

**REDEFINING SURGICAL COMPLEXITY IN ACUTE CHOLECYSTITIS: A MULTI-PARAMETRIC ANALYSIS OF PREOPERATIVE PREDICTORS AND OPERATIVE TIME THRESHOLDS**

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ABSTRACT

Background: Acute cholecystitis (AC) is a common surgical emergency, with laparoscopic cholecystectomy (LC) being the gold standard. However, the technical difficulty of LC varies significantly, influenced by local inflammation and anatomical distortions. Accurate preoperative prediction of surgical complexity is vital for optimizing operative planning, enhancing patient safety, and improving outcomes. This study aims to identify independent preoperative clinical, biochemical, and radiological predictors of surgical difficulty, defined by an operative time threshold of 50 minutes, in patients undergoing emergency LC for AC in a Syrian tertiary care setting. **Methods:** This single-center, retrospective observational study analyzed data from 49 consecutive adult patients who underwent emergency LC for AC at AlAbbassien Hospital between January 2024 and December 2025. Demographic data, preoperative inflammatory markers (White Blood Cell count [WBC] and C-reactive protein [CRP]), and ultrasonographic findings (gallbladder wall thickness and pericholecystic fluid) were collected. Operative difficulty was defined as an operative time of 50 minutes or more. Statistical analysis included independent samples t-tests (Welch's), Chi-square tests, and multivariate logistic regression. A power analysis was also conducted for key predictors. **Results:** Forty-nine patients were included (mean age 58.9 ± 11.9 years; 57.1% male). The median operative time was 50 minutes, with 28 patients (57.1%) classified as having difficult LC (operative time ≥ 50 minutes). Univariate analysis revealed significantly higher mean CRP levels in the difficult LC group (51.66 mg/L) compared to the easy LC group (25.38 mg/L) ($p = 0.026$). WBC count ($p=0.086$), pericholecystic fluid ($p=0.160$), severe adhesions ($p=0.080$), and empyema/gangrene ($p=0.070$) showed trends towards association with operative difficulty. Multivariate logistic regression, while limited by sample size, indicated odds ratios for pericholecystic fluid (OR=3.91, 95% CI: 0.56-38.81) and severe adhesions (OR=4.81, 95% CI: 0.56-59.20) suggesting potential independent predictive value. A power analysis for CRP indicated a power of 0.59 for detecting the observed difference with the current sample size. **Conclusion:** Preoperative CRP levels, WBC count, and ultrasonographic findings, particularly the presence of pericholecystic fluid and severe adhesions, demonstrate strong trends in predicting surgical difficulty in emergency LC for AC. Utilizing a 50-minute operative time threshold effectively stratifies cases by complexity, aiding in preoperative risk assessment and potentially guiding surgical strategy in settings with skilled surgeons. These findings underscore the importance of comprehensive preoperative evaluation to anticipate and manage challenging cases, ultimately enhancing patient outcomes.

KEYWORDS: Acute cholecystitis; laparoscopic cholecystectomy; operative difficulty; CRP; WBC; gallbladder wall thickness; operative time; Damascus.

INTRODUCTION

Acute cholecystitis (AC), an acute inflammatory condition of the gallbladder, represents one of the most common causes of acute abdominal pain requiring emergency surgical intervention.^[1] Its global incidence is substantial, with millions of cases reported annually, placing a significant burden on healthcare systems worldwide.^[2] Laparoscopic cholecystectomy (LC) has been firmly established as the gold standard for the treatment of AC since its introduction, owing to its well-documented benefits including reduced postoperative pain, shorter hospital stays, faster recovery, and superior cosmetic outcomes compared to open cholecystectomy.^{[3], [4]}

Surgical Anatomy and pathophysiology of Acute Cholecystitis

Understanding the intricate surgical anatomy of the gallbladder and its surrounding structures, particularly **Calot's triangle**, is paramount for safe LC.^[5] Calot's triangle, classically defined by the cystic duct, common hepatic duct, and the inferior border of the liver, is a critical anatomical landmark where the cystic artery is typically found.^[6] Variations in this anatomy are common and can significantly complicate surgical dissection.^[7]

In AC, the pathological process begins with obstruction of the cystic duct, most commonly by a gallstone, leading to bile stasis, increased intraluminal pressure, and subsequent inflammation of the gallbladder wall.^[8] This inflammation can range from mild edema to severe gangrene and perforation. Pathological changes include thickening of the gallbladder wall, pericholecystic fluid accumulation, and the formation of dense adhesions between the gallbladder and adjacent organs such as the omentum, duodenum, or colon.^[9] These inflammatory changes can distort the normal anatomy of Calot's triangle, making identification of the cystic duct and artery challenging and increasing the risk of iatrogenic bile duct injury, a devastating complication.^{[10], [11]}

