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Predicting operative difficulty of laparoscopic cholecystectomy in patients with acute biliary presentations

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Abstract

Background: Early laparoscopic cholecystectomy (LC) is advocated in patients with an acute biliary presentation but may require some precaution. We aimed to assess the intra-operative difficulty of cholecystectomy in patients who underwent early intervention, and to establish a prediction model for a 'complicated' LC.

Methods: Retrospective analysis of prospectively collected data from patients presenting to the emergency department with acute biliary symptoms, and who subsequently underwent early LC between 2015 and 2018. Operative difficulty was assessed by standardized grading of intra-operative findings (grades 1–4). Pre-operative predictors for a 'complicated' LC (grades 3/4) were assessed using univariable and multivariable logistic regression analysis. A prediction model was created using variable regression coefficients. Cut-off and accuracy of the model were assessed using a receiver operating characteristic curve.

Results: A total of 185 patients were included and 59% presented with acute cholecystitis. In this cohort 113 (61%) patients underwent a 'complicated' LC. A prediction model for a 'complicated' LC (0–4.5 points) included: clinical diagnosis of acute cholecystitis (2 points), C-reactive protein >10.5 mg/L (1.5 points) and pericholecystic fluid on pre-operative imaging (1 point). A score ≥2.5 had a sensitivity of 77.7%, specificity of 81.7% and positive and negative predictive values of 87.0% and 69.9%, respectively.

Conclusion: Early LC may be 'complicated' in up to 60% of cases. The presented prediction model uses readily available information in the emergency department and is a simple but accurate way to predict a likely 'complicated' LC in patients with acute biliary presentations.

Introduction

Acute biliary presentations account for approximately 10% of patients seen in the emergency department (ED) of which approximately half have acute cholecystitis (AC).[1] Accurate differentiation between AC and biliary colic at first presentation is challenging.[2,3] The Tokyo Guidelines (TG18) advocate early laparoscopic cholecystectomy (LC) for patients with AC as well as for most other acute biliary presentations.[4] Numerous studies support early LC for patients with AC as this is purported to be associated with reduced morbidity, length of stay and costs.[5–8] Some authors suggest that early LC is often an easier operation to perform than a delayed LC.[9]

In the (semi-)urgent setting, early LC may be done out of normal working hours and many hospitals do not have standardized or uniform protocols for performing these procedures. A complex or prolonged operation may result from unexpected intra-operative findings that cannot be dealt with by on-call surgeons or trainees who do not have the requisite skills or experience. Severe inflammation around the gallbladder (GB) can make safe dissection difficult, and may increase the risk of both minor and major complications.[10–12] When an early LC policy is adopted for patients with acute biliary presentations it would be helpful to predict the degree of operative difficulty. This would assist timing of the procedure and allocation of appropriate resources including the provision of experienced nursing and surgical staff. Numerous groups have attempted this using surrogate markers of difficulty such as the duration of the operation or the need for conversion to open cholecystectomy.[13–18] However, these outcomes are highly dependent on surgeons' experience and institutional preferences.[19]

The aim of the current study was to assess the intra-operative findings at LC using a simplified and easily applicable grading system in patients with acute biliary presentations, and to establish an accurate pre-operative prediction model for difficulty of LC.

Methods

Study design and patient selection

A retrospective analysis of prospectively collected clinical data was performed in the upper gastrointestinal (GI) surgery unit of a tertiary Australian hospital. Patients ≥18 years of age who were admitted via the ED with an acute biliary presentation between July 2015 and February 2018 and underwent emergency LC within the same admission or a semi-elective operation within 1 week of discharge, were included in this study. Timing of the operation was at the discretion of the treating surgical team. LC was performed by one of five upper GI surgeons or by surgical trainees under supervision. Patients who underwent a delayed operation (>1 week after ED admission), or those with a history of malignancy or pregnancy at the time of admission were excluded. This study was approved by the Northern Sydney Local Health District Human Research Ethics Committee (AU/1/D724311).

