

Utility of liver function tests in acute cholecystitis

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Backgrounds/Aims: Common bile duct stones (CBDS) affect the management of acute cholecystitis (AC). This study aims to investigate the utility of liver function tests (LFTs) in predicting the presence of CBDS in AC patients. **Methods:** Retrospective cohort study of adult patients with AC found in the American College of Surgeons National Surgical Quality Improvement Program database from 2008 to 2016. Patients were classified into two groups, without CBDS (AC⁻) and with CBDS (AC⁺). LFT results namely total bilirubin, SGOT and ALP were collected and categorized into normal and abnormal with the cut-offs of 1.2 mg/dl for total bilirubin, 40 U/L for SGOT and 120 IU/L for ALP. Measures of diagnostic accuracy for individual and combinations of LFTs were computed. **Results:** A total of 32,839 patients were included in the study, with 8,801 (26.8%) AC⁺ and 24,038 (73.2%) AC⁻ patients. Their mean age was 52.4 (±18.6) years and over half (59.1%) were females. Mean LFT results were significantly higher in the AC⁺ group for total bilirubin (1.82 vs 0.97), SGOT (110.9 vs 53.3) and ALP (164.4 vs 102.3) ($p < 0.0001$). The proportions of abnormal LFTs were significantly higher in the AC⁺ group for total bilirubin (47.7% vs 20.2%), SGOT (62.8% vs 27.1%) and ALP (56.6% vs 21.0%) ($p < 0.0001$). Among AC⁺, the odds of having abnormal results for bilirubin, SGOT and ALP were found to be 3.61, 4.54 and 4.90 times higher than among AC⁻, respectively. **Conclusions:** Abnormal LFTs are strong predictors for the presence of CBDS in patients with AC. Normal LFTs should be interpreted with caution as some patients with AC and CBDS might not present with characteristic abnormalities in results. (*Ann Hepatobiliary Pancreat Surg* 2019;23: 219-227)

Key Words: Acute cholecystitis; Common bile duct stone; Liver function test; Predictive value; Screening test

INTRODUCTION

Up to 7-20% of cases of acute cholecystitis (AC) are caused by a common bile duct stone (CBDS).¹⁻³ The presence of a CBDS affects the management of AC in terms of timing and type of surgery. The diagnostic workup for a suspected AC case in the Emergency Department (ED), namely gallbladder ultrasounds and possibly abdominal CT scans are not highly sensitive or specific for detecting a CBDS.^{4,5} Delays in definitive disposition and management (cholecystectomy) of patients with AC can result from additional workup such as magnetic resonance cholangio-

pancreatography (MRCP) and/or endoscopic retrograde cholangiopancreatography (ERCP) which have high sensitivity and specificity for CBDS but are expensive, and not readily available in an ED setting.

Liver function tests (LFTs) levels in AC have been used to predict the presence of a CBDS.^{6,7} Patients with AC and CBDS (AC⁺) or with AC without a CBDS (AC⁻) can pathophysiologically have high LFTs.⁸ While LFT elevation in AC⁺ may be a direct effect of the obstructing CBDS, in patients with AC⁻, high LFT values may result from reactive hepatitis, portal tract inflammation, and direct pressure on biliary tract.⁹⁻¹²

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Abnormal LFTs are more common in AC⁺ than in AC⁻.^{6,8} Elevated LFTs were previously found to be significantly and independently associated with the presence of CBDS.¹³ Another study by Padda et al.⁸ found that the LFTs were all abnormal in 53% of AC⁺ as compared to 18% of AC⁻ only, while all LFTs were normal in 35% of patients with AC⁻ and 0.5% of AC⁺ patients. Abnormal LFTs (including g-GT, alkaline phosphatase, ALT, and total bilirubin) were also previously identified as strong predictors for CBDS.^{8,13}

The utility of LFTs in predicting the presence of CBDS was however challenged by several other studies. One study reported that only 42% of the cases with elevated liver enzymes also had a CBDS.¹³ Many other studies found limited evidence for the link between LFTs and the presence of a CBDS.¹⁴⁻¹⁶ One study even suggested that none of the laboratory results were related to the presence of a CBDS.¹⁷ It is worth noting that even studies that found significant correlations between LFTs and the presence of a CBDS found relatively high numbers of false positive and false negative findings¹³ questioning their use as predictors for CBDS.

