

A Study to Assess the Role of C-Reactive Protein Estimation in Predicting Surgical Difficulty in Laparoscopic Cholecystectomy at a Tertiary Care Centre in Ranchi

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Abstract

Background: Laparoscopic cholecystectomy is the standard surgical treatment for symptomatic gallstone disease and acute cholecystitis. However, severe inflammation, adhesions, distorted anatomy, and fibrosis may make the procedure technically difficult and increase the risk of prolonged operative time, conversion to open surgery, and postoperative morbidity. Preoperative identification of patients likely to undergo difficult laparoscopic cholecystectomy may facilitate operative planning and patient counselling. C-reactive protein (CRP), an established marker of systemic inflammation, may reflect the severity of gallbladder inflammation and therefore have potential value in predicting operative difficulty.

Objective: To evaluate the role of preoperative serum C-reactive protein estimation in predicting surgical difficulty during laparoscopic cholecystectomy and to assess its association with Parkland grading, conversion to open cholecystectomy, operative duration, and postoperative complications.

Materials and Methods: A hospital-based observational study was conducted in the Department of General Surgery, Rajendra Institute of Medical Sciences (RIMS), Ranchi, over 18 months. Although the calculated minimum sample size was 96 patients, 110 consecutive eligible patients undergoing laparoscopic cholecystectomy were included in the final analysis. Preoperative serum CRP was measured before surgery. Intraoperative gallbladder severity was assessed using the Parkland Grading Scale, and procedures were classified as easy or difficult laparoscopic cholecystectomy. Operative duration, conversion to open surgery, and postoperative complications were recorded. Statistical analysis was performed using IBM SPSS Statistics version 26.0. Associations were evaluated using appropriate chi-square, Student's t-test, and ANOVA, correlation, and ROC analyses. A two-tailed p value <0.05 was considered statistically significant.

Results: Among 110 patients, 59 (53.6%) were male and 51 (46.4%) were female. Difficult laparoscopic cholecystectomy occurred in 49 (44.5%) patients. Increasing CRP categories were significantly associated with operative difficulty ($\chi^2=95.770$, $p<0.001$). Mean CRP was significantly different across Parkland grades, from 18.89 ± 13.81 mg/L in Grade 1 to 157.33 ± 21.59 mg/L in Grade 5 (ANOVA $F=114.171$, $p<0.001$). Preoperative CRP showed a strong positive correlation with Parkland grade (Spearman's $\rho=0.787$, $p<0.001$). ROC analysis demonstrated excellent discriminatory performance, with an area under the curve of 0.969 (95% CI: 0.937–1.000; $p<0.001$). A CRP cut-off of 30 mg/L demonstrated 91.8% sensitivity and 72.1% specificity. Higher CRP was also significantly associated with conversion to open surgery ($\chi^2=15.356$, $p=0.002$), longer operative duration ($F=135.522$, $p<0.001$), and postoperative complications ($\chi^2=80.222$, $p<0.001$).

Conclusion: Preoperative serum CRP demonstrated excellent predictive performance for difficult laparoscopic cholecystectomy in this study. Higher CRP concentrations were associated with greater Parkland grade, longer operative duration, increased conversion to open surgery, and postoperative complications. CRP may therefore serve as a simple and readily available adjunct to clinical and radiological assessment for preoperative risk stratification.

Keywords: C-reactive protein; laparoscopic cholecystectomy; Parkland grading scale; surgical difficulty; acute cholecystitis; gallstone disease.

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Introduction

Gallstone disease is a common gastrointestinal disorder and represents an important cause of morbidity and surgical intervention worldwide. Its prevalence increases with several demographic and metabolic factors, and a proportion of affected individuals subsequently develop symptomatic disease or complications requiring cholecystectomy. [1,2]

Laparoscopic cholecystectomy has become the standard operative approach for symptomatic gallstone disease and is associated with advantages over open surgery, including reduced postoperative pain, shorter hospitalisation, faster recovery, and lower wound morbidity. [2,3] Acute calculous cholecystitis is diagnosed and severity-graded using established clinical criteria such as the Tokyo Guidelines 2018. [4] Early laparoscopic cholecystectomy is recommended for appropriate patients when expertise and facilities are available. [3]

Despite its widespread use, laparoscopic cholecystectomy may be technically difficult in the presence of severe inflammation, dense adhesions, gallbladder distension, fibrosis, gangrenous changes, or distorted Calot's triangle anatomy. These factors can increase operative duration and the likelihood of conversion to open surgery and may contribute to postoperative complications. [5,6] Several preoperative factors have been investigated for predicting difficult laparoscopic cholecystectomy, including age, sex, clinical presentation, previous inflammation, gallbladder wall thickness, pericholecystic fluid, and other clinical and radiological variables. However, prediction models have shown variable performance, and there remains a need for simple and readily available markers that can complement conventional assessment. [7,8]

