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C-Reactive Protein (CRP) as a Predictive Factor for Difficulty of Laparoscopic Cholecystectomy

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Abstract

Background: Acute cholecystitis with difficult laparoscopic surgery has impact on operating time and training of juniors. The clinical diagnosis of complicated acute cholecystitis (CAC) remains difficult with several pathological or ultrasonography criteria used to differentiate it from uncomplicated acute cholecystitis (UAC).

Aim of Study: Was to evaluate CRP (C-reactive protein) as a parameter that predict operative difficulty of LC (laparoscopic cholecystectomy) or conversion to open surgery.

Patients and Methods: A prospective randomized clinical trial was carried out on 150 Laparoscopic cholecystectomies performed from January 2019 to February 2022 at General Surgery Department, Al-Azhar University Hospitals (Cairo) Egypt. Association of intra-operative difficulties or conversion with the following factors was studied: Age, gender, CRP and white blood cell count (WBC).

Results: 150 patients were analysed [124 laparoscopic, 22 difficult laparoscopic cholecystectomy (LC) and 4 C (Conversion to open)]. All patients had a recorded CRP. Median CRP was highest for patients who were converted (280.5) compared to those who had difficult LC (67.40) or LC (7.05). High preoperative CRP, WBC and cholangiopancreatography, were predictors of conversion. These factors were only marginally better than CRP alone in predicting conversion.

Conclusion: C-reactive protein can be efficient predictor of conversion of Laparoscopic cholecystectomy (LC).

Key Words: *C-reactive protein – Laparoscopic cholecystectomy – Complicated acute cholecystitis – Gangrenous cholecystitis.*

Introduction

THE pathophysiology of acute cholecystitis is blockage of the cystic duct. Edema of the gallbladder wall will eventually cause ischemia of the wall and become gangrenous. That may be infected by gas-forming organisms, causing acute emphysematous cholecystitis which is a life-threatening condition with high rate of mortality **[1]**.

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1% to 2% of patients with asymptomatic cholelithiasis develop acute cholecystitis. This is a consequence of an impacted cystic duct causing distension of the gallbladder and increased tension on the gallbladder wall, accompanied by an associated inflammatory reaction **[2,3]**. Early diagnosis by physical examination, radiology and laboratory C-reactive protein [CRP], white blood cell [WBC] count is the corner stone for management of acute cholcystitis **[3]**.

Laparoscopic cholecystectomy (LC) can be the easiest or the most difficult laparoscopic surgery. Anticipation of conversion can help in consenting patients and preparing them for longer stay and complications **[4]**.

Laparoscopic surgery conversion of LC was influenced by a lot of factors like patient characteristics (high body mass index, previous abdominal surgery), anatomical variations of extra-hepatic biliary system and gallbladder (GB) pathology (severe inflammation of GB or common bile duct [CBD]) **[4]**.

The studies found significant association of conversion with old age, male gender, previous abdominal surgery, previous endoscopic retrograde cholangiopancreatography (ERCP), and ultrasonogrphic findings (USS) like GB wall thickness etc. With increasing experience in laparoscopic surgery and advancement of technology many of the difficulties due to anatomical and patient factors could be dealt with laparoscopically **[5]**. GB wall thickness on ultrasound scan was a strong predictor of conversion of LC **[6]**.

C-reactive protein (CRP) is an acute phase reactant protein secreted by the liver in response to interleukin-6 and other pro-inflammatory cytokines in the context in inflammation, infection,

trauma, malignancy and tissue infarction. Its circulating concentration is determined by its rate of synthesis reflecting the intensity of the pathological process, and hence it is a good indicator of severity of inflammation. It was observed that many of the patients who had their LC converted to open surgery (either emergency or delayed) had very high CRP at the time of their index admission for GB pathology. Even for those who were not converted, LC was difficult if their preoperative CRP levels were moderately raised [7].