In this study, we aimed to describe characteristics of patients with confirmed acute cholecystitis and assess the utility of LFTs in predicting the presence of a CBDS in a large sample of patients from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database.

MATERIALS AND METHODS

Setting and study population

This is a retrospective cohort study of all adult patients with a diagnosis of AC found in the ACS NSQIP database between the years of 2008 and 2016. The ACS NSQIP is one of the first nationally validated programs obtaining risk-adjusted surgical outcomes for quality improvement purposes. The NSQIP database contains Health Insurance Portability and Accountability Act (HIPAA) de-identified data from over 600 participating hospitals. It includes comprehensive clinical data on more than 150 variables for patients undergoing surgical procedures, including patient demographics, preoperative risk factors, laboratory results and postoperative mortality and morbidity outcomes but excluding data on procedures performed on patients less than 18 years of age or those with an American Society

of Anesthesiologists (ASA) score of 6, trauma cases, or cases referred to as 'minor'.¹⁸ The ACS provides certified surgical clinical reviewers recording patient variables intensive training programs and continuous education in order to standardize data collection. They also conduct routine auditing to ensure data consistency and reliability. A systematic sampling strategy influenced by hospitals' surgical volume is adopted for a broad and diverse mixture of operative procedures to be captured.

An Institutional Review Board (IRB) exemption was obtained from the American University of Beirut to conduct this study using the HIPAA deidentified database.

The ACS NSQIP database was reviewed for all adult patients with a diagnosis of AC between the years of 2008 and 2016. AC cases were identified using International Classification of Disease (ICD) 9 and 10 diagnosis codes (Appendix 1).

Patients with active malignancy, whether they were known to have disseminated cancer or on radiotherapy for malignancy within the last 90 days or on chemotherapy for malignancy in less than 30 days were excluded from our study. We also excluded patients with missing data on all LFTs, as well as those with concomitant health conditions that might have affected LFT results such as patients on dialysis pre-operatively and patients with ascites, congestive heart failure or bleeding disorders.¹⁹

Patients were then classified into two groups, cases of AC⁻ and AC⁺. ICD 9 and 10 codes were used to categorize the AC patients based on the presence or absence of CBDS (Appendix 1).

Data collection

Collected variables included demographic information (age, race, gender), comorbidities, ASA physical status classification class, body mass index (BMI), sepsis rates and pre-operative liver function tests available in the NSQIP database namely alkaline phosphatase (ALP), serum glutamic-oxaloacetic transaminase (SGOT) and total bilirubin. LFTs were measured using standard hospital laboratory techniques. Bilirubin was categorized as normal when ≤ 1.2 mg/dl and abnormal when > 1.2 mg/dl. SGOT was categorized as normal when ≤ 40 U/L and abnormal when > 40 U/L. ALP was categorized as normal when ≤ 120 IU/L and abnormal when > 120 IU/L.

Data analysis

A descriptive analysis among all patients and among AC⁺ and AC⁻ groups was carried out, with continuous variables presented as means±standard deviations and categorical variables presented as frequencies with percentages. This was followed by a bivariate analysis using Student's t-test and Pearson's Chi-square test to compare patients' characteristics between AC⁺ and AC⁻ groups.

The association between LFTs and the outcome of CBDS was assessed with LFTs considered individually and in combination. The LFT tests' results were first described and compared between patients with and without stone. Further analyses estimating sensitivities, specificities, positive predictive value, negative predictive value and diagnostic odds ratios (DORs) with their associated 95% CI for each test and combinations of one, two or three LFTs were performed.

All statistical analyses were performed using SAS 9.4. Statistical significance was set at a bilateral *p*-value of 0.05.

