed as a reason for delay in operative intervention. Therefore, a subgroup analysis of 30-day surgical outcomes by ASA-PS class 1 or 2, representing mild systemic disease, vs. 3–5, representing severe to life threatening systemic disease, was performed in an attempt to control for baseline health status as a confounder for poor surgical outcomes.

All statistical analyses were performed using Stata 13.1 (StataCorp LP, College Station, TX) and a p-value <0.05 as significant. This study was exempt from Institutional Review Board approval since the ACS-NSQIP database contains only de-identified patient information.

Results

Temporal trends in cholecystectomy

From 2007 to 2015, open cholecystectomy for the treatment of acute cholecystitis declined from 21% down to 9% (Fig. 1A). Use of intra-operative cholangiogram remained relatively stable and was performed in approximately 25% of cholecystectomies while common bile duct exploration halved, from 2% of cases in 2007 down to 1% of cases in 2015.

Nationally, approximately one-third of cholecystectomies were delayed to HD 3–7 of admission, a trend that remained relatively constant over the study period (Fig. 1B). Starting in 2012, our cohort was limited to non-elective surgeries. By definition, elective operations are mostly performed on HD 1 of admission. Therefore, we believe introduction of this variable resulted in the sharp decline in cholecystectomies performed on HD 1 observed between 2011 and 2012.

Baseline characteristics

Of 34,151 cholecystectomies for acute cholecystitis performed from 2012 to 2015, 33% were on HD 1, 37% on HD 2, and 30% were delayed until HD 3–7. Patients who had a delay in operation until HD 3–7 had a higher median age (58 yrs) than HD 1 (48 yrs) or HD 2 (51 yrs; $p < 0.001$, Table 1). Patients on HD 3–7 also had poorer baseline health status with 50% of patients being classified as ASA class 3–5 as compared to 26% on HD 1 and 33% on HD 2 ($p < 0.001$). Rates of open cholecystectomy and intra-operative common bile duct exploration significantly increased with surgical delay, while rates of cholangiogram remained relatively stable. Likewise,

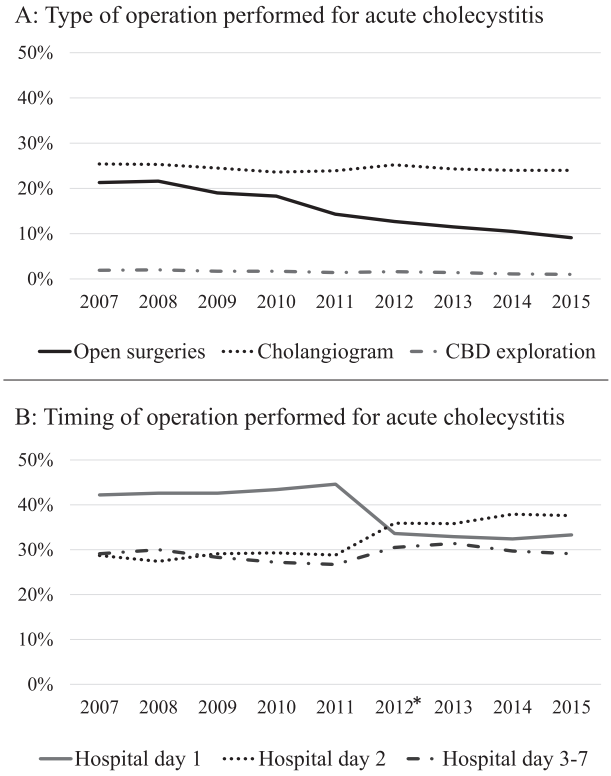

Fig. 1. Temporal trends in cholecystectomy for acute cholecystitis. *A variable for elective surgeries was added to the ACS-NSQIP database in 2012. For all years after 2012, only non-elective surgeries were included in the analysis. Abbreviations: CBD = common bile duct.

Table 1
Baseline characteristics, comorbid conditions and clinical risk factors of patients with acute cholecystitis undergoing cholecystectomy by hospital day of operation.

