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# Predictors of a Difficult Laparoscopic Cholecystectomy

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## Abstract

Laparoscopic cholecystectomy (LC) is the gold standard for surgical treatment of cholecystitis with gallstones. In one of the Philippines' high-volume centers for LC which does about 600 procedures a year, the authors retrospectively reviewed 2,698 records from January 2017 to December 2021 to identify significant factors associated with difficult LC. The authors identified common clinical, biochemical and radiologic factors that affected the difficulty level of such procedure. Patients predicted to have a high risk of difficult LC should be scheduled for longer operating room slots, informed of possibility of longer hospitalization and monitored more closely postoperatively. This information may help the institution improve efficiency. This study showed that around 21.98% of the patients had difficult LC. Almost all (99.2%) were considered difficult as the procedure lasted for more than two hours. Among the 18 laparoscopic surgeries converted to open, 88.89% were because there was failure to identify the critical view of safety. The overall conversion-to-open rate was 0.67 %. There are predictive factors that can be assessed preoperatively to anticipate the difficulty of a laparoscopic cholecystectomy such as being male, per unit increase in body mass index (BMI), having a history of jaundice, having a history of fever, history of laparoscopic abdominal surgery and having right upper quadrant tenderness. Radiologic factors also strongly associated with difficult LC are thickened gallbladder wall, dilated common bile duct, impacted gallbladder stone, pericholecystic fluid, cirrhosis, and per centimeter increase in size of the largest stone.

***Keywords:*** Cholecystectomy; Cholecystitis; Conversion; Difficult; Gallbladder; Gallstones; Laparoscopy; Laparoscopic; Predictors

## Introduction

Laparoscopic cholecystectomy (LC) has emerged as one of the most common surgical procedures in the world. LC is the gold standard for surgical treatment of cholecystitis with gallstones [1]. LC is associated with a significantly shorter hospital stay and a quicker convalescence compared with the classical open cholecystectomy [2]. Moreover, the benefits of laparoscopic cholecystectomy are less postoperative pain, faster recovery, earlier return of bowel function, and shorter hospital stay when compared to conventional cholecystectomy. There is no significant difference between early and late laparoscopic cholecystectomy on primary outcomes [3]. However, early laparoscopic cholecystectomy is preferred over delayed, due to overall better quality of life, lower morbidity rates, and lower hospital cost [4].

In one of the Philippines' high-volume centers for LC which does about 600 procedures a year, the authors reviewed their data to identify significant factors that were associated with difficult LC. The conversion from laparoscopic to open cholecystectomy in this institution was <1% in the past 5 years. In a study by Sakpal, et al., in New Jersey, USA, their overall conversion rate was 4.9%. The most common reason for conversion was adhesions and the majority of these patients had prior abdominal surgery. Males and patients 50 years old had a significantly higher likelihood of open conversion [5].

There are no published studies in the Philippines on predictive factors of difficult LC. This study identified, from retrospective data, which factors were associated with difficult LC. The authors identified common clinical, biochemical and radiologic factors that may affect the difficulty level of such procedure. Based upon the risk factors like patient demographics, such as age, gender, body weight, comorbidity, and ASA score, along with clinical findings (acute versus chronic cholecystitis), and the surgeon's experience; the chance of possible complications, and conversion into open surgery can be estimated [6]. The surgical care team can better prepared and the patient be informed of potential risks and outcomes of a difficult LC as compared to an easy LC if this could be preoperatively predicted.

Patients predicted to have a high risk of difficult LC should be scheduled for longer operating room slots by the staff, informed of possibility of longer hospitalization and monitored more closely postoperatively. And, given the limited resources in a developing country, this information may help the institution improve efficiency.

## Methodology

This was a retrospective study of 2,698 records of eligible patients who underwent a standard four-port laparoscopic cholecystectomy for symptomatic gall stones from January 2017 to December 2021 in The Medical City, Pasig City, Philippines.

### *Inclusion criteria*

- ≥18who underwent a laparoscopic cholecystectomy between January 2017 to December 2021.
- Standard 4-port technique.
- Symptomatic.
- Preoperative blood tests and radiologic imaging done at least 30 days prior to surgery.
- Complete in-patient record with demographic data.

### *Exclusion criteria*

- Incidental or prophylactic cholecystectomy.
- Patients who had planned open cholecystectomy.
- Laparoscopic cholecystectomy with 3-port or single port technique.
- Patients who had planned biliary exploration.
- Neoplastic disease.
- Patients with no radiologic imaging.
- Patients with incomplete data record.
- Acalculous cholecystitis.

### *Method of assigning subjects to treatment groups*

- Difficult Laparoscopic Cholecystectomy is categorized as those cases with any of the following:
    - Operative time of more than two hours.

- Need for conversion to open cholecystectomy.
- With vascular and biliary injuries.
- Need for intraoperative cholangiogram.
- Necessity of a "bail-out" procedure.
- Presence of a biliary-enteric fistula.

• Easy laparoscopic cholecystectomy has none of the features of difficult laparoscopic cholecystectomy.

***Clinical assessments***

- Demographics - age, gender.
- Medical History - number of attacks of cholecystitis, time from first symptom to intervention, Comorbidity, previous abdominal operation, history of endoscopic retrograde cholangiopancreatography (ERCP), history of biliary pancreatitis.
- Physical examination and anthropometrics - episode of hemodynamic instability, right upper quadrant (RUQ) tenderness, body mass index (BMI).

***Clinical laboratory measurements- Leukocyte count***

*Radiologic studies* - Ultrasound, computed tomography (CT) scan or magnetic resonance imaging (MRI) done preoperatively.