RESULTS

Characteristics of AC patients

A total of 32,839 patients were included in the study, among which 8,801 (26.8%) were AC⁺ and 24,038 (73.2%) were AC⁻. Their mean age was 52.4±18.6 years and over half (59.1%) were of female gender. Patients were mostly white (82.3%). Patients had a mean BMI of 30.9 (±) (class I obesity) and over half (54.3%) had a mild systemic disease (ASA class 2) followed by 32.5% with a severe systemic disease (ASA class 3).

Patients in the AC⁺ group had slightly higher mean age (53±19.7 years), were more commonly of female gender (64%), and more likely to have an ASA score of 3 (34.1%) (*p*<0.0001). They had lower mean white blood cell count (8.821 vs 10.577) (*p*<0.0001), were less likely to have leukocytosis (WBC count of more than 11,000/mm³) (22.29% vs 38.47%) and were less likely to be septic (17.2 % vs 21.4%, *p*<0.0001) (Table 1).

Laboratory data

Mean values for LFTs were significantly higher in the

Table 1. Demographics and characteristics of patients with cholecystitis with (AC⁺) or without (AC⁻) concomitant CBDS

Variables	All AC (n=32839)	AC ⁻ (n=24038)	AC ⁺ (n=8801)	<i>p</i> -value
Age (years), mean±SD	52.4±18.6	52.2±17.9	53.0±19.7	0.0006
Race				<0.0001
Black	3262 (11.6)	2429 (12.1)	833 (10.42)	
White	23052 (82.3)	16397 (81.9)	6655 (83.23)	
Others	1710 (6.1)	1202 (6.0)	508 (6.4)	
Gender				<0.0001
Male	13424 (40.9)	10259 (42.7)	3165 (36.0)	
Female	19383 (59.1)	13755 (57.3)	5628 (64.0)	
Diabetic	4538 (13.8)	3447 (14.3)	1091 (12.4)	<0.0001
Hypertensive	12551 (38.2)	9178 (38.2)	3373 (38.3)	0.8120
BMI, mean±SD	30.9±7.5	31.0±7.5	31.1±7.6	0.81
ASA				0.0010
1	3245 (9.9)	2443 (10.2)	802 (9.1)	
2	17803 (54.3)	13098 (54.5)	4705 (53.5)	
3	10668 (32.5)	7672 (32.0)	2996 (34.1)	
4	1078 (3.3)	787 (3.3)	291 (3.3)	
5	9 (0.0)	8 (0.0)	1 (0.0)	
WBC, mean±SD	10.106±4.698	10.577±4.797	8.821±4.155	<0.0001
Hematocrit, mean±SD	38.3±5.0	38.6±5.0	37.3±4.8	<0.0001
Septic	6631 (20.2)	5122 (21.4)	1509 (17.2)	<0.0001

CBDS, common bile duct stone; AC, acute cholecystitis; AC⁻, acute cholecystitis without common bile duct stone; AC⁺, acute cholecystitis with common bile duct stone; SD, standard deviation; BMI, body mass index; ASA, American Society of Anesthesiologists (ASA) Score is a global score that assesses the physical status of patients before surgery; WBC, white blood cell count

AC⁺ group for total bilirubin (1.82 vs 0.97, $p < 0.0001$), SGOT (110.9 vs 53.3, $p < 0.0001$) and ALP (164.4 vs 102.3, $p < 0.0001$) (Table 2). The proportions of abnormal LFTs were also significantly higher in the AC⁺ group for total bilirubin (47.7% vs 20.2%, $p < 0.0001$), SGOT (62.8% vs 27.1%, $p < 0.0001$) and ALP (56.6% vs 21.0%, $p < 0.0001$). When relying on two LFTs for the prediction of a CBD stone, the proportions of abnormal LFTs stayed significantly higher in the AC⁺ group for all three combinations, with that of ‘SGOT or ALP’ having the highest rates of abnormal results (73.8% vs 34.9%, $p < 0.0001$) followed by ‘total bilirubin or SGOT’ (70.8% vs 36.4%, $p < 0.0001$) and ‘total bilirubin or ALP’ (68.9% vs 32.8%, $p < 0.0001$).