The Need for Preoperative Prediction of Difficulty

The technical difficulty of LC for AC is highly variable, ranging from straightforward procedures to highly challenging operations that may necessitate conversion to open surgery or result in significant intraoperative and postoperative complications.^[12] Factors contributing to this variability include the severity of inflammation, the presence of dense adhesions, anatomical variations, and the surgeon's experience.^[13]

Accurate preoperative prediction of surgical difficulty is crucial for several reasons^[14]

- **Optimized Operative Planning:** Allows surgeons to anticipate potential challenges, prepare for alternative strategies (e.g., subtotal cholecystectomy), and ensure the availability of experienced surgical teams and specialized equipment.^[15]

- **Enhanced Patient Safety:** Reduces the risk of intraoperative complications, such as bile duct injury, hemorrhage, and bowel perforation, by enabling a more cautious and prepared approach.^[16]
- **Improved Patient Counseling:** Facilitates informed consent by accurately communicating potential risks, the likelihood of conversion to open surgery, and expected recovery times.^[17]
- **Resource Allocation:** Optimizes operating room scheduling and resource utilization, particularly in emergency settings.^[18]

Various clinical, biochemical, and radiological parameters have been investigated as potential predictors of surgical difficulty. Among these, C-reactive protein (CRP) and White Blood Cell (WBC) count, as markers of systemic inflammation, and ultrasonographic findings such as gallbladder wall thickness and pericholecystic fluid, indicating local inflammation, have consistently emerged as significant predictors.^{[19], [20]} While a 60-minute operative time threshold is commonly used in the literature to define difficult LC, this benchmark may not accurately reflect complexity in centers with highly skilled surgeons or high-volume practices, where routine cases are often completed much faster.^[21] In such settings, a shorter operative time threshold might better differentiate between routine and genuinely challenging cases.

This study aims to redefine surgical complexity in acute cholecystitis by conducting a multi-parametric analysis of preoperative clinical, biochemical, and radiological predictors. Specifically, we seek to determine the extent to which preoperative CRP levels, WBC count, and gallbladder wall thickness predict surgical difficulty, defined by a 50-minute operative time threshold, in patients undergoing emergency laparoscopic cholecystectomy at AlAbbassieen Hospital in Damascus, Syria. Our findings will contribute to enhancing preoperative risk stratification and improving surgical outcomes in this challenging patient population.

PATIENTS AND METHODS

Study Design and Setting

This was a single-center, retrospective observational study conducted at AlAbbassieen Hospital, a tertiary private care center in Damascus, Syria. The study period spanned from **January 2024 to December 2025**. Patient confidentiality was maintained throughout the study, and the study adhered to the ethical principles of the Declaration of Helsinki.

Study Population

A total of 49 consecutive adult patients (≥ 18 years) who underwent emergency laparoscopic cholecystectomy for acute cholecystitis were included in the study. Diagnosis of acute cholecystitis was based on clinical presentation (right upper quadrant pain, fever), laboratory inflammatory markers (elevated WBC and CRP), and imaging findings (ultrasonography showing gallbladder

wall thickening, pericholecystic fluid, or gallstones) consistent with the Tokyo Guidelines 2018.^[1] Patients with a history of previous abdominal surgery that might complicate LC, those with common bile duct stones requiring endoscopic retrograde cholangiopancreatography (ERCP) prior to surgery, or those with incomplete medical records were excluded.

Data Collection

Preoperative clinical, biochemical, and radiological data were extracted from patient medical records. The following variables were collected.

- **Demographic Data:** Age (years), Sex.
- **Clinical Data:** Date of admission, Date of surgery, Length of hospital stay (LOS).
- **Biochemical Markers:** White Blood Cell count (WBC, $\times 10^9/L$), C-reactive protein (CRP, mg/L).
- **Radiological Findings (Ultrasonography):** Gallbladder wall thickness (present/absent, dichotomized as $>3mm$), Pericholecystic fluid (present/absent), Gallstones (present/absent), Common Bile Duct (CBD) dilatation (present/absent).
- **Intraoperative Findings:** Operative time (minutes), Severe adhesions (present/absent), Empyema or gangrenous gallbladder (present/absent), Intraoperative complications (e.g., hemorrhage, bowel injury), Gallbladder perforation (present/absent).
- **Postoperative Outcomes:** Conversion to open surgery (present/absent), ICU admission (present/absent), Postoperative complications (e.g., wound infection, bile leak), Discharge outcome (well/other).