C-reactive protein is an acute-phase inflammatory biomarker that increases in response to tissue inflammation. Because the inflammatory process underlying acute cholecystitis may contribute directly to adhesions, tissue oedema, fibrosis, and distortion of normal anatomy, an elevated preoperative CRP concentration may provide an indirect indication of operative difficulty. Previous studies have demonstrated associations between preoperative CRP and difficult laparoscopic cholecystectomy, including significant

discriminatory performance in patients with acute calculous cholecystitis. [9-11] The Parkland Grading Scale provides an intraoperative five-grade assessment of gallbladder inflammation and anatomical complexity. The scale was originally developed as a simple and reliable method for characterising gallbladder severity, and subsequent prospective validation demonstrated that increasing Parkland grades were associated with greater operative difficulty and adverse operative outcomes. [12,13] Further studies have also demonstrated an association between Parkland grade and surgical difficulty. [14]

The relationship between inflammatory markers and operative difficulty is clinically relevant because accurate preoperative risk assessment may assist in operative scheduling, allocation of experienced surgeons, informed consent, and anticipation of possible conversion or bail-out procedures. Studies evaluating CRP have reported associations with difficult surgery, prolonged operative duration, and conversion to open cholecystectomy. [9-11]

However, evidence from individual tertiary-care centres in India remains limited. The present study was therefore undertaken at Rajendra Institute of Medical Sciences, Ranchi, to evaluate the association between preoperative serum CRP and surgical difficulty during laparoscopic cholecystectomy. The study additionally assessed the relationship of CRP with Parkland grade, conversion to open surgery, operative duration, and postoperative complications.

Materials and Methods

Study Design: A hospital-based observational study was conducted in the Department of General Surgery, Rajendra Institute of Medical Sciences (RIMS), Ranchi.

Study Setting: The study was conducted at Rajendra Institute of Medical Sciences (RIMS), Ranchi, Jharkhand, a tertiary-care teaching hospital.

Study Duration: The study was conducted over a period of 18 months.

Study Population: Adult patients diagnosed with symptomatic gallstone disease or acute or chronic cholecystitis who underwent laparoscopic

cholecystectomy during the study period were considered for inclusion.

Sample Size

The calculated minimum sample size was 96 patients. However, 110 consecutive eligible patients fulfilling the study criteria during the study period were included in the final analysis.

Sampling Technique

Consecutive sampling was used.

Inclusion Criteria

- Age ≥ 18 years.
- Symptomatic gallstone disease.
- Acute or chronic cholecystitis.
- Planned elective or emergency laparoscopic cholecystectomy.
- Written informed consent.

Exclusion Criteria

- Suspected or confirmed gallbladder malignancy.
- Primary open cholecystectomy.
- Common bile duct stones requiring additional biliary procedures.
- Severe systemic inflammatory disease unrelated to gallbladder pathology.
- Pregnancy.
- Refusal to participate.

Study Procedure: After admission, demographic characteristics, clinical history, examination findings, laboratory investigations, and radiological findings were recorded using a predesigned case record form. Preoperative serum CRP was measured before surgery using the standard immunoturbidimetric method available in the institutional biochemistry laboratory. All patients subsequently underwent laparoscopic cholecystectomy performed by experienced consultant surgeons according to standard operative protocols. The intraoperative appearance of the gallbladder was assessed using the Parkland Grading Scale, which grades gallbladder inflammation and anatomical complexity from Grade 1 to Grade 5. [12,13] For analysis, laparoscopic cholecystectomy was classified as easy or difficult according to the study's predefined operative criteria. Operative duration, intraoperative events, conversion to open surgery, postoperative complications, and hospital outcomes were documented.

Outcome Measures

Primary outcome: Difficult laparoscopic cholecystectomy.

Secondary outcomes: Parkland grade; conversion to open cholecystectomy; duration of surgery; postoperative complications; and predictive performance of preoperative CRP using ROC analysis.

Statistical Analysis: Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics version 26.0. Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were presented as frequencies and percentages. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Continuous variables were compared using the independent Student's t-test or one-way ANOVA. Pearson's or Spearman's correlation coefficient was used according to the distribution of the variables.

ROC curve analysis was performed to evaluate the discriminatory ability of preoperative CRP for predicting difficult laparoscopic cholecystectomy. The AUC and 95% confidence interval were calculated. A two-tailed p value < 0.05 was considered statistically significant.