Our study hypothesised that high CRP level due to GB pathology (biliary colic or acute inflammation) is associated with difficulties and conversion.

The aim of this study was to evaluate CRP (C-reactive protein) as a parameter that predict operative difficulty of LC (laparoscopic cholecystectomy) or conversion to open surgery.

Patients and Methods

A prospective randomized clinical trial was carried out on 150 Laparoscopic cholecystectomies performed from January 2019 to February 2022 at General Surgery Department Al-Azhar University Hospitals (Cairo) Egypt performed by experience upper gastrointestinal surgeon.

Inclusion criteria: All the patients 18 years and above who had cholecystectomy.

Exclusion criteria: The study aims to look at the association between CRP and difficult cholecystectomy/conversion due to GB pathology; the following patients were excluded to avoid confounding effect of these factors:

- High BMI (>35).
- Previous abdominal surgery.
- Preoperative ERCP and pancreatitis
- Patient with concurrent non-biliary cause of raised CRP concentration (chest infection).

Patient demographics, radiological findings, duration of surgery, conversion to open, perioperative complications, readmissions and mortality will retrieved. Surgical difficulty is based on the Nassar scale [8] and a CRP level below 6mg/l is considered normal.

Nassar difficultly grading scale:

Surgeons were asked to grade the difficulty of the procedure using the Nassar scale (grades 1-4). This scale was published in 1995 and graded operative findings from the gallbladder, cystic pedicle and associated adhesions [8].

The scale is as follows:

Grade 1:

- Gallbladder-floppy, non-adherent.
- Cystic pedicle-thin and clear.
- Adhesions-Simple up to the neck/Hartmann's pouch.

Grade 2:

- Gallbladder-Mucocele, Packed with stones.
- Cystic pedicle-Fat laden.
- Adhesions-Simple up to the body.

Grade 3:

- Gallbladder-Deep fossa, Acute cholecystitis, Contracted, Fibrosis, Hartmans adherent to CBD, Impaction.
- Cystic pedicle-Abnormal anatomy or cystic duct-short, dilated or obscured.
- Adhesions-Dense up to fundus; Involving hepatic flexure or duodenum.

Grade 4:

- Gallbladder-Completely obscured, Empyema, Gangrene, Mass.
- Cystic pedicle-Impossible to clarify.
- Adhesions-Dense, fibrosis, wrapping the gallbladder, Duodenum or hepatic flexure difficult to separate.

The grading system is designed to be used as an overall summary of the operative conditions found, and the worst factor found in the individual aspect of either the 'Gallbladder', 'Cystic Pedicle' or 'Adhesions' should be used to define the final overall grade [8].

Patient management:

All patients with gall bladder stone by clinical and ultrasound findings are admitted to general surgery department. Laparoscopic cholecystectomy is performed after the patient is assessed as fit for general anesthesia. All cases undergo chest X-ray and urine analysis to exclude other causes of increased CRP.

CRP (mg/L), and white blood cell count (WBC) on admission were recorded for all the patients. Logistic analysis is used to assess predictors of high operative difficulty (grade III or above) versus low difficulty (grades I and II), and included the following variables: Age, sex, and CRP level.

Statistical analysis:

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test (χ^2) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples *t*-test was used to compare between two independent groups of normally distributed variables (parametric data). *p*-value <0.05 was considered significant.