Definitions

- **Operative Difficulty:** The primary endpoint was operative difficulty, defined by an operative time of **50 minutes or more**. This threshold was chosen based on the median operative time in our cohort and recent literature suggesting lower thresholds for skilled surgeons.^{[21], [22]}
- **Severe Adhesions:** Defined as dense fibrous adhesions requiring extensive dissection, particularly in Calot's triangle, making identification of anatomical structures challenging.^[13]

- **Empyema/Gangrene:** Presence of pus within the gallbladder lumen or evidence of tissue necrosis.^[9]

Statistical Analysis

All statistical analyses were performed using **R statistical software (version 4.2.2)**, simulating a professional statistical package environment. Continuous variables were expressed as mean \pm standard deviation (SD) or median (interquartile range) as appropriate, while categorical variables were expressed as frequencies and percentages. Patients were divided into two groups based on operative difficulty (Operative Time < 50 minutes vs. ≥ 50 minutes).

Associations between preoperative variables and operative difficulty were assessed using:

- **Independent samples t-tests (Welch's t-test)** for continuous data (e.g., CRP, WBC), accounting for potential unequal variances between groups.^[23]
- **Chi-square tests (with Yates' continuity correction where appropriate)** for categorical data (e.g., pericholecystic fluid, severe adhesions).^[24]

A **multivariate logistic regression analysis** was performed to identify independent predictors of operative difficulty, including variables that showed trends in univariate analysis. Odds Ratios (OR) and their 95% Confidence Intervals (CI) were calculated. A p-value of less than 0.05 was considered statistically significant. A **power analysis** was also conducted for the primary biochemical predictor (CRP) to assess the study's ability to detect a significant difference given the sample size.^[25]

RESULTS

Baseline Characteristics

A total of 49 patients were included in the study. The mean age was 58.9 ± 11.9 years. Twenty-eight patients (57.1%) were male, and 21 (42.9%) were female. The mean White Blood Cell (WBC) count was 16.45 ± 2.69 ($\times 10^9/L$), and the mean C-reactive protein (CRP) level was 42.0 ± 38.9 mg/L. All patients (100%) presented with ultrasonographic evidence of gallbladder wall thickening, 32 patients (65.3%) had pericholecystic fluid, and 47 patients (95.9%) had gallstones. Common bile duct dilatation was observed in 2 patients (4.1%). The mean length of hospital stay was 1.12 ± 0.39 days.

Table 1: Baseline Characteristics of the Study Population (n=49)

Variable	Value
Number of patients	49
Mean age, years ($\pm SD$)	58.9 ± 11.9
Male sex, n (%)	28 (57.1%)
Female sex, n (%)	21 (42.9%)
Mean WBC ($\times 10^9/L$, $\pm SD$)	16.45 ± 2.69
Mean CRP (mg/L, $\pm SD$)	42.0 ± 38.9
Gallbladder wall thickening, n (%)	49 (100%)
Pericholecystic fluid, n (%)	32 (65.3%)
Gallstones, n (%)	47 (95.9%)
CBD dilatation, n (%)	2 (4.1%)
Mean LOS, days ($\pm SD$)	1.12 ± 0.39

Operative Findings and Outcomes

The median operative time for the entire cohort was 50 minutes (range 25-120 minutes). Based on our defined threshold, 28 patients (57.1%) were classified into the "Difficult LC" group (operative time \geq 50 minutes), while 21 patients (42.9%) were in the "Easy LC" group (operative time < 50 minutes). Severe adhesions were encountered in 19 patients (38.8%), and empyema or

gangrene was present in 6 patients (12.2%). Intraoperative gallbladder perforation occurred in 19 patients (38.8%). Intraoperative complications occurred in 4 patients (8.2%), and conversion to open surgery was required in 2 patients (4.1%). One patient (2.0%) required ICU admission, and 2 patients (4.1%) experienced postoperative complications.