Ethical Considerations: The study was conducted after obtaining approval from the Institutional Ethics Committee of Rajendra Institute of Medical Sciences (RIMS), Ranchi.

Written informed consent was obtained from all participants before enrolment. Patient confidentiality was maintained throughout the study, and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Results

Study Population: A total of 110 patients undergoing laparoscopic cholecystectomy were included in the final analysis.

The majority belonged to the 51–60-year age group (26.4%), followed by the 41–50-year age group (25.5%). There was a slight male predominance, with 59 (53.6%) males and 51 (46.4%) females.

Forty-nine patients (44.5%) had BMI 18.5–24.9 kg/m², 42 (38.2%) had BMI 25–29.9 kg/m², and 19 (17.3%) had BMI 30–35 kg/m². Acute presentation was observed in 47 (42.7%) patients, whereas 63 (57.3%) had chronic presentation.

Table 1: Baseline demographic and clinical characteristics of study participants (n=110).

Variable	Frequency	Percentage (%)
Age 18–30 years	12	10.9
31–40 years	22	20.0
41–50 years	28	25.5
51–60 years	29	26.4
>60 years	19	17.3
Male	59	53.6
Female	51	46.4
BMI 18.5–24.9 kg/m ²	49	44.5
BMI 25–29.9 kg/m ²	42	38.2
BMI 30–35 kg/m ²	19	17.3
Acute presentation	47	42.7
Chronic presentation	63	57.3

Distribution of CRP and Parkland Grade: CRP levels varied considerably across the study population. Thirty-two patients (29.1%) had CRP <10 mg/L, 33 (30.0%) had CRP 10–50 mg/L, 20 (18.2%) had CRP 51–100 mg/L, and 25 (22.7%) had CRP >100 mg/L. Parkland Grade 1 was observed in 27 (24.5%) patients, Grade 2 in 34 (30.9%), Grade 3 in 15 (13.6%), Grade 4 in 19 (17.3%), and Grade 5 in 15 (13.6%). Overall, 61 (55.5%) procedures were classified as easy and 49 (44.5%) as difficult.

Table 2. Distribution of preoperative CRP level, Parkland grade, and surgical difficulty (n=110).

Variable	Frequency	Percentage (%)
CRP <10 mg/L	32	29.1
CRP 10–50 mg/L	33	30.0
CRP 51–100 mg/L	20	18.2
CRP >100 mg/L	25	22.7
Parkland Grade 1	27	24.5
Grade 2	34	30.9
Grade 3	15	13.6
Grade 4	19	17.3
Grade 5	15	13.6
Easy LC	61	55.5
Difficult LC	49	44.5

Figure 1 illustrates the distribution of Parkland grades among study participants.

Association between CRP and Surgical Difficulty: A highly significant association was observed between preoperative CRP category and surgical difficulty. All 32 patients with CRP <10 mg/L underwent easy laparoscopic

cholecystectomy. Among patients with CRP 10–50 mg/L, 4 (12.1%) underwent difficult surgery. All patients with CRP 51–100 mg/L and >100 mg/L underwent difficult laparoscopic cholecystectomy. The association was statistically significant ($\chi^2=95.770$, $p<0.001$).

Table 3. Association between preoperative CRP level and surgical difficulty. Chi-square=95.770; $p<0.001$.

CRP (mg/L)	Difficult n (%)	Easy n (%)
<10	0 (0.0)	32 (100.0)
10–50	4 (12.1)	29 (87.9)
51–100	20 (100.0)	0
>100	25 (100.0)	0

Figure 2 illustrates the association between preoperative CRP categories and surgical difficulty.

Association between CRP and Parkland Grade: Mean preoperative CRP differed significantly across Parkland grades. Mean CRP was

18.89±13.81 mg/L in Grade 1, 17.88±14.65 mg/L in Grade 2, 64.67±28.42 mg/L in Grade 3, 125.79±50.56 mg/L in Grade 4, and 157.33±21.59 mg/L in Grade 5. The overall difference was statistically significant (ANOVA $F=114.171$, $p<0.001$).

Table 4: Mean CRP according to Parkland grade. ANOVA: F=114.171; p<0.001.

Parkland grade	Mean CRP $\pm$ SD (mg/L)
Grade 1	18.89 $\pm$ 13.81
Grade 2	17.88 $\pm$ 14.65
Grade 3	64.67 $\pm$ 28.42
Grade 4	125.79 $\pm$ 50.56
Grade 5	157.33 $\pm$ 21.59

Figure 3 illustrates the distribution of CRP according to Parkland grade.