	Total n = 34,151(%)	HD 1 n = 11,280 (%)	HD 2 n = 12,624 (%)	HD 3–7 n = 10,247 (%)	p-value
Age (yrs.), median (IQR)	52 (37–66)	48 (35–62)	51 (36–65)	58 (41–72)	<0.001
Gender					<0.001
Male	13,514 (40)	4,291 (38)	4,814 (38)	4,409 (43)	
Female	20,637 (60)	6,989 (62)	7,810 (62)	5,838 (57)	
Race/Ethnicity					<0.001
Non-Hispanic White	19,716 (64)	6,411 (63)	7,466 (65)	5,839 (63)	
Non-Hispanic Black	3,335 (11)	911 (9)	1,253 (11)	1,171 (13)	
Hispanic	6,227 (20)	2,247 (22)	2,189 (19)	1,791 (19)	
Asian	1,270 (4.1)	460 (4.5)	431 (3.8)	379 (4.1)	
Other	374 (1.2)	134 (1.3)	136 (1.2)	104 (1.1)	
BMI (kg/m^2), median (IQR) (n = 32,545)	30 (26–35)	30 (26–35)	30 (26–35)	30 (26–35)	<0.001
ASA-PS class (n = 34,109)					<0.001
1- No disturbance	3,424 (10)	1,389 (12)	1,354 (11)	681 (6.7)	
2- Mild disturbance	18,311 (54)	6,871 (61)	7,062 (56)	4,378 (43)	
3- Severe disturbance	10,971 (32)	2,754 (24)	3,805 (30)	4,412 (43)	
4- Life threatening	1,390 (4.1)	244 (2.2)	388 (3.1)	758 (7.4)	
5- Moribund	13 (0.04)	5 (0.04)	2 (0.02)	6 (0.06)	
Procedure Type					<0.001
Laparoscopic	30,501 (89)	10,337 (92)	11,445 (91)	8,719 (85)	
Open	3,650 (11)	943 (8)	1,179 (9)	1,528 (15)	
Cholangiogram	8,297 (24)	2,608 (23)	3,103 (25)	2,586 (25)	0.001
CBD exploration	415 (1.2)	91 (0.8)	132 (1.1)	192 (1.9)	<0.001
Comorbid conditions					
Hypertension	12,804 (37)	3,469 (31)	4,449 (35)	4,886 (48)	<0.001
Current smoker[a]	6,377 (19)	2,185 (19)	2,424 (19)	1,768 (17)	<0.001
Diabetes mellitus	4,904 (14)	1,313 (12)	1,680 (13)	1,911 (19)	<0.001
Bleeding disorder[b]	1,788 (5.2)	291 (2.6)	556 (4.4)	941 (9.2)	<0.001
Dyspnea					<0.001
With moderate exertion	1,243 (3.6)	258 (2.3)	405 (3.2)	580 (5.7)	
At rest	137 (0.4)	21 (0.2)	51 (0.4)	65 (0.6)	
Severe COPD	1,054 (3.1)	249 (2.2)	314 (2.5)	491 (4.8)	<0.001
Chronic steroid use[c]	788 (2.3)	191 (1.7)	274 (2.2)	323 (3.2)	<0.001
Congestive heart failure[d]	297 (0.9)	43 (0.4)	56 (0.4)	198 (1.9)	<0.001
>10% loss of body weight[e]	254 (0.7)	50 (0.4)	72 (0.6)	132 (1.3)	<0.001
Open wound	251 (0.7)	39 (0.4)	71 (0.6)	141 (1.4)	<0.001
Dialysis[f]	250 (0.7)	38 (0.3)	55 (0.4)	157 (1.5)	<0.001
Disseminated cancer	192 (0.6)	38 (0.3)	69 (0.6)	85 (0.8)	<0.001
Ascites[d]	93 (0.3)	17 (0.2)	27 (0.2)	49 (0.5)	<0.001
Any comorbid condition	19,357 (57)	5,702 (51)	6,929 (55)	6,726 (66)	<0.001
Clinical Risk Factors					
Systemic Sepsis[g]					<0.001
SIRS	5,676 (17)	1,780 (16)	2,355 (19)	1,541 (15)	
Sepsis	2,025 (6)	541 (4.8)	808 (6.4)	676 (6.6)	
Septic shock	171 (0.5)	28 (0.3)	65 (0.5)	78 (0.8)	
RBC Transfusion[h]	210 (0.6)	22 (0.2)	35 (0.3)	153 (1.5)	<0.001
Acute renal failure[i]	123 (0.4)	16 (0.1)	37 (0.3)	70 (0.7)	<0.001
Ventilator dependent[g]	62 (0.2)	8 (0.1)	17 (0.1)	37 (0.4)	<0.001
Concurrent bile duct stone[j]	4,173 (12)	696 (6)	1,091 (9)	2,386 (23)	<0.001