Outcomes and collected data

The primary outcome was the operative difficulty of the cholecystectomy. Intra-operative findings were systematically graded on a scale of 1–4 by the surgeon during the operation. The grading system represents a concise but simplified modification of intra-operative factors known to be associated with the degree of difficulty of LC.[10,11] Grades 1 and 2 were considered 'straightforward' operations, and grades 3 and 4 were considered 'complicated' operations as illustrated in Figure 1.

Secondary outcomes were associations between clinical, biochemical and radiological characteristics and the difficulty of the LC, and the associated prediction model.

Data deducted from the data set included: patient characteristics, medical history, clinical presentation, pre-operative diagnosis, abdominal ultrasound report and blood chemistry, operative characteristics (GB morphology and extent of inflammatory change, the duration of the operation and conversion to an open procedure), and post-operative data on length of stay, histopathology, 30-day complications (according to the Clavien-Dindo classification) and readmissions. Missing data were retrospectively collected from patient's medical records. Patients for whom no intra-operative complexity data were available were excluded. The TG18 score was applied to grade the severity of AC.[20] The full list of characteristics assessed, is provided in the Appendix S1.

Statistical analysis

Dichotomous variables were presented as percentages and analysed using the chi-squared test. Continuous variables were expressed as means and standard deviations and analysed using the independent Student's t-test where there was normal distribution. In cases of non-normal distribution, median and range were reported, and variables were analysed using the Mann–Whitney U-test. For continuous variables that were significantly associated with difficulty of surgery, optimum cut-off points were determined using receiver operating characteristic (ROC) curves. Associations of variables with difficulty of LC were assessed using univariable and multivariable regression analysis. Collinearity of the individual variables was tested and no correlation between any of the variables was found. All univariable variables with a P-value <0.1 were included in the multivariable model. Backward elimination was used as variable selection method. The results were reported as adjusted odds ratio (OR) and 95% confidence intervals (CIs).

The regression coefficients of multivariable analysis were used to build the prediction model. Accuracy of the model was assessed using area under the ROC curve (AUC). The ROC curve was used to establish the optimum cut-off score for the prediction of difficult LC. Sensitivity, specificity and positive and negative predictive values of the cut-off were calculated. For all analyses a P-value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS Statistic 25.0 software package (IBM, Amsterdam, The Netherlands).

Results

During the study period, 257 patients were admitted for acute biliary disease through the ED and subsequently underwent LC. Of these, 72 patients were excluded (50 delayed LCs (>1 week after discharge), 20 with unavailable intra-operative information, one concurrent malignancy and one <18 years of age), leaving 185 patients for inclusion in the study. Indications for surgery and clinical characteristics of the full cohort are shown in Table 1. Table 2 consists of the univariable and multivariable analysis with OR and 95% CI.

Difficulty of cholecystectomy

Difficulty of LC was reported as grade 1 in 25 patients, grade 2 in 47 patients, grade 3 in 69 patients and grade 4 in 44 patients. Table 1 summarizes the difference between the 'straightforward' procedures (72 patients, 38.9%) and 'complicated' procedures (113 patients, 61.1%). 'Complicated' procedures were associated with the following clinical characteristics: older age, a positive Murphy's sign, duration of symptoms >24 h prior to presentation at ED, higher median white blood cell count, neutrophil and C-reactive protein (CRP) levels and ultrasound findings associated with cholecystitis. 'Complicated' procedures were associated with the following peri-operative characteristics: increased operation time, more conversion to an open procedure, longer post-operative stay, increased complications and more severe complications (Clavien-Dindo classification ≥3) (Table 1). The TG18 severity grade of AC and total duration of symptoms prior to LC were not significantly associated with a 'complicated' procedure.