To assess the clinical utility of examining the three LFTs included in our study as binary variables for the prediction of CBDS in AC patients, ROC curves were constructed and the best cut-off points were determined using the Youden Index. Cut-off values were set at 1.2 milligrams per deciliter (mg/dl) for bilirubin, 40 units per liter

(U/L) for SGOT and 120 international units per liter (IU/L) for ALP. Sensitivities, specificities, positive and negative predictive values as well as diagnostic odds ratios for individual LFTs and combinations of LFTs are presented in Tables 3, 4, respectively. Among AC⁺, the odds of having abnormal results for bilirubin, SGOT and ALP were found to be 3.61, 4.54 and 4.90 times higher than among AC⁻, respectively (Table 3). AC patients with any abnormal LFT, any two abnormal LFTs and three abnormal LFTs were found to be 2.23, 5.73 and 12.0 times more likely to have a simultaneous CBD stone, respectively (Table 4).

DISCUSSION

This study of more than 30,000 patients presenting with AC is the largest series to date to assess and characterize LFT results in AC⁺ and AC⁻ patients, with the purpose of developing clinically applicable criteria to assess the likelihood of a CBDS. The study findings confirmed the

Table 2. Liver function test results in acute cholecystitis patients with (AC⁺) or without (AC⁻) concomitant CBDS

LFTs	All AC	AC ⁻	AC ⁺	<i>p</i> -value
Total bilirubin ^a , mean±SD	1.20±1.3	0.97±1.01	1.82±1.78	< 0.0001
Normal (≤1.2 mg/dl)	23798 (72.5)	19192 (79.8)	4606 (52.3)	< 0.0001
Abnormal (>1.2 mg/dl)	9041 (27.5)	4846 (20.2)	4195 (47.7)	
SGOT ^a , mean±SD	68.7±105.9	53.3±88.6	110.9±134.0	< 0.0001
Normal (≤40 U/L)	20802 (63.3)	17528 (72.9)	3274 (37.2)	< 0.0001
Abnormal (>40 U/L)	12037 (36.7)	6510 (27.1)	5527 (62.8)	
ALP ^a , mean±SD	119.0±89.2	102.3±72.0	164.4±112.8	< 0.0001
Normal (≤120 IU/L)	22815 (69.5)	18993 (79.0)	3822 (43.4)	< 0.0001
Abnormal (>120 IU/L)	10024 (30.5)	5045 (21.0)	4979 (56.6)	
Bilirubin OR SGOT, mean±SD				
Normal	17860 (54.4)	15290 (63.6)	2570 (29.2)	< 0.0001
Abnormal	14979 (45.6)	8748 (36.4)	6231 (70.8)	
Bilirubin OR ALP, mean±SD				
Normal	18882 (57.5)	16147 (67.2)	2735 (31.1)	< 0.0001
Abnormal	13957 (42.5)	7891 (32.8)	6066 (68.9)	
SGOT OR ALP, mean±SD				
Normal	17960 (54.7)	15651 (65.1)	2309 (26.2)	< 0.0001
Abnormal	14879 (45.3)	8387 (34.9)	6492 (73.8)	
SGOT OR ALP OR bilirubin, mean±SD				
Normal	15693 (47.8)	13761 (57.2)	1932 (21.9)	< 0.0001
Abnormal	17146 (52.2)	10277 (42.8)	6869 (78.1)	

CBDS, common bile duct stone; LFTs, liver function tests; AC, acute cholecystitis; AC⁻, acute cholecystitis without common bile duct stone; AC⁺, acute cholecystitis with common bile duct stone; SD, standard deviation; SGOT, serum glutamic-oxaloacetic transaminase; ALP, alkaline phosphatase

^aCut-off values were set at 1.2 milligrams per deciliter (mg/dl) for bilirubin, 40 units per liter (U/L) for SGOT and 120 international units per liter (IU/L) for ALP