- Gallbladder wall thickness.
- Impacted gallbladder stone/Mirizzi syndrome.
- Pericholecystic fluid.
- Size of the largest stone.
- Cirrhosis.

***Time from symptoms to surgery***

*Surgeon classification* - Hepato-Pancreato-Biliary (HPB) Surgeon or non-HPB Surgeon.

***Operative outcome***

- Time of operation.
- Conversion to open.
- Need for cholangiogram.
- Need for biliary exploration/choledochoscopy.
- Need for bail-out procedure.
- Uncontrollable bleeding.
- Bile duct injury.

***Analysis***

Data were analyzed using Stata 14.0 IC [7]. Throughout the analysis, a 0.05 level of significance was used. The authors ran descriptive statistics to understand the distribution of the different variables after removing outliers of quantitative variables and converted into missing unrealistic values of categorical variables. The authors then cross-tabulated the different sociodemographic, clinical, radiological, and other factors with the outcome variable, which is difficult laparoscopic surgery (dichotomous variable with easy laparoscopic surgery as the baseline).

Chi-square test of associations and/or Fisher's exact test to assess the association of the different categorical exposure variables with the outcome variable. T-tests and/or Wilcoxon rank-sum test to assess the association of the different exposure variables with the outcome variable. Simple logistic regression models were done to assess the crude estimates of association between the different exposure variables and difficult laparoscopic surgery. Penalized likelihood models were done to quantify the association between the different exposure variables and difficult laparoscopic surgery [8, 9] when there was separation (small cell or zero cell issue) in traditional likelihood-based regression models.

Prior to multivariate analysis, the researchers ran a correlation matrix to assess for any potential multicollinearity in the dataset. If pairwise correlation coefficients >0.70 was detected, only one of the variables was included in the multivariate analysis. The authors excluded observations with missing data in any of the remaining variables of interest prior to multivariate analysis.

The authors fitted a logistic regression model, first with the outcome variable and the socio-demographic variables which were known from the literature and from the dataset to be strongly associated with difficult laparoscopic surgery. They then fitted the different clinical, radiological, and laboratory covariates one by one, starting with the covariate with the lowest p-value until all the variables that were known from the literature and from the dataset that was associated with the outcome were fitted into the model that was tolerated by the model without loss of precision or power. Every time a quantitative categorical variable was fitted, they tested for departure from the linearity assumption using likelihood-ratio test.

## Results

### *Description of the cohort*

A total of 2,872 laparoscopic cholecystectomies were performed from January 2017 to December 2021. 2,698 patient records were included in this analysis. Around 64% of the patients were female. The age of the patients ranged from 19-93 years old, with a mean age of 44.55 (±14.70) years and a median age of 42 years (interquartile range: 33-55 years old). The age distribution of the patients is right-skewed (Figure 1). Meanwhile, the body mass index (BMI) of the patients ranged from 16.80 - 53.00 kg/m$^2$, with a mean BMI of 27.19 (± 5.06) kg/m$^2$, and a median BMI of 26.40 (interquartile range: 23.99-30.00) kg/m$^2$. The BMI distribution of the patients is right-skewed (Figure 2).

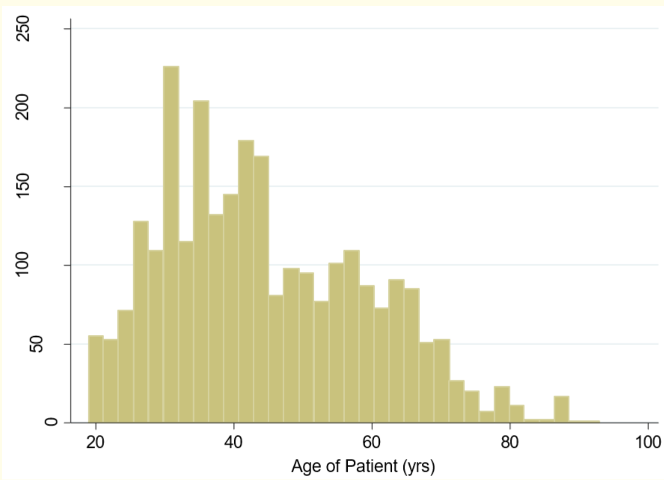


***Figure 1:*** Age distribution of laparoscopic cholecystectomy patients (n=2,698).

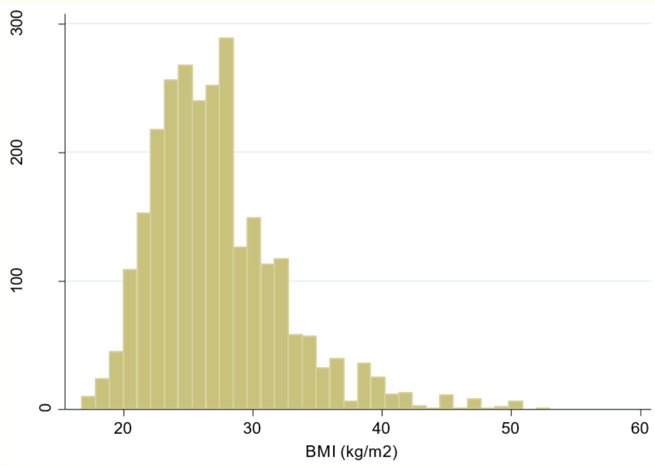


***Figure 2:*** BMI distribution of laparoscopic cholecystectomy patients (n=2,681).

Most of the patients did not have any other comorbidities and did not have history of jaundice, fever, nor biliary pancreatitis. Most of them did not also have previous surgeries/invasive procedures done in the abdomen. Most of them also have normal white blood cell counts and are not taking anticoagulant therapy. Most of them have undergone ultrasonography and only have used one imaging modality. Most of them have also been operated by a non-HPB surgeon. Around 30% have single stones. The size of the largest gallbladder stone ranged anywhere between 0.20-8.00 cm, with a mean size of 1.26 (±0.84) cm, and a median size of 1.00 cm (interquartile range: 0.50-1.60 cm). The distribution of the patients according to size of largest gallbladder stone is right-skewed (Figure 3). 593 (21.98%) of the patients had difficult laparoscopic surgery (Table 1).