Predictive Accuracy of Preoperative CRP: ROC analysis demonstrated excellent discriminatory performance of preoperative CRP for difficult

laparoscopic cholecystectomy. The AUC was 0.969 (95% CI: 0.937–1.000; p<0.001). A CRP cut-off of 30 mg/L provided 91.8% sensitivity and 72.1% specificity. A lower cut-off of 17.5 mg/L achieved 98.0% sensitivity.

Table 5: ROC analysis of preoperative CRP.

Parameter	Value
Area under ROC curve	0.969
95% CI	0.937–1.000
p value	<0.001
Best cut-off	30 mg/L
Sensitivity	91.8%
Specificity	72.1%

Figure 4 shows the ROC curve for preoperative CRP in predicting difficult laparoscopic cholecystectomy.

Operative Outcomes: Increasing CRP levels were significantly associated with operative outcomes. Mean operative duration increased from

approximately 52 minutes among patients with CRP <50 mg/L to approximately 90 minutes among those with CRP $\geq$ 51 mg/L (p<0.001). Conversion to open surgery and postoperative complications were also significantly associated with elevated CRP.

Table 6. Association of elevated CRP with operative outcomes.

Outcome	Statistical test	p value
Duration of surgery	ANOVA F=135.522	<0.001
Conversion to open surgery	$\chi^2=15.356$	0.002
Postoperative complications	$\chi^2=80.222$	<0.001

Figure 5 illustrates operative duration according to CRP category.

Correlation Analysis: A strong positive correlation was observed between preoperative

CRP and Parkland grade (Spearman's $\rho=0.787$, p<0.001). Age was also positively correlated with Parkland grade ($\rho=0.639$, p<0.001), while duration of surgery demonstrated a positive correlation with Parkland grade ($\rho=0.755$, p<0.001).

Table 7: Correlation analysis.

Variables	Correlation coefficient	p value
CRP vs Parkland grade	$\rho=0.787$	<0.001
Age vs Parkland grade	$\rho=0.639$	<0.001
Duration of surgery vs Parkland grade	$\rho=0.755$	<0.001

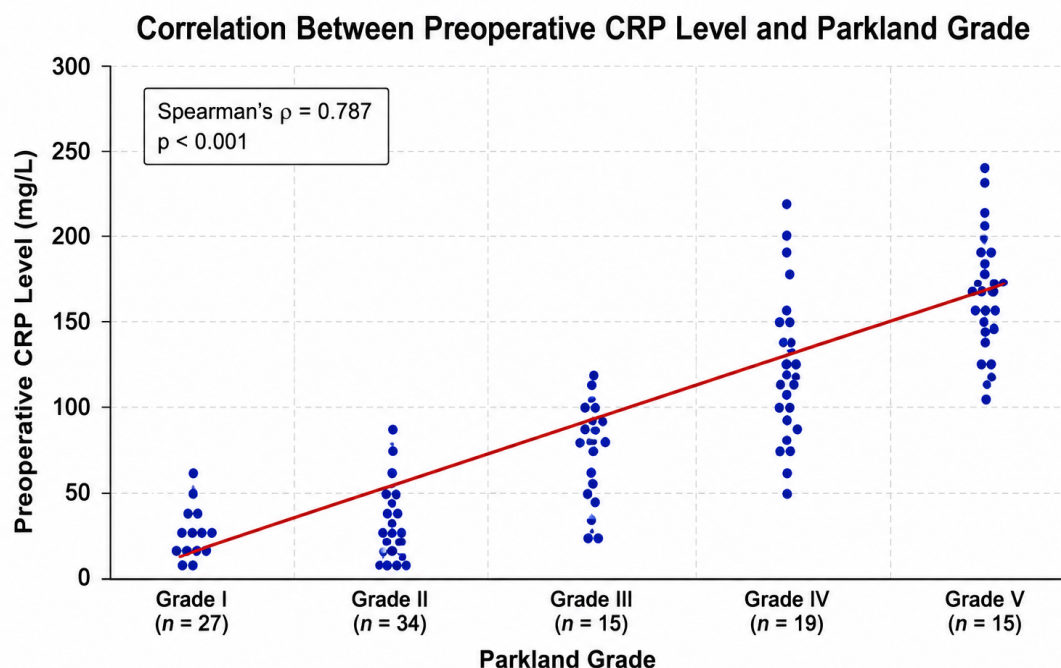


Figure 6. Scatter plot demonstrating the correlation between preoperative C-reactive protein (CRP) level and Parkland grade.

Each dot represents one patient. The red line represents the trend of increasing CRP level with higher Parkland grade.

Figure 1: Distribution of Parkland grades among study participants.