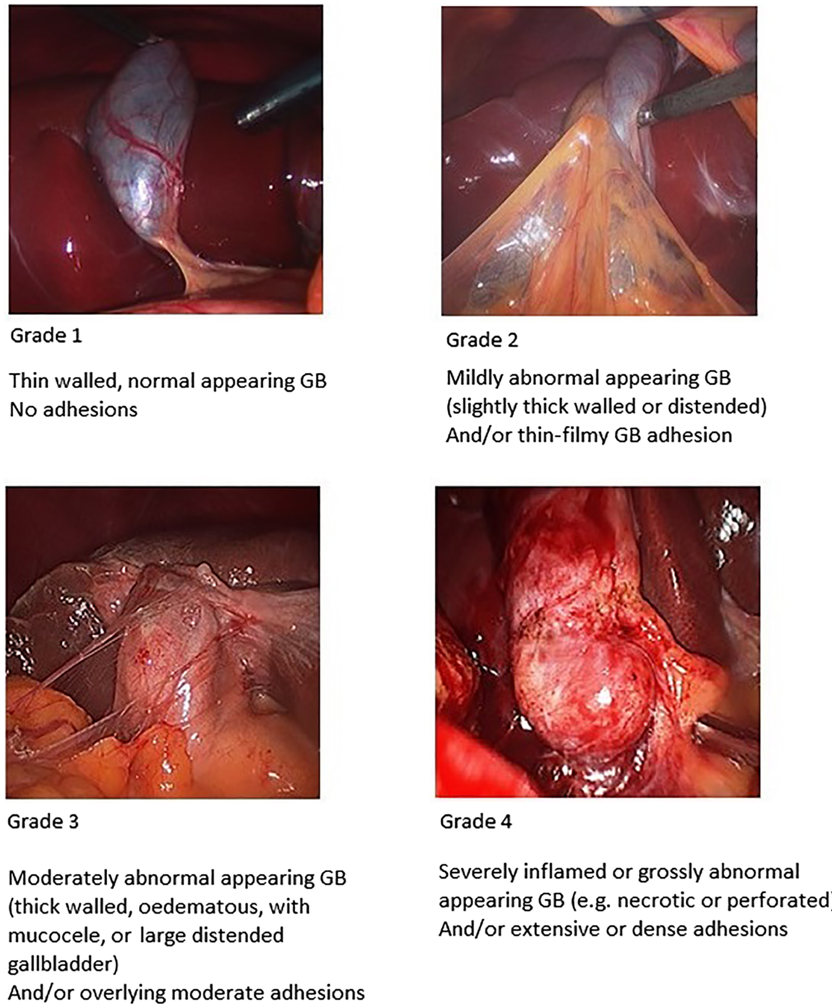

Fig. 1. Intra-operative grade examples.

Predictive factors for a complicated cholecystectomy

Table 2 summarizes the uni- and multivariable analyses of pre-operative predictive factors for a 'complicated' LC. The cut-off values were determined using ROC curves (Fig. S1). Multivariable analysis showed that clinical diagnosis of AC (OR 8.33 (95% CI 3.78–18.36), $P < 0.001$), CRP >10.5 mg/L (OR 3.85 (95% CI 1.78–8.34), $P = 0.001$) and pericholecystic fluid (OR 2.77 (95% CI 1.11–6.95), $P = 0.029$) were independently predictive for a 'complicated' LC.

The AUC of the prediction model was 0.86 (95% CI 0.80–0.91, $P < 0.001$) (Fig. S2). Using the ROC curve the cut-off for a 'complicated' LC was set at ≥2.5. Sensitivity of this score was 77.7%, specificity was 81.7% and positive and negative predictive values were 87.0% and 69.9%, respectively.

Discussion

This study showed that 60% of the operations done as an early LC after an acute biliary presentation were classified as 'complicated' (grade 3 or 4). A 'complicated' LC was associated with worse post-operative outcomes compared with patients who underwent a 'straightforward' operation (grade 1 or 2). Regardless, early LC is still feasible and can be done safely in most patients because it is possible using readily available clinical and radiological data to predict and therefore plan for this likelihood.

Existing grading methods for the difficulty of LC mainly use surrogate markers such as the risk of conversion to an open operation, a prolonged operative time or post-operative complications.[13–18] These outcomes, although partly related to the intra-operative findings, are also dependent on the skills and preferences of the surgeon, or on institutional protocols regarding conversion, and the availability of experienced peri-operative staff and equipment.[11,19,21] Several groups have suggested from retrospective series that a pre-operative diagnosis or grading of AC according to the TG18 criteria alone is often not helpful in predicting the difficulty of a subsequent LC.[20,22,23] We showed that a diagnosis of AC, but not the TG18 grading was an independent predictor for a 'complicated' LC. Interestingly, 29% of 'complicated' LCs in the present study were in patients with a pre-operative diagnosis of biliary colic only.