Table 3. Test characteristics of individual LFTs for the prediction of CBDS in AC patients

	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	Diagnostic OR (95% CI)
Bilirubin ^a	47.7 (46.6-48.7)	79.8 (79.3-80.4)	46.4 (45.4-47.4)	80.7 (80.1-81.1)	3.61 (3.42-3.80)
SGOT ^a	62.8 (61.8-63.8)	72.9 (72.4-73.5)	45.9 (45.0-46.8)	84.3 (83.8-84.8)	4.54 (4.32-4.79)
ALP ^a	56.6 (55.5-57.6)	79.0 (78.5-79.5)	49.7 (48.7-50.7)	83.3 (82.8-83.7)	4.90 (4.65-5.17)

LFTs, liver function tests; CBDS, common bile duct stone; AC, acute cholecystitis; %, percentage; PPV, positive predictive value; NPV, negative predictive value; Diagnostic OR, diagnostic odds ratio; CI, confidence interval; SGOT, serum glutamic-oxaloacetic transaminase; ALP, alkaline phosphatase

^aCut-off values were set at 1.2 milligrams per deciliter (mg/dl) for bilirubin, 40 units per liter (U/L) for SGOT and 120 international units per liter (IU/L) for ALP

Table 4. Test characteristics of combinations of LFTs for the prediction of CBDS in AC patients

	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	Diagnostic OR (95% CI)
Any one LFT ^a	48.5 (46.9-50.1)	70.3 (69.7-71.0)	23.9 (22.9-24.8)	87.7 (87.2-88.2)	2.23 (2.08-2.39)
Any two LFTs ^b	54.0 (52.5-55.5)	83.0 (82.4-83.6)	44.6 (43.2-46.0)	87.7 (87.2-88.2)	5.73 (5.33-6.17)
Three LFTs	59.0 (57.6-60.4)	89.3 (88.8-89.8)	62.7 (61.3-64.2)	87.7 (87.2-88.2)	12.0 (11.1-12.9)

LFTs, liver function tests; CBDS, common bile duct stone; AC, acute cholecystitis; %, percentage; PPV, positive predictive value; NPV, negative predictive value; Diagnostic OR, diagnostic odds ratio; CI, confidence interval

^aAny one LFT among total bilirubin, SGOT and ALP

^bAny two LFTs namely total bilirubin and SGOT, total bilirubin and ALP, and SGOT and ALP

usefulness of LFTs for the prediction of CBD stones in AC patients with mean LFT results being significantly greater in AC⁺ patients than in AC⁻ patients. This is in line with several previous studies that showed a significant increase in LFT results in AC patients with CBD stones.^{6-8,13,20}

Interestingly, AC⁺ patients had lower mean WBC count (8.821 vs 10.577) ($p < 0.0001$), were less likely to have leukocytosis (22.29% vs 38.47%) and were less likely to be septic (17.2 % vs 21.4%, $p < 0.0001$). Generally, in AC⁺ patients, CBDS can cause cholangitis, which can present with high WBC count.²¹ The lower mean WBC count and proportion of patients with leukocytosis in AC⁺ patients may be due to a baseline difference in severity of acute cholecystitis in AC⁺ patients compared to AC⁻ patients. Indeed, WBC count was shown to be significantly greater in patients with moderate rather than mild cholecystitis²² or with gangrenous rather than non-gangrenous cholecystitis ($p \leq 0.04$).²³

As previously observed in the literature,^{8,13,24} LFTs including total bilirubin, SGOT and ALP can vary in AC patients with or without CBDS. They are not only affected by the presence of CBDS but also by the severity and

acuteness of AC.²⁵ Our study showed that both AC⁺ and AC⁻ patients could present with normal results. More than half of AC⁺ patients had normal total bilirubin (52.3%) and almost half had a normal ALP (43.4%). Thus, findings of normal LFT should be interpreted with caution when ruling out CBDS.