Abbreviations: HD = hospital day; IQR = interquartile range; BMI = body mass index; SD = standard deviation; ASA-PS = American Society of Anesthesiologists Physical Status; COPD = chronic obstructive pulmonary disease; SIRS = systemic inflammatory response syndrome; RBC = red blood cell.

[a] Within 1 year before surgery.
[b] Includes medical conditions leading to increased risk of bleeding and chronic anticoagulation therapy (excluding aspirin) not discontinued before surgery.
[c] Use of oral or parenteral steroids within 30 days before surgery for a chronic medical condition.
[d] Within 30 days before surgery.
[e] Unintentional weight loss within 6 months before surgery.
[f] Within 2 weeks before surgery for an acute or chronic condition.
[g] Within 48 h before surgery.
[h] Within 72 h before surgery.
[i] Within 24 h before surgery.
[j] Based on ICD-9 or ICD-10 codes.

patients undergoing operation on HD 3–7 had a higher rate of concurrent bile duct stones (23%) in comparison to HD 1 (6%) or HD 2 (9%; $p < 0.001$). Delay in operation to HD 3–7 was also associated with an increased number of comorbid conditions with hypertension, tobacco use, and diabetes being most common (Table 1). Patients undergoing operation on HD 3–7 had increased rates of clinical risk factors including preoperative blood transfusion, sepsis or septic shock, and evidence of end-organ damage including acute renal failure or ventilator dependence.

30-Day outcomes

Patients who underwent cholecystectomy on hospital day 3–7 had a 2-fold increase in 30-day mortality in comparison to operations performed on hospital day 1 or 2 of admission ($p < 0.001$, Table 2). Hospital day 3–7 cholecystectomies also had increased 30-day major morbidity at 5.2% in comparison to 3.2% on HD 1 and 3.7% on HD 2 ($p < 0.001$). Rate of experiencing any complication increased to 12% when operation was delayed, in comparison to 7%

Table 2
30-day morbidity and mortality after cholecystectomy for acute cholecystitis by hospital day of operation.