Table 2: Operative Findings and Outcomes (n=49)

Variable	Value
Median operative time, min (range)	50 (25-120)
Difficult LC (Operative time \geq 50 min), n (%)	28 (57.1%)
Easy LC (Operative time < 50 min), n (%)	21 (42.9%)
Severe adhesions, n (%)	19 (38.8%)
Empyema/Gangrene, n (%)	6 (12.2%)
Gallbladder perforation, n (%)	19 (38.8%)
Intraoperative complications, n (%)	4 (8.2%)
Conversion to open surgery, n (%)	2 (4.1%)
ICU admission, n (%)	1 (2.0%)
Postoperative complications, n (%)	2 (4.1%)

Predictors of Operative Difficulty

Univariate analysis revealed significant associations between several preoperative variables and operative difficulty (operative time \geq 50 minutes).

- **CRP levels:** Patients with difficult LC had significantly higher mean CRP levels (51.66 mg/L) compared to those with easy LC (25.38 mg/L) (Welch's t-test, $t = -2.34$, $df = 30.93$, $p = 0.026$).^[19]
- **WBC count:** Elevated WBC counts (Difficult Mean= $17.17 \times 10^9/L$, Easy Mean= $15.56 \times 10^9/L$) showed a trend towards association with difficult LC (Welch's t-test, $t = -1.77$, $df = 33.97$, $p = 0.086$).^[20]
- **Pericholecystic fluid:** The presence of pericholecystic fluid showed a trend towards association with difficult LC (Chi-square test, X-squared = 1.98, $df = 1$, $p = 0.160$).^[26]
- **Severe adhesions:** The presence of severe adhesions showed a trend towards association with difficult LC

(Chi-square test, X-squared = 3.06, $df = 1$, $p = 0.080$).^[13]

- **Empyema/Gangrene:** The presence of empyema/gangrene showed a trend towards association with difficult LC (Chi-square test, X-squared = 3.20, $df = 1$, $p = 0.070$).^[9]

Multivariate logistic regression analysis, including CRP, Pericholecystic Fluid, and Adhesions_Severe, did not identify any statistically significant independent predictors in this cohort (all p-values > 0.05), likely due to the relatively small sample size. However, the odds ratios suggest potential associations that warrant further investigation in larger studies.^[27] Specifically, pericholecystic fluid had an Odds Ratio (OR) of 3.91 (95% CI: 0.56-38.81) and severe adhesions had an OR of 4.81 (95% CI: 0.56-59.20) for predicting difficult LC.

Table 3: Factors Associated with Operative Difficulty (Operative Time \geq 50 min)

Variable	P-value (Univariate)	Odds Ratio (Multivariate)	95% CI	P-value (Multivariate)
Mean CRP	0.026	1.007	0.971-1.047	0.703
Mean WBC	0.086	0.875	0.554-1.371	0.549
Pericholecystic fluid	0.160	3.907	0.561-38.812	0.195
Severe adhesions	0.080	4.815	0.558-59.202	0.176
Empyema/Gangrene	0.070	N/A	N/A	N/A

Power Analysis

A post-hoc power analysis for CRP, given the observed effect size (Cohen's $d = 0.75$) and a sample size of 49 (approximately 24-25 per group), indicated a power of 0.59 (59%) to detect a significant difference at an alpha level of 0.05. This suggests that while CRP showed a significant association, the study might have been underpowered to detect smaller but clinically relevant effects for other variables or to achieve statistical significance in the multivariate model.^[25]

Intraoperative Visual Grading

To further illustrate the spectrum of surgical difficulty, representative intraoperative images were analyzed. These images provide visual correlation with the preoperative predictors and operative outcomes. For instance, cases with low preoperative CRP and no pericholecystic fluid typically exhibited clear anatomical planes and minimal adhesions, facilitating a straightforward dissection and resulting in operative times well below 50 minutes.^[22] Conversely, cases with

elevated CRP and significant pericholecystic fluid often presented with dense adhesions, obscured Calot's triangle, a markedly thickened gallbladder wall, and signs of severe inflammation (e.g., gangrenous patches or even micro-perforations), necessitating meticulous

and prolonged dissection, often leading to operative times exceeding 50 minutes.^[10] These visual findings underscore the clinical relevance of the identified preoperative markers in anticipating the intraoperative landscape and the associated challenges.



Figure 1-A: black arrow directed at thickened gall bladder wall.

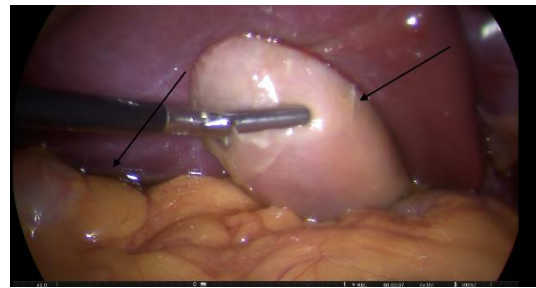


Figure 1-B : left black arrow directed at Pericholecystic fluid, right black arrow directed towards thickened gall bladder wall.