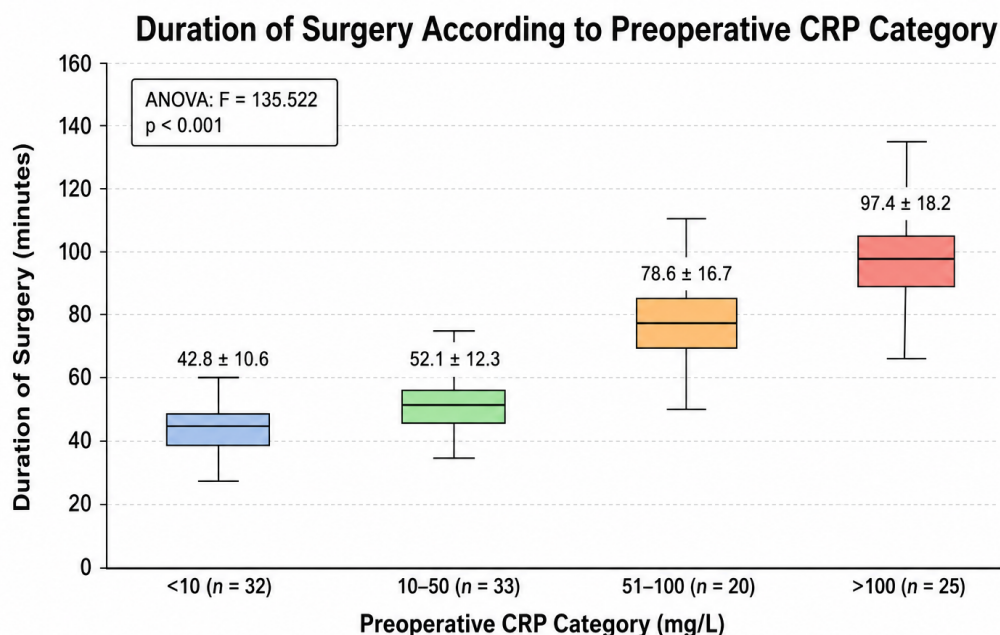


Figure 5. Box-and-whisker plot showing duration of surgery (minutes) according to preoperative C-reactive protein (CRP) category.

Boxes represent interquartile range (IQR), lines inside the boxes indicate median values, and whiskers indicate range.

Figure 2: Association between preoperative CRP categories and surgical difficulty.

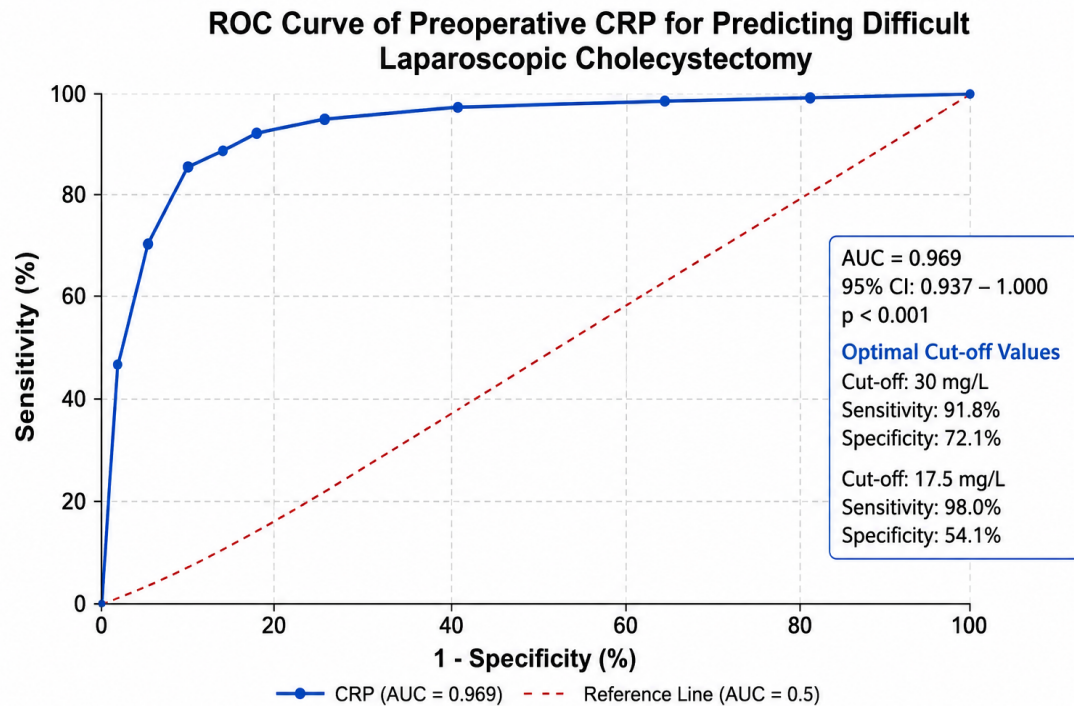


Figure 4. Receiver operating characteristic (ROC) curve of preoperative C-reactive protein (CRP) for predicting difficult laparoscopic cholecystectomy.