	Total n = 34,151 (%)	HD 1 n = 11,280 (%)	HD 2 n = 12,624 (%)	HD 3–7 n = 10,247 (%)	p-value
Mortality	193 (0.6)	31 (0.3)	59 (0.5)	103 (1.0)	<0.001
Major complications	1,357 (4.0)	362 (3.2)	466 (3.7)	529 (5.2)	<0.001
Organ/Space SSI	404 (1.2)	109 (1.0)	143 (1.1)	152 (1.5)	0.002
Reoperation[a]	373 (1.1)	108 (1.0)	137 (1.1)	128 (1.3)	0.12
Pneumonia[b]	283 (0.8)	60 (0.5)	98 (0.8)	125 (1.2)	<0.001
Reintubation	217 (0.6)	53 (0.5)	63 (0.5)	101 (1.0)	<0.001
Deep venous thrombosis	110 (0.3)	23 (0.2)	38 (0.3)	49 (0.5)	0.002
Acute renal failure[c]	92 (0.3)	20 (0.2)	23 (0.2)	49 (0.5)	<0.001
Myocardial infarction	85 (0.3)	25 (0.2)	31 (0.3)	29 (0.3)	0.66
Pulmonary embolism	66 (0.2)	19 (0.2)	23 (0.2)	24 (0.2)	0.51
Cardiac arrest	58 (0.2)	8 (0.1)	19 (0.2)	31 (0.3)	<0.001
CVA/stroke	28 (0.1)	10 (0.1)	7 (0.1)	11 (0.1)	0.38
Minor complications					
Readmission[a]	1,271 (3.7)	381 (3.4)	443 (3.5)	447 (4.4)	<0.001
RBC Transfusion	674 (2.0)	129 (1.1)	195 (1.5)	350 (3.4)	<0.001
Superficial SSI	280 (0.8)	83 (0.7)	113 (0.9)	84 (0.8)	0.40
Sepsis[b]	191 (0.6)	42 (0.4)	56 (0.4)	93 (0.9)	<0.001
Prolonged ventilation[d]	175 (0.5)	36 (0.3)	50 (0.4)	89 (0.9)	<0.001
Urinary tract infection[b]	152 (0.5)	46 (0.4)	57 (0.5)	49 (0.5)	0.73
Septic shock[b]	95 (0.3)	19 (0.2)	34 (0.3)	42 (0.4)	0.003
Renal insufficiency	91 (0.3)	14 (0.1)	31 (0.3)	46 (0.5)	<0.001
Deep SSI	50 (0.2)	13 (0.1)	14 (0.1)	23 (0.2)	0.047
Wound dehiscence	32 (0.1)	9 (0.1)	11 (0.1)	12 (0.1)	0.64
Any complication	3,062 (9.0)	804 (7.1)	1,050 (8.3)	1,208 (12)	<0.001
Length of stay, days median (IQR)	3 (2–4)	1 (1–2)	2 (2–3)	5 (3–7)	<0.001

Abbreviations: HD = hospital day; SSI = surgical site infection; CVA = cerebrovascular accident; RBC = red blood cell; IQR = interquartile range.
[a] Unplanned and related to primary operation.
[b] Excluded if evidence of condition documented in pre-operative period.
[c] Dialysis in patient who did not require dialysis pre-operatively.
[d] Prolonged mechanical ventilation for >48 h post-operatively.

for operations performed on HD 1 and 8% for operations performed on HD 2 ($p < 0.001$). In addition, hospital LOS was significantly increased with delayed operation, with median LOS of 5 days for HD 3–7 operations in comparison to 1 day for HD 1 and 2 days for HD 2 ($p < 0.001$).

On multivariable logistic regression, hospital day of operation was not a significant predictor of major complications ($p = 0.29$). However, when controlling for demographics, comorbid conditions and clinical risk factors, hospital day of operation remained a significant predictor of 30-day mortality (OR 1.15, 95% CI [1.04–1.26]; Table 3).

Subgroup analysis based on ASA-PS class

A subgroup analysis of patients based on ASA-PS class was performed to control for poorer baseline health status observed with delay in operation (Table 4). Among the healthiest subset of patients with ASA-PS class 1–2, peri-operative blood transfusion and hospital LOS were significantly increased with a delay to HD 3–7. Of patients with an ASA-PS class of 3–5, representing the group of patients with the poorest baseline health status, we observed significantly higher rates of mortality, major complications and all complications with a delay in surgery in addition to prolonged LOS (Table 4).

Discussion

We provide further support that cholecystectomy for acute cholecystitis should be treated as an urgent surgical condition and cholecystectomy should be performed within 2 days of hospital admission. We observed a 1.4-times increase in major complications and 2-times increase in mortality when surgery was delayed to HD 3–7. Furthermore, HD of operation was an independent predictor of 30-day mortality. Other contributory factors leading to increased post-operative complications include comorbid conditions, baseline health status, and open operations. Subgroup

Table 3
Factors associated with major complications and mortality following cholecystectomy for acute cholecystitis on logistic regression.