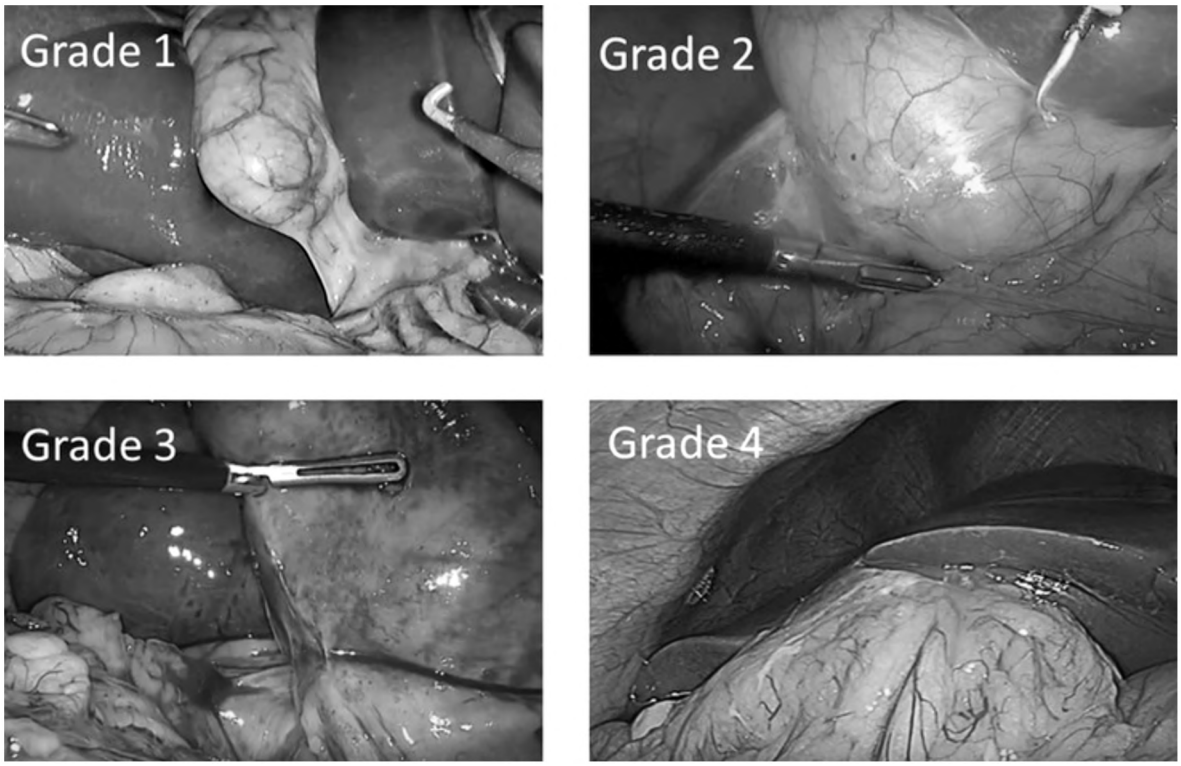

Fig. (1): Illustrates laparoscopic images of each of the Nassar operative difficulties.

Results

150 laparoscopic cholecystectomies performed between 2019 and 2022, all patients had preoperative estimation of CRP concentration, but some cases were excluded owing to preoperative chest or urinary infection.

Table (1): Demographic parameter of patients who had LC with difficult dissection and conversion to open surgery groups.

Demographic parameter	Laparoscopic cholecystectomy	Difficult Dissection	Conversion to open
Age (years): Median (IQR)	47.5 (36.8-55.0)	59.0 (50.5-70.0)	69.0 (56.0-79.5)
Gender: Male/female (%)	25/122 (20.16)	18/22 (81.81)	3/4 (75)

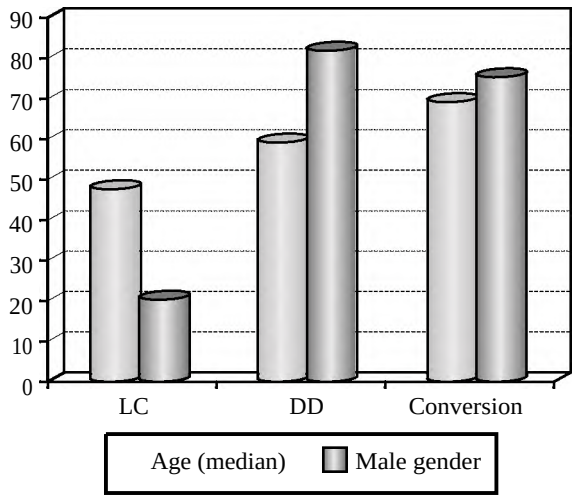

Fig. (2): Demographic parameter of patients who had LC with difficult dissection and conversion to open surgery groups.