Figure 3: Distribution of preoperative CRP levels according to Parkland grade.

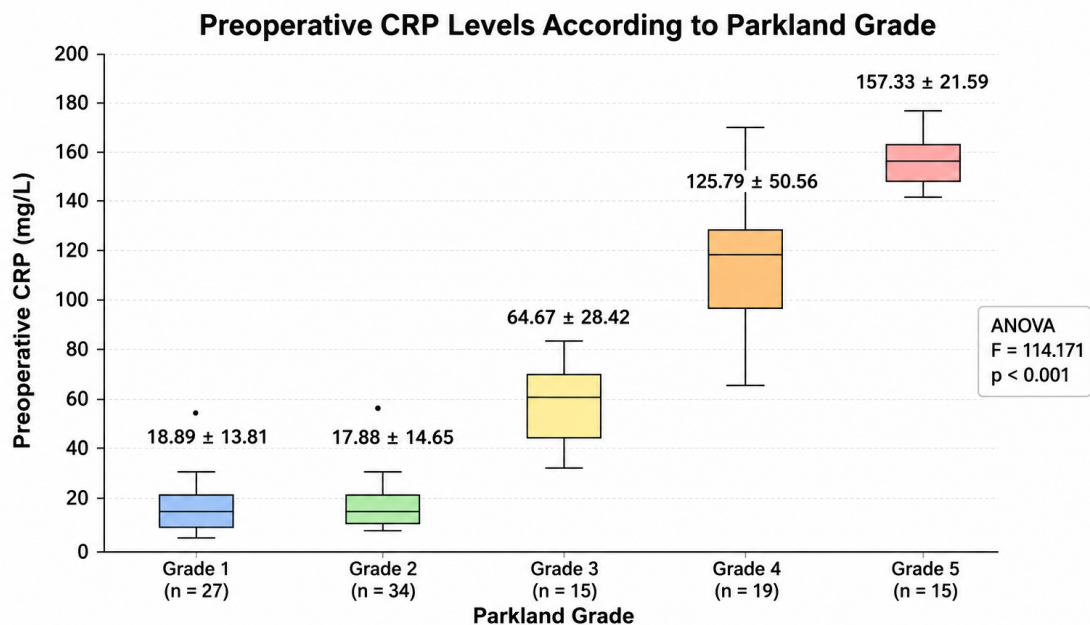


Figure 3. Box-and-whisker plot of preoperative C-reactive protein (CRP) levels according to Parkland grade. Boxes represent interquartile range (IQR), lines inside the boxes indicate median values, whiskers indicate range, and dots represent outliers.

Figure 4: Receiver operating characteristic curve of preoperative CRP for predicting difficult laparoscopic cholecystectomy (AUC=0.969).