Several prediction models for a difficult LC, based on subjective assessment intra-operative difficulty have been proposed (e.g. 'unable to', 'difficult dissection of').[21,24–26] However, these assessments also depend on a surgeons' experience and routine

Table 1 Clinical characteristics

Variable	Total cohort (*n* = 185)	'Straightforward' LC (*n* = 72)	'Complicated' LC (*n* = 113)	*P*-value
Age (year), mean (SD)	51.6 (18.4)	46.2 (18.7)	55.0 (17.5)	0.001
Sex, female, *n* (%)	108 (58.4)	45 (62.5)	63 (55.8)	0.36
ASA, *n* (%)				0.19
1–2	145 (78.4)	60 (83.3)	85 (75.2)	
3–4	40 (21.6)	12 (16.7)	28 (27.8)	
BMI (kg/m^2), mean (SD)	30.3 (24.0)	28.8 (5.86)	31.4 (31.1)	0.55
Clinical diagnosis, *n* (%)				<0.001
Acute cholecystitis	109 (58.9)	18 (25.0)	91 (80.5)	<0.001
Biliary colic	41 (22.2)	29 (40.3)	12 (10.6)	<0.001
Gallstone pancreatitis	15 (8.1)	14 (19.4)	1 (0.9)	<0.001
Choledocholithiasis	10 (5.4)	9 (12.5)	1 (0.9)	0.001
Cholangitis	6 (3.2)	2 (2.8)	4 (3.5)	0.78
Biliary sepsis†	4 (2.2)	0	4 (3.5)	0.11
History, *n* (%)				
Abdominal surgery	57 (31.0)	22 (31.0)	35 (31.0)	0.99
Cholecystitis	10 (5.4)	3 (4.2)	7 (6.3)	0.54
ERCP	17 (9.2)	6 (8.3)	11 (9.7)	0.75
Cholecystostomy	6 (3.2)	1 (3.2)	5 (4.4)	0.26
Pancreatitis	10 (5.4)	5 (6.9)	5 (4.5)	0.47
Cholangitis	1 (0.5)	0	1 (0.9)	0.42
Symptoms, *n* (%)				
First episode	70 (37.8)	22 (30.6)	48 (42.5)	0.10
Fever	29 (15.7)	9 (12.5)	20 (17.7)	0.34
Murphy's sign+	78 (42.2)	19 (26.4)	59 (52.2)	0.001
Duration prior ER >24 h	99 (53.5)	31 (43.1)	68 (60.2)	0.02
Duration until operation (days), median (range)	4 (0.1–54)	4 (0.1–54)	4 (0.1–34)	0.81
Tokyo grade, *n* (%)				0.41
I	42 (22.7)	6 (31.6)	36 (38.3)	0.58
II	45 (24.3)	8 (42.1)	37 (39.4)	0.83
III	7 (3.8)	0	7 (7.4)	0.22
Laboratory values, median (range)				
WBC (×10^9/L)	11.0 (2.6–185)	9.3 (2.9–19.6)	12.0 (2.6–185)	<0.001
Neutrophil (×10^9/L)	8.2 (1.4–173)	6.6 (2.1–16.6)	9.2 (1.4–173)	<0.001
CRP (mg/L)	18 (0.3–523)	6 (0.3–297)	32 (0.6–523)	<0.001
AST (U/L)	37 (12–3032)	57 (16–1105)	31 (12–3032)	<0.001
ALT (U/L)	43 (10–2788)	64 (10–1227)	34 (10–2788)	<0.001
ALP (U/L)	91 (44–767)	104 (44–373)	87 (47–767)	0.25
Bilirubin (total) (μmol/L)	15 (3–136)	14 (3–112)	17 (5–136)	0.21
GGT (U/L)	62 (12–1336)	161 (12–1288)	47 (12–1336)	0.001
Radiological characteristics, *n* (%)				
US diagnosis of AC	88 (47.6)	19 (26.4)	69 (61.1)	<0.001
GB wall >4 mm	87 (47.0)	23 (31.9)	64 (56.6)	0.001
Pericholecystic fluid	63 (34.1)	9 (12.5)	54 (47.8)	<0.001
Stone impacted US	59 (31.9)	12 (16.8)	47 (41.6)	<0.001
Operative outcomes				
Operative time (min), mean (SD)	110.4 (49.6)	86.2 (36.8)	125 (50.7)	<0.001
Conversion, *n* (%)	10 (5.5)	1 (1.4)	9 (8.2)	0.05
Post-operative LOS, median (range)	2 (1–47)	1 (1–9)	2 (1–47)	<0.001
Complications, *n* (%)	28 (15.1)	5 (6.9)	23 (20.4)	0.01
CDC1	10 (35.7)	2 (40)	8 (34.8)	0.21
CDC2	6 (3.2)	1 (1.4)	4 (3.5)	0.38
CDC ≥3	18 (3.8)	2 (2.8)	11 (9.7)	0.07