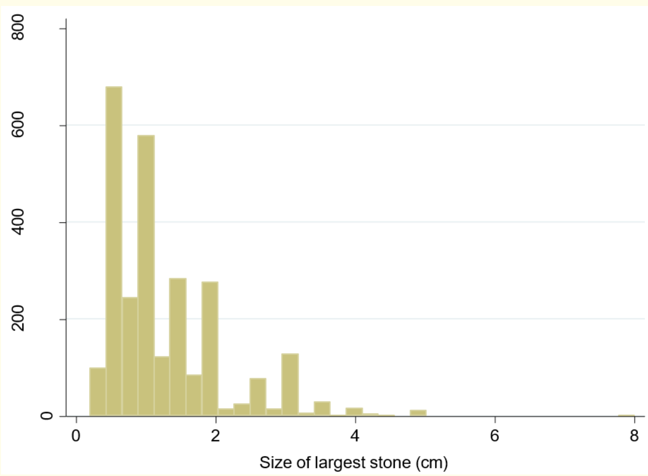


***Figure 3:*** Distribution of patients according to size of largest stone (cm, n=2,698).

| | ***Frequency (%)*** |
|---|---|
| Time from occurrence of symptoms to surgery | |
| <1 month | 1,139 (42.22) |
| 1-2 months | 413 (15.31) |
| > 2 months | 1,146 (42.48) |
| Diabetes | |
| No | 2,250 (83.40) |
| Yes | 448 (16.60) |
| History of jaundice | |
| No | 2,617 (97.00) |
| Yes | 82 (3.00) |
| History of fever | |
| No | 2,670 (98.96) |
| Yes | 28 (1.04) |
| Previous open abdominal surgery | |
| No | 2.323 (86.10) |
| Yes | 375 (13.90) |
| Previous laparoscopic abdominal surgery | |
| No | 2,573 (95.37) |
| Yes | 125 (4.63) |
| Previous endoscopic retrograde cholangiopancreatography (ERCP) | |
| No | 2.623 (97.22) |
| Yes | 75 (2.78) |
| History of biliary pancreatitis | |
| No | 2,674 (99.11) |
| Yes | 24 (0.89) |
| Anti-coagulant therapy | |
| No | 2,647 (98,11) |
| Yes | 51 (1.89) |
| Episode of hemodynamic instability | |
| No | 2,697 (99.96) |
| Yes | 1 (0.04) |
| Right upper quadrant tenderness | |
| No | 2,163 (80.17) |
| Yes | 535 (19.83) |
| White blood cell counts | |
| Normal | 2,288 (84.80) |
| Abnormal | 408 (15.12) |
| *Missing* | 2 (0.07) |
| Ultrasound | |
| No | 84 (3.11) |
| Yes | 2,614 (96.89) |

| | |
|---|---|
| Computerized Tomography Scan | |
| No | 2,576 (95.48) |
| Yes | 122 (4.52) |
| Magnetic Resonance Imaging | |
| No | 2,626 (97.33) |
| Yes | 72 (2.67) |
| Number of imaging modalities | |
| 1 | 2,602 (96.3) |
| 2 | 89 (3.29) |
| 3 | 11 (0.4!) |
| Gallbladder wall thickness | |
| Normal (<3mm) | 1,863 (69.05) |
| Thickened (>3mm) | 823 (30.50) |
| *Missing* | 12 (0.44) |
| Common bile duct size | |
| Normal | 2,614 (96.89) |
| Dilated | 80 (2.97) |
| *Missing* | 4 (0.15) |
| Impacted gallbladder stone | |
| No | 2,327 (86.25) |
| Yes | 371 (13.75) |
| Mirizzi syndrome | |
| No | 2,690 (99.70) |
| Yes | 8 (0.30) |
| Pericholecystic fluid | |
| No | 2,492 (92.36) |
| Yes | 206 (7.64) |
| Number of stones | |
| Multiple | 1,874 (69.46) |
| Single | 803 (29.76) |
| *Missing* | 21 (0.78) |
| Cirrhosis | |
| No | 2,682 (99.41) |
| Yes | 16 (0.59) |
| Surgeon | |
| Non-Hepato-Pancreato-Biliary surgeon | 2,288 (84.80) |
| Hepato-Pancreato-Biliary surgeon | 408 (15.12) |
| *Missing* | 2 (0.07) |
| Laparoscopic cholecystectomy | |
| Easy | 2,105 (78.02) |
| Difficult | 593 (21.98) |

***Table 1:*** Distribution of patients according to select clinical, laboratory, and radiological characteristics (n=2,698).

Out of the 593 difficult laparoscopic surgeries in the cohort, almost all (99.2%) were considered difficult as the procedure lasted for more than two hours, among other complications arising during the surgery. Among the 18 laparoscopic surgeries converted, 88.89% were because there was failure to identify critical view of safety. Out of the 2,698 patients, 10 (0.37%) expired.