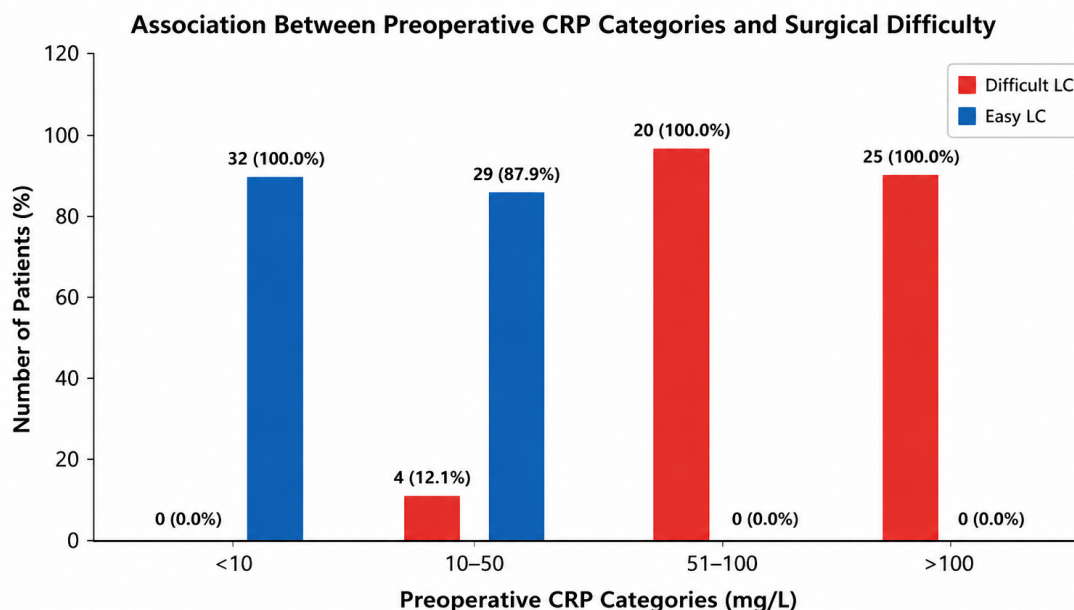


Figure 2. Clustered bar chart showing the association between preoperative CRP categories and surgical difficulty.

Figure 5: Operative duration according to preoperative CRP category.

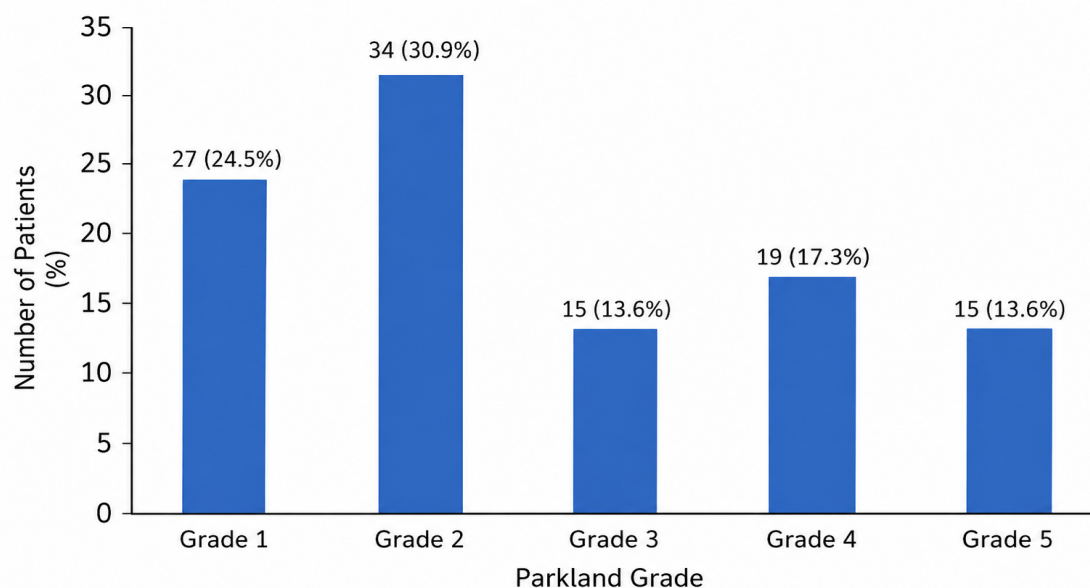


Figure 1. Distribution of Parkland grades among study participants.

Figure 6: Correlation between preoperative CRP level and Parkland grade (Spearman's $\rho=0.787$).

Figure 6 illustrates the correlation between preoperative CRP and Parkland grade.

Discussion

The present hospital-based observational study evaluated the association between preoperative serum CRP and operative difficulty during laparoscopic cholecystectomy. Among 110 patients, 44.5% underwent difficult laparoscopic

cholecystectomy. Higher CRP concentrations were strongly associated with difficult surgery, higher Parkland grades, longer operative duration, conversion to open surgery, and postoperative complications. These findings support the potential utility of CRP as an adjunctive preoperative marker for anticipating operative complexity. The demographic profile showed a slight male predominance, with most participants between 41

and 60 years of age. Demographic characteristics such as age and sex have previously been incorporated into prediction models for difficult laparoscopic cholecystectomy, although their predictive performance varies between populations. [7,8]

The principal finding of this study was the strong association between preoperative CRP and operative difficulty. Patients with CRP below 10 mg/L uniformly underwent easy procedures, whereas all patients with CRP above 50 mg/L underwent difficult laparoscopic cholecystectomy in the present dataset. This association was highly significant ($\chi^2=95.770$, $p<0.001$). These findings are consistent with previous studies demonstrating that elevated preoperative CRP is associated with difficult laparoscopic cholecystectomy. [9-11]

Díaz-Flores et al. reported that preoperative CRP was a significant predictor of difficult laparoscopic cholecystectomy in patients with acute calculous cholecystitis, with an AUC of 0.96 in their multivariable model. [9] Similarly, a large study involving 804 emergency patients demonstrated a significant relationship between increasing preoperative CRP concentrations and increasing operative difficulty, although the reported AUC was lower than that observed in the present study.¹⁰ Differences in patient selection, disease severity, operative difficulty definitions, timing of CRP measurement, and case mix may explain the variation in discriminatory performance between studies.