	Major Complications		*p*-value	Mortality		*p*-value
	OR	[95% CI]		OR	[95% CI]	
Age (yrs.)	1.02	[1.01–1.02]	<0.001	1.07	[1.06–1.09]	<0.001
Female gender	0.87	[0.77–0.98]	0.02	–		NS
ASA-PS class	1.52	[1.38–1.68]	<0.001	2.89	[2.20–3.81]	<0.001
Open procedure	2.09	[1.82–2.39]	<0.001	1.51	[1.07–2.12]	0.02
Cholangiogram	–		NS	0.48	[0.31–0.75]	0.001
# of Comorbid conditions	1.26	[1.19–1.32]	<0.001	1.28	[1.13–1.45]	<0.001
Preoperative sepsis	1.52	[1.41–1.63]	<0.001	1.52	[1.28–1.80]	<0.001
Acute renal failure	2.69	[1.73–4.19]	<0.001	2.41	[1.07–5.42]	0.03
Ventilator dependent	–		NS	6.78	[3.08–14.9]	<0.001
Hospital day of operation	–		NS	1.15	[1.04–1.26]	0.01

Abbreviations: OR = odds ratio; CI = confidence interval; NS = not significant; ASA-PS = American Society of Anesthesiologists Physical Status.

Table 4
30-day outcomes after cholecystectomy stratified by ASA-PS class and hospital day of operation.

Outcome	ASA-PS class 1-2				ASA-PS class 3-5			
	HD 1 n=8,260 (%)	HD 2 n=8,416 (%)	HD 3-7 n=5,059 (%)	*p*-value	HD1 n=3,020 (%)	HD2 n=4,208 (%)	HD3-7 n=5,188 (%)	*p*-value
Mortality	3 (0.04)	7 (0.08)	7 (0.14)	0.12	28 (0.9)	52 (1.2)	96 (1.9)	<0.01
Reoperation [a]	65 (0.8)	70 (0.8)	30 (0.6)	0.28	43 (1.4)	67 (1.6)	98 (1.9)	0.25
Readmission [a]	237 (2.9)	240 (2.9)	163 (3.2)	0.43	144 (4.8)	203 (4.8)	284 (5.5)	0.25
SSI [b]	99 (1.2)	134 (1.6)	78 (1.5)	0.08	97 (3.2)	132 (3.1)	173 (3.3)	0.86
Pulmonary [c]	30 (0.4)	36 (0.4)	30 (0.6)	0.15	86 (2.9)	133 (3.2)	214 (4.1)	<0.01
Cardiovascular [d]	9 (0.1)	6 (0.1)	8 (0.2)	0.32	32 (1.1)	46 (1.1)	58 (1.1)	0.97
Genitourinary [e]	33 (0.4)	33 (0.4)	24 (0.5)	0.75	46 (1.5)	77 (1.8)	119 (2.3)	0.04
Thromboembolic [f]	29 (0.4)	23 (0.3)	14 (0.3)	0.61	10 (0.3)	31 (0.7)	53 (1.0)	<0.01
RBC transfusion	38 (0.5)	51 (0.6)	44 (0.9)	0.01	91 (3.0)	144 (3.4)	306 (5.9)	<0.01
Sepsis [g]	23 (0.3)	29 (0.3)	27 (0.5)	0.06	38 (1.3)	60 (1.4)	105 (2.0)	0.01
Major complication	168 (2.0)	182 (2.2)	120 (2.4)	0.43	194 (6.4)	284 (6.8)	409 (7.9)	0.02
Any complication	419 (5.1)	473 (5.6)	304 (6.0)	0.06	385 (13)	577 (14)	904 (17)	<0.01
Length of stay, d median (IQR)	1 (1-2)	2 (2-3)	4 (3-5)	<0.01	2 (1-4)	3 (2-5)	6 (4-8)	<0.01

Abbreviations: ASA = American Society of Anesthesiologists; HD = hospital day; SSI = surgical site infection; RBC = red blood cell; IQR = interquartile range.
[a] Unplanned and related to primary operation.
[b] Includes superficial, deep and organ/space SSI.
[c] Includes pneumonia, prolonged mechanical ventilation, and reintubation.
[d] Includes myocardial infarction, cardiac arrest and cerebrovascular accident.
[e] Includes urinary tract infection, renal insufficiency and acute renal failure.
[f] Includes deep venous thrombosis and pulmonary embolism.
[g] Includes post-operative sepsis and septic shock.

analysis performed to look at patients with the worst baseline health as defined by ASA-PS class 3–5 revealed surgical delay was even more detrimental in this group.