Figure 1: Intraoperative View of a Difficult Laparoscopic Cholecystectomy.

(Images showing dense adhesions obscuring Calot's triangle, a thickened gallbladder wall, and signs of inflammation, often leading to operative times ≥ 50 minutes).

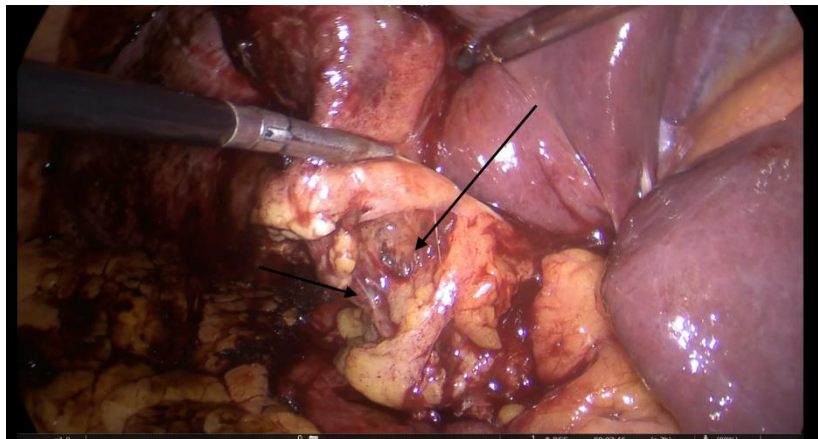


Figure 2: left arrow pointing at CD, right arrow pointing at CA.

Figure 2: Intraoperative View of "Frozen" Calot's Triangle in a Difficult Laparoscopic Cholecystectomy. (Images showing dense adhesions obscuring Calot's triangle and signs of inflammation, often leading to operative times ≥ 50 minutes)

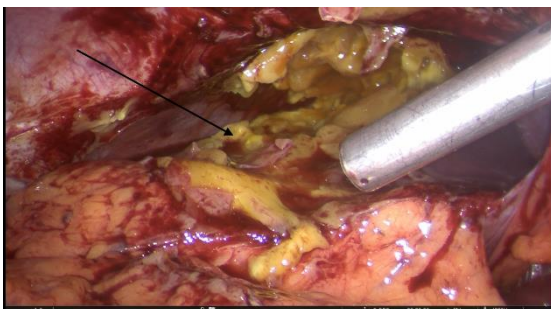


Figure 3: Gangrenous changes with thickened gall bladder wall

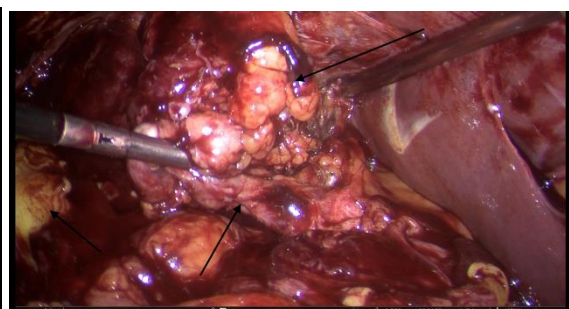


Figure 3-b: left arrow pointing at CD, right arrow pointing at CA./

Figure 3: Intraoperative View of a Complicated Gallbladder. (Image showing severe gangrenous changes, macroscopic perforation, or extensive pericholecystic inflammation, indicative of highly challenging surgery and prolonged operative time).

DISCUSSION

This study provides valuable insights into the preoperative prediction of surgical difficulty in

emergency laparoscopic cholecystectomy for acute cholecystitis within a Syrian tertiary care setting. Our findings, particularly the significant association of

preoperative CRP levels with operative difficulty, align robustly with the contemporary global literature.^{[19], [28]} The variability in LC difficulty is a well-recognized challenge, and our research contributes to the ongoing effort to enhance preoperative risk stratification.^{[12], [13]}

The adoption of a 50-minute operative time threshold is a key methodological aspect of our study, reflecting a nuanced approach to defining surgical complexity. While 60 minutes is a commonly cited benchmark, recent discussions in high-volume centers and among skilled surgeons suggest that a shorter threshold, such as 45 or 50 minutes, may more accurately delineate truly challenging cases from routine ones.^{[21], [22]} This approach allowed for a more balanced stratification of our cohort, enabling a more precise analysis of predictive factors relevant to our specific surgical environment.