Clinical characteristics are summarized as: The admission diagnosis was biliary colic in 120 of the 150 patients (80%), acute cholecystitis in 30 (20%), A medical history of previous admission was recorded for 19 patients (12.67 per cent). All patients who had laparoscopic cholecystectomy were evaluated by ultrasound imaging of the abdomen.

The duration of surgical procedure ranged from 22 to 187min. The median time for laparoscopic cholecystectomy was 75min. There were 4 cases conversions to open surgery. Duration of hospital stay ranged from 1 to 15 (median 3) days.

No association was found between Nassar scale grades and the timing of laparoscopic cholecystectomy, but patients with a previous admission for had increased operative difficulty than those with a first admission.

Table (2): CRP and WBC comparison of patients who had LC with difficult dissection and conversion to open surgery groups.

Variable	Laparoscopic cholecystectomy	Difficult Dissection	Conversion to open
WBC: Median (IQR)	7.75 (6.20-9.45)	9.50 (7.10-13.00)	12.35 (7.60-16.75)
CRP: Median (IQR)	9.25 (7.05-62.20)	67.40 (18.95-300.55)	280.5 (201.48-320.50)

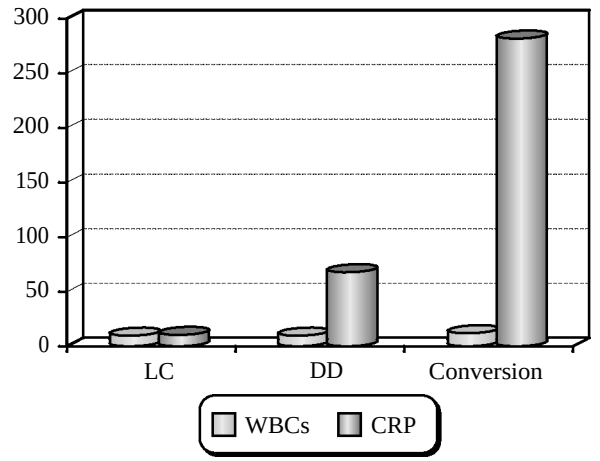

Fig. (3): CRP and WBC comparison of patients who had LC with difficult dissection and conversion to open surgery groups.

C-reactive protein:

All patients had a preoperative peak CRP level of more than 6mg/l. The preoperative peak CRP level ranged from 7.05 to 320.50mg/l. A statistically significant association was found between the proportions of patients with a CRP level greater than or equal to 6mg/l and Nassar scale grades.

Table (3): Nassar scale grade and peak C-reactive protein levels.

Peak CRP (mg/l)	Grade I	Grade II	Grade III	Grade IV
Mean (±SD)	9.35±2.33	12.50±3.12	70.81±17.7	210.05±51.36
Median (range)	7.05-62.020	18.5- 67.5	65-98.5	198-32.5

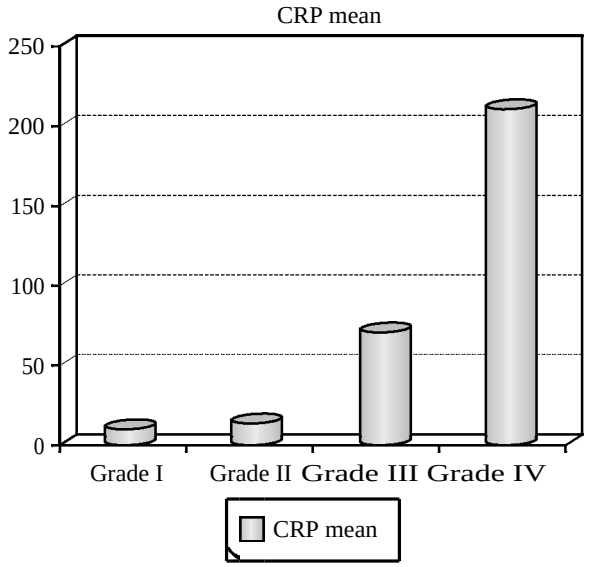

Fig. (4): Nassar scale grade and peak C-reactive protein levels.