***Bivariate analysis***

Considering the skewed nature of the quantitative exposure variables, Wilcoxon rank-sum test was used in assessing the association of age, body mass index, and size of largest stone (cm) with having difficult laparoscopic surgery. The authors did not find any strong evidence of differences in the age distribution of patients who have easy and difficult laparoscopic surgeries (p=0.22; crude OR (cOR): 1.00; 95% Confidence Interval: 0.99, 1.00), but they found strong evidence of differences in the distributions of body mass index (p<0.01; cOR: 1.03; 95% CI: 1.01, 1.05) and size of largest stone (cm, p<0.01; cOR: 1.42; 95% CI: 1.29, 1.58) between those who have easy and difficult laparoscopic surgeries.

Among the categorical variables and without adjusting for confounding, patient's sex, time from occurrence of symptoms to surgery, history of jaundice, history of fever, previous open abdominal surgery, previous laparoscopic abdominal surgery, previous endoscopic retrograde cholangiopancreatography, right upper quadrant tenderness, white blood cell counts, using ultrasound, using computerized tomography scan, using magnetic resonance imaging, number of imaging modalities used, gallbladder wall thickness, common bile duct size, presence of impacted gallbladder stone, presence of Mirizzi syndrome, presence of pericholecystic fluid, number of stones, presence of cirrhosis, and surgeon were all found to have strong evidence of association with difficult laparoscopic cholecystectomy (all have p<0.01). History of biliary pancreatitis was also found to have strong evidence of association with difficult laparoscopic cholecystectomy (p=0.01, Table 2).

| | ***Laparoscopic Cholecystectomy (N, %)*** | | ***p-value*** | ***Crude odds ratio (95% Confidence Interval)*** | ***p-value*** |
|---|---|---|---|---|---|
| | ***Easy*** | ***Difficult*** | | | |
| Sex of the Patient | | | <0.01 | | |
| Female | 1,419 (82.60) | 299 (17.40) | | 1 | |
| Male | 686 (70.07) | 293 (29.93) | | 2.03 (1.69, 2.44) | <0.01 |
| *Missing* | 0 (0.00) | 1 (100.0) | | | |
| Time from occurrence of symptoms to surgery | | | <0.01 | | |
| <1 month | 822 (72.11) | 318 (27.89) | | 1 | |
| 1-2 months | 337 (81.60) | 76 (18.40) | | 0.58 (0.44, 0.77) | <0.01 |
| > 2 months | 949 (82.59) | 200 (17.41) | | 0.39 (0.34, 0.44) | <0.01 |
| Diabetes | | | 0.67 | | |
| No | 1,752 (77.87) | 498 (22.13) | | 1 | |
| Yes | 353 (78.39) | 95 (21.21) | | 0.95 (0.73, 1.21) | 0.67 |

| | | | | | |
|---|---|---|---|---|---|
| History of jaundice | | | <0.01 | | |
| No | 2,075 (79.29) | 542 (20.71) | | 1 | |
| Yes | 30 (37.04) | 51 (62.96) | | 6.51 (4.11, 10.32) | <0.01 |
| History of fever | | | <0.01 | | |
| No | 2,097 (78.54) | 573 (21.46) | | 1 | |
| Yes | 8 (28.57) | 20 (71.43) | | 9.15 (4.01, 20.88) | <0.01 |
| Previous open abdominal surgery | | | <0.01[a] | | |
| No | 1,732 (74.56) | 591 (25.44) | | 1 | |
| Yes | 373 (99.47) | 2 (0.53) | | 0.02 (0.00, 0.06) | <0.01 |
| Previous laparoscopic abdominal surgery | | | <0.01[a] | | |
| No | 2,100 (81.62) | 473 (18.38) | | 1 | |
| Yes | 5 (4.00) | 120 (96.00) | | 106.56 (43.32, 262.18) | |
| Previous endoscopic retrograde cholangiopancreatography (ERCP) | | | <0.01 | | <0.01 |
| No | 2,074 (79.07) | 549 (20.93) | | 1 | |
| Yes | 31 (41.33) | 44 (58.67) | | 5.36 (3.35, 8.57) | |
| History of biliary pancreatitis | | | 0.01 | | 0.01 |
| No | 2,092 (78.23) | 582 (21.77) | | 1 | |
| Yes | 13 (54.17) | 11 (45.83) | | 3.04 (1.36, 6.82) | |
| Anti-coagulant therapy | | | 0.34 | | |
| No | 2,068 (78.13) | 579 (21.87) | | 1 | |
| Yes | 37 (72.55) | 14 (27.45) | | 1.35 (0.73, 2.52) | 0.34 |
| Episode of hemodynamic instability | | | 0.22[a] | | |
| No | 2,105 (78.05) | 592 (21.95) | | 1 | |
| Yes | 0 (0.00) | 1 (100.0) | | 10.66[b] (0.43, 262.04) | 0.15[b] |
| Right upper quadrant tenderness | | | <0.01 | | |