†Three based on cholecystitis and one based on cholangitis. AC, acute cholecystitis; ALP, alkaline phosphatase; ALT, alanine transaminase; ASA, American Society of Anesthesiologists classification; AST, aspartate transaminase; BMI, body mass index; CDC, Clavien-Dindo classification; CRP, C-reactive protein; ER, emergency room; ERCP, endoscopic retrograde cholangio-pancreaticography; GB, gallbladder; GGT, gamma-glutamyltransferase; LC, laparoscopic cholecystectomy; LOS, length of stay; SD, standard deviation; US, ultrasound; WBC, white blood cell count.

practice and are therefore not easily transferable between institutions. The best attempt to date to identify objective intra-operative findings for a 'complicated' LC was a Japan–Korea–Taiwan expert Delphi consensus in 2017. This included factors related to inflammation of the GB and surrounding structures, fibrotic or adhesive changes in Calot's triangle and other anatomical variations.[10,11] However, the list of intra-operative factors used in this grading system is extensive, and the associated scoring system is complicated which is likely to limit routine and universal adoption.

Instead, we propose a simple grading system incorporating the main elements of the intra-operative factors outlined in the above model, except for anatomical variations which are hard to predict pre-operatively. Pragmatically, 'straightforward' operations were defined as grade 1 or 2 intra-operative findings (which can be performed by less experienced surgeons and trainees) and 'complicated' operations as grade 3 or 4 intra-operative findings (often requiring an experienced laparoscopic surgeon or even a specialist hepato-pancreatico-biliary surgeon).

Table 2 Univariable and multi-variable analysis

Variable	'Straightforward' LC	'Complicated' LC	Univariable OR (95% CI)	*P*-value	Multivariable OR (95% CI)	*P*-value	Regression coefficient	Points Prediction model
Acute cholecystitis†, *n* (%)	18 (25.0)	94 (83.2)	14.84 (7.18–30.69)	<0.001	8.33 (3.78–18.36)	<0.001	2.12	2
Murphy's sign positive, *n* (%)	19 (26.4)	59 (52.2)	3.05 (1.61–5.79)	0.001				
CRP >10.5 mg/L, *n* (%)	23 (32.4)	84 (75.0)	6.26 (3.25–12.06)	<0.001	3.85 (1.78–8.34)	0.001	1.35	1.5
Pericholecystic fluid, *n* (%)	9 (12.5)	54 (47.8)	6.41 (2.91–14.12)	<0.001	2.77 (1.11–6.95)	0.029	1.02	1
Impacted stone GB neck, *n* (%)	12 (16.8)	47 (41.6)	3.56 (1.73–7.34)	<0.001				
Neutrophils >8 × 10^9/L, *n* (%)	24 (33.3)	73 (64.6)	3.65 (1.96–6.81)	<0.001				
US diagnosis AC, *n* (%)	19 (26.4)	69 (61.1)	4.37 (2.29–8.35)	<0.001				
Age >50 years, *n* (%)	26 (36.1)	70 (61.9)	2.88 (1.56–5.32)	0.001				
First episode, *n* (%)	22 (30.6)	48 (42.5)	1.68 (0.90–3.14)	0.104				
Symptoms >24 h prior to ER, *n* (%)	31 (43.1)	68 (60.2)	2.00 (1.10–3.64)	0.024				
WBC >9.5 × 10^9/L, *n* (%)	35 (48.6)	80 (70.8)	2.56 (1.39–4.73)	0.003				
GB wall >4 mm, *n* (%)	23 (31.9)	64 (56.6)	2.78 (1.50–5.17)	<0.001				