Rates of morbidity and mortality when cholecystectomy for acute cholecystitis is delayed has been previously presented with mixed results. Our findings are consistent with those of Banz et al. who observed a similar 2-fold increase in post-operative complications when operation was performed on day of admission compared to delay past HD 6.[11] Furthermore, Blohm et al. observed significantly lower rates of bile duct injury when operation was performed on HD 1, with a stepwise increase in risk of this most dreaded complication with each subsequent day of operative delay.[12]

However, a similar study using data from ACS-NSQIP from 2005 to 2010 concluded a delay in surgery past HD 4 did not increase 30-day morbidity or mortality.[13] One major difference in methodology is that this study utilized emergent surgeries as an inclusion criteria, defined as needing to proceed to the operating room within 12 h of presentation by the operating surgeon. As such, 83% of the cohort had operations performed on HD 1 or 2 of admission in comparison to 67% of our cohort. Utilizing only cases classified as an emergency likely eliminated a large subset of patients presenting with acute cholecystitis as most surgeons may not classify this condition as a surgical emergency.

Over the study period, we observed a decreasing rate of open cholecystectomies, from 21% in 2007 to 9% in 2015. This trend persisted even after our cohort was limited to non-elective operations after 2012. Previous reports have established non-elective cholecystectomies to have higher rates of open operations due to increased technical difficulty and patient factors in the non-elective setting.[14,15] As such, the persistent decline in open cholecystectomy after 2012, when operations were limited to non-elective procedures, may reflect surgeons' increased experience with laparoscopic technique over time.

Furthermore, we observed a low rate of open cholecystectomy occurring in 11% of cases, ranging from 8% on HD 1 to15% on HD 3–7. This rate is considerably lower than previous studies including Brooks et al. and Degrate et al. with reported rates of open cholecystectomy >20%, and consistent with conversion rates ranging from 9 to 15% reported by To et al. and 8%–22% reported by Sugrue et al.[13–16] With increased experience and technical skill over the years, laparoscopic cholecystectomy has become the gold standard for acute cholecystitis with lower rates of major morbidity and mortality in addition to shorter hospital LOS.[17] We suspect the increased rate of open cholecystectomies with subsequent HD likely reflects increasing complexity of operation secondary to inflammatory changes when operation is delayed, contributing to the overall increase in major morbidity and mortality observed on HD 3–7.

Oftentimes, surgery is delayed for medical optimization in patients with a multitude of comorbid conditions. On subgroup analysis of patients with ASA class of 3–5, we revealed that delay in operation to HD 3–7 had significantly increased 30-day morbidly and mortality, with 8% of patients experiencing a major complication, 17% of patients experiencing any complication, and a mortality rate of 1.9%. Similarly, Haltmeier et al. observed early cholecystectomy for elderly patients with an ASA-PS class >2 was an independent predictor of shorter operative times and LOS without an increase in post-operative complications.[18] From this data, it appears early operative intervention is preferable to delay in surgery in this cohort. On the contrary, patients with a low ASA-PS class can better tolerate a delay in operation without increased morbidity or mortality.