| | | | | | |
|---|---|---|---|---|---|
| No | 1,910 (88.30) | 253 (11.70) | | 1 | |
| Yes | 195 (36.45) | 340 (63.55) | | 13.16 (10.57, 16.39) | <0.01 |
| White blood cell counts | | | <0.01[a] | | |
| Normal | 1,917 (83.78) | 371 (16.22) | | 1 | |
| Abnormal | 188 (46.08) | 220 (53.92) | | 6.05 (4.83, 7.57) | <0.01 |
| *Missing* | 0 (0.00) | 2 (100.0) | | | |
| Ultrasound | | | <0.01 | | |
| No | 23 (27.38) | 61 (72.62) | | 1 | |
| Yes | 2,082 (79.65) | 532 (20.35) | | 0.10 (0.06, 0.16) | <0.01 |
| Computerized Tomography Scan | | | <0.01 | | |
| No | 2,068 (80.28) | 508 (19.72) | | 1 | |
| Yes | 37 (30.33) | 85 (69.67) | | 9.35 (6.28, 13.92) | <0.01 |
| Magnetic Resonance Imaging | | | <0.01 | | |
| No | 2,080 (79.21) | 546 (20.79) | | 1 | |
| Yes | 25 (34.72) | 47 (65.28) | | 7.16 (4.37, 11.74) | <0.01 |
| Number of imaging modalities | | | <0.01[a] | | |
| 1 | 2,072 (79.72) | 527 (20.28) | | 1 | |
| 2 | 27 (30.68) | 61 (69.32) | | 8.79[b] (5.55, 13.91) | <0.01[b] |
| 3 | 6 (54.55) | 5 (45.45) | | 3.32[b] (1.06, 10.39) | 0.04[b] |
| Gallbladder wall thickness | | | <0.01[a] | | |
| Normal (<3mm) | 1,684 (90.39) | 179 (9.61) | | 1 | |
| Thickened (>3mm) | 410 (49.82) | 413 (50.18) | | 9.48 (7.71, 11.64) | <0.01 |
| *Missing* | 11 (91.67) | 1 (8.33) | | | |
| Common bile duct size | | | <0.01 | | |
| Normal | 2,071 (79.23) | 543 (20.77) | | 1 | |

| | | | | | |
|---|---|---|---|---|---|
| Dilated | 33 (41.25) | 47 (58.75) | | 5.43 (3.45, 8.56) | <0.01 |
| *Missing* | 1 (25.00) | 3 (75.00) | | | |
| Impacted gallbladder stone | | | <0.01 | | |
| No | 1,934 (83.11) | 393 (16.89) | | 1 | |
| Yes | 171 (46.09) | 200 (53.91) | | 5.76 (4.57, 7.25) | <0.01 |
| Mirizzi syndrome | | | <0.01 | | |
| No | 2,105 (78.25) | 585 (21.75) | | | |
| Yes | 0 (0.00) | 8[a] (100.0) | | 4.11[b] (1.26, 6.97) | <0.01[b] |
| Pericholecystic fluid | | | <0.01 | | |
| No | 2,017 (80.94) | 475 (19.06) | | 1 | |
| Yes | 88 (42.72) | 118 (57.28) | | 5.69 (4.25, 7.64) | <0.01 |
| Number of stones | | | <0.01 | | |
| Multiple | 1,410 (75.24) | 464 (24.76) | | 1 | |
| Single | 681 (84.81) | 122 (15.19) | | 0.54 (0.44, 0.67) | <0.01 |
| *Missing* | 14 (66.67) | 7 (33.33) | | | |
| Cirrhosis | | | <0.01[a] | | |
| No | 2,099 (78.26) | 583 (21.74) | | 1 | |
| Yes | 6 (37.50) | 10 (62.50) | | 6.00 (2.17, 16.58) | <0.01 |
| Surgeon | | | <0.01 | | |
| Non-Hepato-Pancreato-Biliary surgeon | 1,744 (76.22) | 544 (23.78) | | 1 | |
| Hepato-Pancreato-Biliary surgeon | 359 (87.99) | 49 (12.01) | | 0.44 (0.33, 0.62) | <0.01 |
| *Missing* | 2 (100.0) | 0 (0.00) | | | |

[a] Fisher's exact test due to small cells.
[b] Firth's logistic regression was used due to separation (0-cell)

***Table 2:*** Crude associations between clinical, radiological, and laboratory variables with difficult laparoscopic cholecystectomy (n=2,698).

The authors encountered separation when they estimated the crude odds ratio for the associations between episodes of hemodynamic instability, white blood cell counts, number of imaging modalities used, presence of Mirizzi syndrome, and surgeon with difficulty of laparoscopic surgery. To address these issues, the authors used Firth's penalized logistic regression to estimate the crude odds ratios of these associations [8, 9]. However, only one patient had episodes of hemodynamic instability, and this variable was not found to be associated with the outcome, and thus, this variable was no longer considered in multivariate analysis.

Diabetes was also not found to be associated with the outcome in both previous studies and the dataset, and thus it was no longer considered in the multivariate analysis. History of anticoagulant therapy, while found to not be associated with the outcome in this dataset, will still be included in the multivariate analysis as previous studies confirmed its association with the outcome [10].

A correlation matrix to assess potential multicollinearity was ran and the authors found that usage of magnetic resonance imaging is highly correlated with number of imaging modalities used (r=0.80), thus, they excluded the number of imaging modalities from the multivariate analysis. The authors also found that usage of ultrasound and computerized tomography scans were highly correlated with each other (r=0.77), thus they excluded usage of computerized tomography scans from the multivariate analysis. Lastly, prior to multivariate analysis, the authors removed some 57 (2.11%) observations with missing data in any of the remaining variables of interest.

***Multivariate analysis***

The authors included 2,641 complete patient records for multivariate analysis. Considering the separation issues for some clinically important variables (e.g., Mirizzi syndrome) detected during bivariate analysis, they used Firth's penalized logistic regression to come up with their multivariate model. In the model building process, the authors tried to test for the departure from the linearity assumption of the time from occurrence of symptoms to surgery, but they got a statistically significant result (p=0.01) for the likelihood ratio test which meant showing stratum-specific odds ratios.