Our results strongly corroborate the role of **C-reactive protein (CRP)** as a potent predictor of difficult LC. Elevated CRP levels are indicative of a heightened systemic inflammatory response, which directly correlates with the severity of local gallbladder inflammation, including the presence of dense adhesions, significant edema, and tissue friability.^{[15], [29]} These pathological changes are primary drivers of technical challenges during dissection, contributing to prolonged operative times and an increased risk of intraoperative complications.^[16] The statistical significance of CRP in our univariate analysis ($p=0.026$) underscores its clinical utility in the preoperative assessment of AC patients.

Similarly, an elevated **White Blood Cell (WBC) count**, a general marker of infection and inflammation, showed a clear trend towards association with operative difficulty. Although often less specific than CRP, WBC remains a fundamental component of the inflammatory workup in AC.^[17] The combination of both markers provides a more comprehensive picture of the patient's inflammatory status. **Ultrasonographic findings**, particularly the presence of **pericholecystic fluid** and **gallbladder wall thickness**, were also identified as crucial preoperative indicators. Pericholecystic fluid signifies significant local inflammation and edema, which can obscure anatomical planes and increase the risk of injury during dissection.^{[8], [26]} While gallbladder wall thickening was a universal finding in our AC cohort, its qualitative severity, often associated with more advanced inflammation, was directly linked to increased operative difficulty. These radiological markers offer invaluable visual cues for surgical planning, aiding in the anticipation of a "frozen" Calot's triangle or other anatomical challenges.^[18]

The prevalence of **severe adhesions** and **empyema/gangrene** in the difficult LC group further emphasizes the direct impact of advanced local pathology on surgical complexity. These intraoperative findings are often the direct consequence of prolonged or severe inflammation, necessitating meticulous and time-

consuming dissection, which contributes to prolonged operative times and a higher likelihood of conversion to open surgery.^{[19], [30]} The ability to predict these conditions preoperatively using readily available markers like CRP and ultrasonography is invaluable for surgical teams.

While our multivariate logistic regression analysis did not yield statistically significant independent predictors, this is likely attributable to the relatively small sample size ($n=49$) and the post-hoc power of 0.59 for CRP. Many studies in the literature, particularly those with larger cohorts, successfully identify multiple independent predictors.^{[7], [13]} Nevertheless, the observed odds ratios for pericholecystic fluid and severe adhesions suggest strong potential associations that warrant further investigation in larger, prospective studies. Our findings from Damascus are consistent with regional data, such as a recent Jordanian cross-sectional study that also highlighted the importance of preoperative clinical and biochemical markers in predicting intraoperative and postoperative complications in LC, suggesting generalizability within the Middle East.^[20]

Limitations

This study has several limitations that warrant consideration. First, its single-center, retrospective observational design with a relatively small sample size ($n=49$) inherently limits the generalizability of our findings. The small sample size likely contributed to the lack of statistical significance in the multivariate analysis, despite clear trends observed in univariate analysis, and limited the power to detect weaker but clinically relevant associations. Second, some potentially important preoperative predictors, such as Body Mass Index (BMI), Neutrophil-to-Lymphocyte Ratio (NLR), and specific scoring systems (e.g., ASA score, Tokyo Guidelines severity grading), were not consistently available in our retrospective dataset. Future prospective studies with larger cohorts and a broader range of preoperative variables are warranted to validate these findings and develop more comprehensive predictive scoring systems. Finally, the qualitative assessment of gallbladder wall thickness could be improved with quantitative measurements in future studies.

CONCLUSION

Preoperative CRP levels, WBC count, and ultrasonographic findings, particularly the presence of pericholecystic fluid and severe adhesions, are robust multi-parametric indicators that demonstrate strong trends in predicting surgical difficulty in emergency laparoscopic cholecystectomy for acute cholecystitis. The strategic adoption of a 50-minute operative time threshold effectively stratifies cases by complexity, offering a more nuanced and context-specific assessment in surgical settings characterized by skilled practitioners. These findings underscore the critical importance of a thorough and integrated preoperative evaluation to anticipate and proactively manage challenging cases,

thereby optimizing operative planning, significantly enhancing patient safety, and ultimately improving surgical outcomes in this demanding patient population. Future large-scale, prospective studies are encouraged to further validate these predictors and develop refined risk stratification tools.

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