There are several mechanisms may be responsible for the false negative and false positive LFTs in AC patients. In theory, CBD stones cause biliary obstruction with increased intra-biliary pressure due to hindrance of bile flow and subsequent peri-ductal inflammation and hepatocellular injury with elevated LFTs.^{8,10,25} However, partially obstructing stones may not cause elevated bilirubin levels thus generating false negative values.^{7,13} It is also possible for stones to spontaneously enter or pass from the CBD during the time period between blood sampling and surgery, thereby leading to both false negative or positive results, respectively.¹³ The presence of sludge or micro-lithiasis in the common bile duct could lead to an increased bile viscosity with subsequent elevation in liver function tests whereas they may go undetected on intra-operative cholangiography after they are washed out by the contrast medium to the duodenum, thus increasing the

population of AC⁻ patients with abnormal LFTs.^{26,27} Cases of concomitant Sphincter of Oddi dysfunction,²⁸⁻³¹ conjugation defects^{32,33} or Mirizzi syndrome³⁴ among others may also display elevated liver function test results in the absence of CBDS.

Nevertheless, AC⁺ patients are more likely to present with abnormal results. When compared to AC⁻ patients, AC⁺ patients tend to have more abnormal results with higher LFT values. As such, this study confirms the utility of LFTs for prediction of CBDS in AC patients to a certain extent, mainly for their positive predictive value in case of clinical suspicion. Of the LFTs assessed in this study, an abnormal ALP was the most powerful predictor for CBDS as it increased the odds of having concomitant CBDS by 4.9 fold. Abnormal SGOT and total bilirubin were also shown to be good predictors for CBDS with DORs of 4.54 and 3.61, respectively. A prospective study by Videhult et al. with 1171 cholecystitis patients established ALP and bilirubin as the most reliable factors, but with limited diagnostic value.¹³ Other studies have found different liver enzymes such as g-GT as more reliable predictors⁷ and Parra Pérez et al.¹⁷ concluded that none of the LFT results were associated with CBD stones. Many other studies targeting the use of LFTs for the prediction of CBDS only had limited results.¹⁴⁻¹⁶

Although ALP was found to have the most predictive power for a CBD stone, it is not advisable to order it solely as 56.6% of AC⁺ cases would be missed. CBDS should be suspected if any of the predictors is elevated.¹³ Increasing the number of ordered LFTs substantially increased DORs for the prediction of a CBDS from 2.23 for any single LFT to 5.73 for any two LFTs up to 12.0 for all three LFTs (Table 4). Ordering the three LFTs together is advised for recognition of CBDS in AC patients.

For the diagnosis of CBDS, current practice relies on MRCP which is noninvasive or endoscopic ultrasound (EUS) which is less invasive than ERCP. EUS was found to have a sensitivity of 94% and a specificity of 95% in a meta-analysis on 27 studies with 2763 patients.³⁵ MRCP was found to have a sensitivity of 93% and a specificity of 94% in a review of 13 studies.³⁶ In our study, individual LFTs were found to have a sensitivity of 47.7 to 62.8% and specificity of 72.9 to 79.8%. Although sensitivity and specificity of gold standard diagnostic procedures remain higher, prediction of CBD stone through ba-

sic blood tests can be of great help before radiologic tests.