After adjusting for other variables, the authors found that being male (adjusted OR (aOR): 2.07; 95% CI: 1.55, 2.77), per unit increase in body mass index (aOR: 1.03, 95% CI: 1.01, 1.06), having a history of jaundice (aOR: 5.06; 95% CI: 2.31, 11.08), having a history of fever (aOR: 14.13; 95% CI: 2.11, 94.79), history of laparoscopic abdominal surgery (aOR: 99.84; 95% CI: 35.73, 278.94), having right upper quadrant tenderness (aOR: 10.89; 95% CI: 7.56, 15.68), thickened gallbladder wall (aOR: 6.16; 95% CI: 4.48, 8.47), dilated common bile duct (aOR: 3.25; 95% CI: 1.32, 8.02), having impacted gallbladder stone (aOR: 1.61; 95% CI: 1.06, 2.44), having pericholecystic fluid (aOR: 2.45; 95% CI: 1.47, 4.09), having cirrhosis (aOR: 5.02; 95% CI: 1.18, 21.40), and per centimeter increase in size of largest stone (aOR: 1.64; 95% CI: 1.37, 1.97) were all strongly associated with difficult laparoscopic surgery. On the other hand, having history of open abdominal surgery (aOR: 0.02; 95% CI: 0.01, 0.07), having used ultrasound (aOR: 0.38; 95% CI: 0.18, 0.78), having single stones (aOR: 0.54; 95% CI: 0.38, 0.76), and being operated by a Hepato-Pancreato-Biliary surgeon (aOR: 0.11; 95% CI: 0.06, 0.19) showed strong evidence of being a protective factor against difficult laparoscopic surgery (Table 3).

| | ***Adjusted odds ratio (95% Confidence Interval)*** | ***p-value*** |
|---|---|---|
| Age (per year increase) | 1.01 (1.00, 1.02) | 0.12 |
| Sex | | |
| Female | 1 | |
| Male | 2.07 (1.55, 2.77) | <0.01 |
| Body mass index (per year increase) | 1.03 (1.01, 1.06) | 0.02 |
| Time from symptoms to surgery | | |
| < 1 month | 1 | |
| 1-2 months | 1.31 (0.84, 2.05) | 0.24 |

| | | |
|---|---|---|
| > 2 months | 1.27 (0.91, 1.76) | 0.16 |
| History of jaundice | | |
| No | 1 | |
| Yes | 5.06 (2.31, 11.08) | <0.01 |
| History of fever | | |
| No | 1 | |
| Yes | 14.13 (2.11, 94.79) | 0.01 |
| History of open abdominal surgery | | |
| No | 1 | |
| Yes | 0.02 (0.01, 0.07) | <0.01 |
| History of laparoscopic abdominal surgery | | |
| No | 1 | |
| Yes | 99.84 (35.73, 278.93) | <0.01 |
| Previous endoscopic retrograde cholangiopancreatography (ERCP) | | |
| No | 1 | |
| Yes | 0.61 (0.22, 1.75) | 0.36 |
| Right upper quadrant tenderness | | |
| No | 1 | |
| Yes | 10.89 (7.56, 15.68) | <0.01 |
| White blood cell counts | | |
| Normal | 1 | |
| Abnormal | 1.09 (0.73, 1.63) | 0.66 |
| Ultrasound | | |
| No | 1 | |
| Yes | 0.38 (0.18, 0.78) | 0.01 |
| Magnetic Resonance Imaging | | |
| No | 1 | |
| Yes | 0.74 (0.27, 2.01) | 0.55 |
| Gallbladder wall thickness | | |
| Normal (<3mm) | 1 | |
| Thickened (>3mm) | 6.16 (4.48, 8.47) | <0.01 |
| Common bile duct size | | |
| Normal | 1 | |
| Dilated | 3.25 (1.32, 8.02) | 0.01 |
| Impacted gallbladder stone | | |
| No | 1 | |
| Yes | 1.61 (1.06, 2.44) | 0.03 |
| Mirizzi syndrome | | |
| No | 1 | |
| Yes | 3.69 (0.12, 113.40) | 0.48 |

| | | |
|---|---|---|
| Pericholecystic fluid | | |
| No | 1 | |
| Yes | 2.45 (1.47, 4.09) | <0.01 |
| Number of stones | | |
| Multiple | 1 | |
| Single | 0.54 (0.38, 0.76) | <0.01 |
| Cirrhosis | | |
| No | 1 | |
| Yes | 5.02 (1.18, 21.40) | 0.03 |
| Size of largest stone (per cm increase) | 1.64 (1.37, 1.97) | <0.01 |
| Surgeon | | |
| non-Hepato-Pancreato-Biliary surgeon | 1 | |
| Hepato-Pancreato-Biliary surgeon | 0.11 (0.06, 0.19) | <0.01 |
| History of biliary pancreatitis | | |
| No | 1 | |
| Yes | 0.68 (0.19, 2.47) | 0.56 |
| Anti-coagulant therapy | | |
| No | 1 | |
| Yes | 0.65 (0.16, 2.66) | 0.55 |

***Table 3:*** Multivariate model describing adjusted associations of select sociodemographic, clinical, laboratory, and radiological variables with difficult laparoscopic surgery (n=2,641).