The Parkland Grading Scale provides a structured intraoperative assessment of gallbladder inflammation and anatomical complexity. The scale was originally developed by Madni et al. and demonstrated good inter-rater reliability. [12] Subsequent prospective validation showed that increasing Parkland grades were associated with operative difficulty, open or partial cholecystectomy, longer operative duration, and bile leak. [13] More recent validation studies have also demonstrated significant associations between Parkland grade and operative difficulty. [14]

In the present study, mean CRP differed significantly across Parkland grades, with markedly higher values observed in Grades 3–5 than in Grades 1–2. Furthermore, CRP showed a strong positive correlation with Parkland grade ($\rho=0.787$, $p<0.001$). This finding provides biological and clinical plausibility for the use of CRP as a preoperative indicator of the inflammatory burden that may translate into greater intraoperative complexity.

The ROC analysis demonstrated an AUC of 0.969, indicating excellent discriminatory ability of preoperative CRP in this study population. A cut-

off of 30 mg/L provided 91.8% sensitivity and 72.1% specificity. Previous investigations have identified different optimal CRP thresholds. Díaz-Flores et al. reported a cut-off of 11 mg/dL in patients with acute calculous cholecystitis, while other studies have demonstrated that increasing CRP concentrations are associated with greater operative difficulty. [9-11] The difference between reported cut-offs highlights the importance of validating thresholds in individual populations rather than applying a universal CRP value.

The present study also demonstrated a significant association between elevated CRP and conversion to open surgery. This is clinically relevant because conversion is frequently related to severe inflammation, adhesions, and difficulty in safely identifying biliary anatomy. Previous studies have identified inflammation and other clinical and operative factors as important contributors to conversion.¹⁵ CRP may therefore provide additional preoperative information regarding the likelihood of technically challenging surgery, although it should not be considered a substitute for clinical judgement or imaging.

Higher CRP was also associated with longer operative duration. This observation is consistent with the concept that increasing inflammatory severity may result in adhesions, oedema, tissue friability, and distorted anatomy, thereby increasing the time required for safe dissection. Previous studies examining CRP and operative difficulty have similarly demonstrated relationships between inflammatory burden and operative complexity. [9-11]

Postoperative complications were significantly more frequent among patients with elevated CRP in the present study. This association should be interpreted as an indicator of the relationship between inflammatory severity and operative complexity rather than evidence that CRP itself causes postoperative complications. Severe inflammatory disease may simultaneously increase operative difficulty and postoperative morbidity.

The clinical relevance of these findings lies in the simplicity and availability of CRP measurement. Unlike complex prediction models requiring multiple clinical and radiological variables, CRP is routinely available in most hospital laboratories. It may therefore serve as an adjunct to preoperative assessment, allowing surgeons to anticipate potentially difficult dissection, plan appropriate operative expertise, and counsel patients regarding the possibility of conversion.

However, CRP should not be used in isolation. Clinical presentation, imaging findings, surgeon experience, and intraoperative assessment remain essential components of safe laparoscopic

cholecystectomy. The current findings should also be interpreted in the context of the single-centre observational design and relatively modest sample size. External validation in larger multicentre cohorts would be useful before adopting the identified 30 mg/L threshold as a universal cut-off.

Limitations

This study has several limitations. It was conducted at a single tertiary-care institution and included a relatively modest sample of 110 patients, which may limit generalisability. The observational design does not establish causality between CRP and operative outcomes. In addition, CRP may be influenced by inflammatory conditions other than gallbladder disease, although patients with severe systemic inflammatory diseases unrelated to gallbladder pathology were excluded. The optimal CRP threshold identified in this cohort should therefore be externally validated before routine adoption in other populations.

Conclusion

Preoperative serum CRP demonstrated excellent discriminatory performance for predicting difficult laparoscopic cholecystectomy in this study. Higher CRP concentrations were significantly associated with difficult surgery, higher Parkland grades, prolonged operative duration, conversion to open cholecystectomy, and postoperative complications.

A CRP cut-off of 30 mg/L demonstrated 91.8% sensitivity and 72.1% specificity for predicting difficult laparoscopic cholecystectomy in the present cohort. CRP is inexpensive, routinely available, and objective, and may therefore serve as a useful adjunct to clinical and radiological assessment during preoperative planning.

Further multicentre prospective studies with larger sample sizes are warranted to validate the observed associations and determine whether the identified CRP threshold can be generalised to other patient populations.

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