Additionally, in an era when healthcare costs and resource utilization has become a top priority, we observed a significantly increased LOS with operative delay. Zafar et al. reported that delaying cholecystectomy for acute cholecystitis has a linear increase in healthcare costs, from $8,964 for HD 1 operations to $17,745 for operations performed past HD 6.[19] As cholecystectomy is the 6th most common operation in the United States requiring hospital admission, there is a real potential to increase healthcare savings with earlier surgical intervention.[1]

A limitation of this study is the inability to determine whether operative delay was secondary to concurrent choledocholithiasis, requiring magnetic resonance cholangiopancreatography (MRCP) or endoscopic retrograde cholangiopancreatography (ERCP) prior to surgical intervention. We observed a significantly higher rate of bile duct stones in patients with delayed cholecystectomy to HD 3–7. However, bile duct stones by ICD code were not predictors of either major morbidity or mortality on logistic regression. The rate

of reported choledocholithiasis in the setting of acute cholecystitis varies widely in the literature from <1% to 18%, therefore making it difficult to ascertain the impact of this variable on our results.[20,21]

Additional limitations of our study include its retrospective nature and limitations inherent to the ACS-NSQIP database. The ACS-NSQIP random sampling process of limiting laparoscopic cholecystectomies to 3 procedures per 8-day cycle may have falsely decreased the proportion of laparoscopic to open cholecystectomies reported. We were also unable to assess time from symptom onset to hospital admission which may contribute to the total time from start of pathology to operative intervention. Furthermore, information on preoperative management such as antibiotic use or cholecystostomy tube placement, pre-operative diagnosis, and specific complications related to cholecystectomy, including bile duct injury or retained common bile duct stones, are not available within the database. Lastly, diagnosis of acute cholecystitis was based on ICD-9 or 10 codes and not pathology which remains the gold standard for diagnosis.

Conclusions

Population level data reveals that 30% of cholecystectomies for acute cholecystitis are delayed to HD 3–7 nationally. We observed increased 30-day morbidity and mortality of cholecystectomy when delayed past HD 2. Other contributory factors include decreased baseline health status and increased complexity of operation in the delayed group. However, HD was an independent predictor of mortality. Our results suggest that cholecystectomy in the setting of acute cholecystitis should be treated as an urgent operation.

Disclosures

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) and the hospitals participating in the ACS-NSQIP are the source of the data used herein; they have not verified and are not responsible for the statistical validity of the data or the conclusions.

Conflicts of interest

The authors declare no conflicts of interest, either personal or financial.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjsurg.2019.08.008.