## Discussion

This study showed that around 593 (21.98%) of the patients had difficult LC. Of the 593 difficult cases, 544 (23.78%) were done by non-Hepato-Pancreato-Biliary surgeons and 49 (12.01%) were done by Hepato- Pancreato-Biliary surgeons. Almost all (99.2%) were considered difficult as the procedure lasted for more than two hours. Among the 18 laparoscopic surgeries converted to open, 88.89% were because there was failure to identify the critical view of safety. The overall conversion-to-open rate was 0.67 % (18 of 2,698 patients). Of the 18 laparoscopic converted to open cholecystectomies only 3 were by Hepato-Pancreato- Biliary surgeons and 15 were by non-Hepato-Pancreato-Biliary surgeons. Based on the multivariate analysis, after adjusting for other variables, the study showed that factors that were strongly associated with difficult LC are being male, per unit increase in body mass index, having a history of jaundice, having a history of fever, history of laparoscopic abdominal surgery and having right upper quadrant tenderness. Radiologic factors also strongly associated with difficult LC were thickened gallbladder wall, dilated common bile duct, having impacted gallbladder stone, having pericholecystic fluid, having cirrhosis, and per centimeter increase in size of largest stone. On the other hand, having history of open abdominal surgery, having used ultrasound, having single stones, and being operated by a Hepato-Pancreato-Biliary surgeon showed strong evidence of being a protective factor against difficult laparoscopic surgery.

In a similar study in Nepal, Bhandari, et al., had a total difficult LC of 52 patients (15.4%) and overall conversion rate was 8.9% in their retrospective cross-sectional review of 338 patients. They concluded that gender (male), past history of acute cholecystitis, gallbladder wall thickness (≥4-5 mm), fibrotic gallbladder, and adhesion at Calot's triangle are significant predictors for difficult LC [6]. Rothman, et al. concluded in their Systematic Review and Meta-Analysis of Observational Studies that in 32 studies, including 460,995 patients, a gallbladder wall thicker than 4-5 mm, a contracted gallbladder, age above 60 or 65, male gender, and acute cholecystitis were risk factors for the conversion of laparoscopic cholecystectomy to open surgery. Furthermore, there was no association between diabetes mellitus or white blood cell count and conversion to open surgery [11]. There are no definite scientific explanations for the preponderance of difficult LC in males but results have been similar in other literature reviewed. This may suggest a greater pain threshold, dietary practices or late health-seeking behavior for males. The scope of which is beyond this study.

The factors of right upper quadrant pain and history of fever pertains to acute inflammation which were strongly associated with difficult LC in this study. Similarly, in a retrospective study of Wennmacker et. al. wherein they looked at predicting operative difficulty of LC with acute biliary presentations using a prediction model of "complicated" cases comprising of clinical diagnosis of acute cholecystitis, C-reactive protein >10.5 mg/L and pericholecystic fluid on pre-operative imaging. They concluded that 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 preoperative radiological findings of pericholecystic fluid [12].

Surgery not only deals with the clinical aspect but also the physical aspect of the disease. Thus, body habitus may play a role in difficulty especially in laparoscopy wherein the physics is based on a "lever and fulcrum" mechanism. The laparoscopic instruments serve as the lever and the abdominal wall serve as the fulcrum. Theoretically, with a wide fulcrum, such as a thick subcutaneous tissue layer in obesity, this limits the movement of the instruments making dissection more difficult. As body mass index (BMI) remains the standard measuring tool for obesity, it was included in this study. The BMI of the patients ranged from 16.80 - 53.00 kg/m$^2$, with a mean BMI of 27.19 (± 5.06) kg/m$^2$, and a median BMI of 26.40 (interquartile range: 23.99-30.00) kg/m$^2$. The study indeed showed a strong association with difficult LC per unit increase in BMI.

As preoperative radiologic studies provide valuable tools for surgeons, these factors are important to possibly predict a difficult LC. In this study, radiologic findings associated with a difficult LC are a thickened gallbladder wall, dilated common bile duct, having impacted gallbladder stone, having pericholecystic fluid, having cirrhosis, and per centimeter increase in size of the largest stone. Meanwhile, having a single stone is a protective factor against difficult LC. Nidoni et al. also concluded in their prospective study of 180 patients to predict difficult LC using Clinical and Radiologic parameters, difficult laparoscopic cholecystectomy and conversion to open surgery can be predicted preoperatively based on the number of previous attacks of cholecystitis, white blood cell count, gallbladder wall thickness and presence or absence of pericholecystic collection [13].

In the era of modern medicine, specialists and subspecialists are trained mostly in a specific clinical or anatomical organ system. This high-volume LC institution where this study was conducted is a tertiary private hospital with an 800-bed capacity, with almost 30 years of laparoscopy experience, and has several surgical fellowship training programs including Hepato-Pancreato-Biliary (HPB) Surgery. As expected in the results of the study, HPB surgeons showed strong evidence of being a protective factor against difficult laparoscopic cholecystectomy. Out of the 593 total difficult LCs, 18 (0.67%) were converted to open cholecystectomies. Only 3 (0.1% conversion-to-open rate) of the 18 converted-to-open cases were by HPB surgeons. Difficult LC was categorized in only 12.01% (49 of 408) in HPB surgeons as compared to 23.78% (544 of 2288) in non-HPB surgeons. As "difficulty" is also partly subjective, this is possibly a reflection of the knowledge and skill of HPB surgeons in this particular field of interest.