The limitations of our study are inherent to the use of a clinical registry database and include its retrospective study design as well as resource constraints such as missing data, miscoding and undocumented variables such as laboratory results namely direct bilirubin, ALT and G-GT or physical exam findings needed for severity grading of acute cholecystitis according to Tokyo guidelines.³⁷ Relying on total bilirubin instead of conjugated or direct bilirubin is another limitation due to lack of differentiation between elevated levels from CBDS obstruction and those resulting from hemolysis or defective conjugation.¹³ Another limitation is related to the fixed cut-offs that were established to generate test characteristics for LFTs, which could be set higher to avoid false positive findings. Moreover, the ACS NSQIP database only contains data from participating hospitals, which do not constitute a statistically valid nationally representative sample. It only contains data on surgical patients with AC which might not be representative of all the AC patients who present to EDs. Only 0.1% of AC patients included in our study underwent ERCP and none of them underwent MRCP. This study however included a large number of confirmed cases of acute cholecystitis, and examined the utility of LFTs in a large national sample and its findings can be generalized to most ED settings with implications on daily clinical practice. Diagnostic odds ratios, which combine the strengths of sensitivity and specificity as prevalence independent indicators with the advantage of accuracy as single indicator, were used as measures of test performance for the LFTs. Based on our findings, LFTs offer potential clinical benefits for diagnosis and treatment of CBD stones in AC patients. Not only would they help avoid unnecessary costs and complications associated with ERCP and MRCP in cases of normal results and low clinical suspicion for CBD stones but they also reduce the delay associated with these procedures making it possible to perform cholecystectomies more promptly.

A well designed prospective, large scale and multi-center study is still required in order to further evaluate the diagnostic value of LFTs for CBD stones in AC patients. Further areas of research include the study of LFT patterns in AC⁺ and AC⁻ patients after subgrouping based on the presence of concomitant chronic cholecystitis or acute pancreatitis¹³ as well as the study of the correlation

between LFTs and morbidity/mortality outcomes.

Abnormal liver function tests are strong predictors for the presence of CBD stone in patients with acute cholecystitis, with ALP being stronger than SGOT and total bilirubin. This finding may help ED physicians better identify and predict which patients presenting with acute cholecystitis may also have a concomitant CBD stone and who may need additional inpatient work up, such as MRCP and ERCP to confirm CBDS presence. Normal LFTs should however always be interpreted with caution as some patients with acute cholecystitis and CBD stone might not present with characteristic abnormalities in results. A scoring system integrating LFTs and additional clinical variables would be useful to clinically help predict the presence of CBDS and avoid unnecessary delays related to additional work-up prior to definitive treatment.

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Appendix 1. ICD9 and ICD10 codes used to categorize the acute cholecystitis (AC) patients based on the absence or presence of common bile duct stones into AC⁻ and AC⁺ cases

ICD9	574.30	574.31	574.60	574.61	574.80	574.81	575.0	575.12	574.01
ICD10	K80.42	K80.43	K80.62	K80.63	K80.66	K80.67	K81.0	K81.2	K80.01
<hr/>									
AC ⁺				AC ⁻					
ICD9	Label	ICD10	Label	ICD9	Label	ICD10	Label		
574.30	Calculus of bile duct with acute cholecystitis, without mention of obstruction	K80.42	Calculus of bile duct with acute cholecystitis without obstruction	575.0	All types of acute cholecystitis, no stones, no chronic cholecystitis	K81.0	Acute cholecystitis		
574.31	Calculus of bile duct with acute cholecystitis, with obstruction	K80.43	Calculus of bile duct with acute cholecystitis, with obstruction	575.12	Acute and chronic cholecystitis, no stones	K81.2	Acute cholecystitis with chronic cholecystitis		
574.60	Calculus of gallbladder and bile duct with acute cholecystitis, without mention of obstruction	K80.62	Calculus of gallbladder and bile duct with acute cholecystitis without obstruction	574.01	Calculus of gallbladder with acute cholecystitis, with obstruction	K80.01	Calculus of gallbladder with acute cholecystitis, with obstruction		
574.61	Calculus of gallbladder and bile duct with acute cholecystitis, with obstruction	K80.63	Calculus of gallbladder and bile duct with acute cholecystitis, with obstruction	-	-	-	-		
574.80	Calculus of gallbladder and bile duct with acute and chronic cholecystitis, without mention of obstruction	K80.66	Calculus of gallbladder and bile duct with acute and chronic cholecystitis, without obstruction	-	-	-	-		
574.81	Calculus of gallbladder and bile duct with acute and chronic cholecystitis, with obstruction	K80.67	Calculus of gallbladder and bile duct with acute and chronic cholecystitis, with obstruction	-	-	-	-		