References

1. Fingar KR, Stocks C, Weiss AJ, Steiner CA. *Most Frequent Operating Room Procedures Performed in U.S. Hospitals, 2003-2012. Healthcare Cost and Utilization Project*; 2014. https://www.hcup-us.ahrq.gov/reports/statbriefs/sb186-Operating-Room-Procedures-United-States-2012.jsp. Accessed March 6, 2019.
2. Alli VV, Yang J, Xu J, et al. Nineteen-year trends in incidence and indications for laparoscopic cholecystectomy: the NY State experience. *Surg Endosc*. 2017;31(4):1651–1658. https://doi.org/10.1007/s00464-016-5154-9.
3. Mayumi T, Okamoto K, Takada T, et al. Tokyo Guidelines 2018: management bundles for acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Sci*. 2018;25:96–100. https://doi.org/10.1002/jhbp.519.
4. Strasberg SM. Clinical practice: acute calculous cholecystitis. *N Engl J Med*. 2008;358(26):2804–2811.
5. de Mestral C, Rotstein OD, Laupacis A, et al. Comparative operative outcomes of early and delayed cholecystectomy for acute cholecystitis: a population-based propensity score analysis. *Ann Surg*. 2014;259(1):10–15. https://doi.org/10.1097/SLA.0b013e3182a5cf36.
6. Gurusamy K, Samraj K, Gluud C, Wilson E, Davidson BR. Meta-analysis of randomized controlled trials on the safety and effectiveness of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. *Br J Surg*. 2010;97:141–150. https://doi.org/10.1002/bjs.6870.
7. Ansaloni L, Pisano M, Coccolini F, et al. WSES guidelines on acute calculous cholecystitis. *World J Emerg Surg*. 2016;11(25):1–23. https://doi.org/10.1186/s13017-016-0082-5, 2016.
8. Kluger Y, Ben-Ishay O, Sartelli M, et al. World society of emergency surgery study group initiative on Timing of Acute Care Surgery classification (TACS). *World J Emerg Surg*. 2013;8(17):1–6. https://doi.org/10.1186/1749-7922-8-17.
9. American College of Surgeons. ACS NSQIP participant use data file. https://www.facs.org/quality-programs/acs-nsqip/participant-use. Accessed March 9, 2019.
10. American College of Surgeons. *User Guide for the 2015 ACS NSQIP Participant Use Data File (PUF)*; 2016. https://www.facs.org/~/media/files/quality programs/nsqip/nsqip_puf_user_guide_2015.ashx. Accessed March 9, 2019.
11. Banz V, Gsponer T, Candinas D, Guller U. Population-based analysis of 4113 patients with acute cholecystitis: defining the optimal time-point for laparoscopic cholecystectomy. *Ann Surg*. 2011;254(6):964–970. https://doi.org/10.1097/SLA.0b013e318228d31c.
12. Blohm M, Österberg J, Sandblom G, Lundell L, Hedberg M, Enochsson L. The sooner, the better? The importance of optimal timing of cholecystectomy in acute cholecystitis: data from the National Swedish Registry for Gallstone Surgery, GallRiks. *J Gastrointest Surg*. 2017;21:33–40. https://doi.org/10.1007/s11605-016-3223-y.
13. Brooks KR, Scarborough JE, Vaslef SN, Shapiro ML. No need to wait: an analysis of the timing of cholecystyectomy during admission for acute cholecystitis using the American College of Surgeons National Surgical Quality Improvement Program database. *J Trauma Acute Care Surg*. 2012;74(1):167–174. https://doi.org/10.1097/TA.0b013e3182788b71.
14. Sugrue M, Coccolini F, Bucholc M, Johnston A, and contributors from WSES. Intra-operative gallbladder scoring predicts conversion of laparoscopic to open cholecystectomy: a WSES prospective collaborative study. *World J Emerg Surg*. 2019;14:12. https://doi.org/10.1186/s13017-019-0230-9.
15. To KB, Cherry-Bukowiec JR, Englesbe MJ, et al. Emergent versus elective cholecystectomy conversion rates and outcomes. *Surg Infect*. 2013;14(6). https://doi.org/10.1089/sur.2012.160.
16. Degrate L, Ciravegna AL, Luperto M, et al. Acute cholecystitis: the golden 72-h period is not a strict limit to perform early cholecystectomy. Results from 316 consecutive patients. *Langenbeck's Arch Surg*. 2013;398:1129–1136. https://doi.org/10.1007/s00423-013-1131-0.
17. Coccolini F, Catena F, Pisano M, et al. Open versus laparoscopic cholecystectomy in acute cholecystitis. Systematic review and meta-analysis. *Int J Surg*. 2015;18:196–204. https://doi.org/10.1016/j.ijsu.2015.04.083.
18. Haltmeier T, Benjamin E, Inaba K, Lam L, Demetriades D. Early versus delayed same-admission laparoscopic cholecystectomy for acute cholecystitis in elderly patients with comorbidities. *J Trauma Acute Care Surg*. 2015;78(4):801–807. https://doi.org/10.1097/TA.0000000000000577.
19. Zafar SN, Obirieze A, Adesibikan B. *Optimal Time for Early Laparoscopic Cholecystectomy for Acute Cholecystitis*. vol. 20060. 2015:129–136. https://doi.org/10.1001/jamasurg.2014.2339, 2.
20. Gouveia C, Loureiro R, Ferreira R, et al. Performance of the choledocholithiasis diagnostic score in patients with acute cholecystitis. *GE Port J Gastroenterol*. 2018;25:24–29. https://doi.org/10.1159/000479973.
21. Chrisholm PR, Patel AH, Law RJ, et al. Preoperative predictors of choledocholithiasis in patients presenting with acute calculous cholecystitis. *Gastrointest Endosc*. 2019;89(5):977–983. https://doi.org/10.1016/j.gie.2018.11.017.