†Including three patients with biliary sepsis based on cholecystitis. AC, acute cholecystitis; CI, confidence interval; CRP, C-reactive protein; ER, emergency room; GB, gallbladder; OR, odds ratio; US, ultrasound; WBC, white blood cell count.

In the present study, an elevated pre-operative CRP and the presence of pericholecystic fluid were associated with a 'complicated' LC (grade 3 or 4). These are consistent with previous findings in the literature.[13–15,27] A pre-operative clinical diagnosis of AC was also an independent predictor of a likely 'complicated' LC. By combining all three pre-operative variables we produced a highly accurate pre-operative prediction model (AUC 0.86). The variables were assigned different scores based on the regression coefficients, and a cumulative score of ≥2.5 had a sensitivity of 77.7%, specificity of 81.7% and positive and negative predictive values of 87.0% and 69.9% for predicting a 'complicated' LC.

This simple predictive model using readily available clinical and radiological information can predict the likelihood of a 'complicated' LC in patients presenting with acute biliary symptoms. If patients present out of normal working hours or if appropriately skilled surgical staff are not available, a conservative approach may be warranted in the first instance until 'normal' working hours or until experienced staff are available. In support of this, we found that a prolonged duration of symptoms prior to LC was not associated with a 'complicated' LC in the present study. In fact, delayed operations >72 h after presentation were no more difficult than operations done within 72 h from the time of presentation (data not shown). In modern surgical practice neither the TG18 grading nor the duration of symptoms should be used as an excuse to postpone surgery beyond the primary admission.

A strength of this study was the development of an accurate prediction model using readily assessable pre-operative factors that are part of standard clinical evaluation of patients with biliary symptoms in the ED. The score can be quickly determined without any difficult calculations. Limitations of the study include the relatively small cohort size which limited the number of factors that could be included in the multivariable analysis, and the fact that there was no subset of patients for external validation. Importantly, this prediction model needs to be validated in an independent and prospectively collected cohort of patients presenting at the ED with acute biliary symptoms.

Conclusion

In conclusion, 60% of patients with acute biliary disease who undergo early surgical intervention have a 'complicated' LC and this is associated with worse post-operative outcomes compared with 'straightforward' procedures. An 'immediate cholecystectomy' protocol for patients presenting with acute biliary symptoms is certainly feasible but is likely to have an impact on operating room and hospital resources. In order to schedule operations accurately and provide appropriate resources, the expected difficulty of an early LC can be assessed pre-operatively using a simple prediction model based on the clinical diagnosis of AC, CRP level >10.5 mg/L and pre-operative radiological findings of pericholecystic fluid.

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Conflicts of interest

None declared.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Appendix S1. Full list of assessed characteristics.

Figure S1. ROC-curves age and biochemical predictors. (a) Age > 50 years; sensitivity: 0.62; specificity: 0.64; AUC: 0.64 (95% CI 0.56–0.72); $P = 0.001$. (b) WBC > 9.5×10^9/L; sensitivity: 0.71; specificity: 0.51; AUC: 0.66 (95% CI 0.58–0.74); $P < 0.001$. (c) Neutrophils 8×10^9/L; sensitivity: 0.65; specificity: 0.68; AUC: 0.69 (95% CI 0.62–0.77); $P < 0.001$. (d) CRP 10.5 mg/L; sensitivity: 0.65; specificity: 0.68; AUC: 0.78 (95% CI 0.72–0.85); $P < 0.001$.

Figure S2. ROC-curve prediction model. Prediction score ≥ 2.5; sensitivity: 0.78; specificity: 0.82; AUC 0.86 (95% CI 0.80–0.91); $P < 0.001$.