Discrepancies in this study between bivariate and multivariate analysis results exists as explained previously. Separation despite high nominal sample size - while the nominal sample size was high throughout the analysis and allowed for precise estimation of associations between the different exposure variables and outcome variables, and very few observations were excluded, many of the important clinical variables have lopsided distributions which resulted in separation. The authors chose to retain these clinical variables in their multivariate analyses and handled it using best practices for handling separation, namely by using penalized likelihood models [9]. One alternative would be to exclude these clinical variables from multivariable analysis and estimate it using traditional likelihood models, but this would result in uncontrolled confounding. However, since the authors used penalized logistic regression, they were unable to estimate area under the respondent operating characteristic curve which prevented them from assessing the model's performance in predicting the outcome. There were also unmeasured confounding factors - no data for some clinical variables known to be associated with difficult laparoscopic cholecystectomy (Calot's triangle, fibrosis, etc.). As this was also a retrospective study, the limitations of study such as record keeping and incomplete data could possibly exist. Although the institution caters to charity cases, socioeconomic biases can likely exist as this is a private institution which caters mostly to the more fortunate patients who can afford. Therefore, this study cannot generalize for all patients of the country but would be a good basis.

## Conclusion

There are predictive factors that can be assessed preoperatively to anticipate the difficulty of a laparoscopic cholecystectomy such as being male, per unit increase in body mass index, having a history of jaundice, having a history of fever, history of laparoscopic abdominal surgery and having right upper quadrant tenderness. Radiologic factors also strongly associated with difficult LC are thickened gallbladder wall, dilated common bile duct, having impacted gallbladder stone, having pericholecystic fluid, having cirrhosis, and per centimeter increase in size of largest stone.

## Recommendations

The authors highly recommend that to further pursue predictive factors for a difficult LC, a preoperative scoring system model utilizing the significant factors in this study can be created and validate this with a prospective study. This can later on be applied to other institutions and tested if indeed, these are predictive factors. Then, if this still exhibits significance, this can be used later on as a tool to preoperatively predict which laparoscopic cholecystectomy cases can be done in outpatient setting thereby conserving health care resources.

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## References

1. He XiangYi and Shi Jian. "Consensus on diagnosis and treatment of chronic cholecystitis and gallstones in China". J Clin Hepatol 35.6 (2019): 1231-1236.
2. Keus F., et al. "Laparoscopic versus open cholecystectomy for patients with symptomatic cholecystolithiasis". Cochrane Database of Systematic Reviews 4 (2006): CD006231.
3. Gurusamy KS., et al. "Early versus delayed laparoscopic cholecystectomy for people with acute cholecystitis". Cochrane Database of Systematic Reviews 6 (2013): CD005440.
4. Thangavelu A, Rosenbaum S and Thangavelu D. "Timing of Cholecystectomy in Acute Cholecystitis". J Emerg Med 54.6 (2018): 892-897.
5. Sakpal SV, Bindra SS and Chamberlain RS. "Laparoscopic cholecystectomy conversion rates two decades later". JSLS 14.4 (2010): 476-483.

6. Bhandari TR, Khan SA and Jha JL. "Prediction of difficult laparoscopic cholecystectomy: An observational study". Ann Med Surg (Lond) 72 (2021): 103060.
7. StataCorp. Stata 14.0 IC. College Station, TX: StataCorp (2015).
8. Firth D. "Bias reduction of maximum likelihood estimates". Biometrika 80.1 (1993): 27-38.
9. Mansournia MA., et al. "Separation in Logistic Regression: Causes, Consequences, and Control". American Journal of Epidemiology 187.4 (2018): 864-70.
10. Inoue K., et al. "Risk factors for difficulty of laparoscopic cholecystectomy in grade II acute cholecystitis according to the Tokyo guidelines 2013". BMC Surgery 17.1 (2017): 114.
11. Philip Rothman J., et al. "Preoperative Risk Factors for Conversion of Laparoscopic Cholecystectomy to Open Surgery - A Systematic Review and Meta-Analysis of Observational Studies". Dig Surg 33.5 (2016): 414-23.
12. Wennmacker SZ., et al. "Predicting operative difficulty of laparoscopic cholecystectomy in patients with acute biliary presentations". ANZ J Surg 89.11 (2019): 1451-1456.
13. Nidoni R., et al. "Predicting Difficult Laparoscopic Cholecystectomy Based on Clinicoradiological Assessment". J Clin Diagn Res 9.12 (2015): PC09-12.
14. Griniatsos John. "Factors predisposing to conversion from laparoscopic to open cholecystectomy". Annals of Laparoscopic and Endoscopic Surgery 3 (2018): 12-12.
15. Onoe S., et al. "A preoperative predictive scoring system to predict the ability to achieve the critical view of safety during laparoscopic cholecystectomy for acute cholecystitis". HPB 19 (2017): 406-10.
16. Bourgouin S., et al. "How to predict difficult laparoscopic cholecystectomy? Proposal for a simple preoperative scoring system". Am J Surg 212 (2016): 873-81.
17. Wevers KP, van Westreenen HL and Patijin GA. "Laparoscopic cholecystectomy in acute cholecystitis: C-reactive protein level combined with age predicts conversion". Surg Laparosc Endosc Percutan Tech 23 (2013): 163-6.
18. Suman Baral, Raj Kumar Chhetri and Neeraj Thapa. "Utilization of an Intraoperative Grading Scale in Laparoscopic Cholecystectomy: A Nepalese Perspective". Gastroenterology Research and Practice (2020).
19. Koichi Inukai. "Predictive Factors for a Long Postoperative Stay after Emergency Laparoscopic Cholecystectomy Using the 2013 Tokyo Guidelines: A Retrospective Study". Minimally Invasive Surgery (2019).
20. Gupta N., et al. "Validation of a scoring system to predict difficult laparoscopic cholecystectomy". Int J Surg 11.9 (2013): 1002-6.