Discussion

Due to the variability of operative findings, laparoscopic cholecystectomy is one of the most unpredictable operations in general surgery, this can be due to anatomical reasons, but is mainly due to the effect of cholecystitis and fibrosis on the dissection planes in Calot's triangle [9].

A recent study for AC found that CRP level at admission (≥3.6mg/dL) and male gender were strongly related to conversion of emergency LC. In this study, the measurement of CRP in predicting a DD or conversion to open surgery was investigated alone for the subset of patients [10].

Two studies have been done previously to predict difficult LC rather than predicting conversion [11,12]. Randhawa and Pujahari looked at 15 factors that make the operation difficult, but not necessarily requiring conversion [11]. The other study by Sakuramoto et al., is the only study that looked at "difficult LC due to GB pathology" a concept similar to this study, but required 41 factors to predict intraoperative difficulties [12].

Previous studies in this field reported an association between a raised CRP level and cholecys-

titis, although with limited results in relation to duration of symptoms or timing of laboratory test evaluation. Another study 7 found a CRP concentration above 200mg/l to be a good predictor of gangrenous cholecystitis, consistent with the present findings and Nassar scale grading **[13]**.

In this study, patients were treated by experience surgical team despite CRP levels. However, the median hospital stay of 3 days was due to the exclusion criteria of another factor.

Some authors have acknowledged the importance of grading the difficulty of cholecystectomy and the use of operative risk predictive scores. The Nassar scale has been suggested to optimize the perioperative management of patients with gallstone disease **[14]**.

In this study, the Nassar scale grade was higher when the preoperative peak CRP concentration was raised. An increased CRP level can be a predictor of a high operative difficulty grade, and this finding could be of use in planning surgical management and also to select patients appropriate for surgical training.

Although a number of important clinical applications of the Nassar grading system have been reported, the scale has yet to be evaluated and validated in large cohorts of patients such as the present study **[8]**.

All Difficult Dissection/Conversions cases in this study group refer to difficulty in getting satisfactory views of the Calot's triangle. The rate of conversion was higher in patients with preoperative CRP than those without. Median CRP was highest for patients who were converted to open surgery from laparoscopic.

Patients in the DD group were significantly older, had significantly higher CRP and WBC, and a higher percentage of males compared with patients in the LC group. Patients in the Conversion group were significantly older, had significantly higher CRP and WBC, a higher percentage of males.

In this study, the median CRP was significantly higher in the patients converted to open operation (286.2) compared to those with difficult LC (67.4) and laparoscopic group (7.05). This is the first study to assess value of CRP as a single predictor of difficult surgery.

Conclusion:

C-reactive protein can be efficient predictor of conversion of Laparoscopic cholecystectomy (LC).

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Conflict of interest: Nil.

References

1- JANOWITZ P., KRATZER W., ZEMMLER T., TUDYKA J. and WECHSLER J.G.: Gallbladder sludge: Spontaneous course and incidence of complications in patients without stones. Hepatology, 20 (2): 291-4, 1994.

2- FRIEDMAN G.D.: Natural history of asymptomatic and symptomatic gallstones. Am. J. Surg., 165 (4): 399-404, 1993.

3- GIGER U.F., MICHEL J.M., OPITZ I., TH INDERBITZIN D., KOCHER T., KRÄHENBÜHL L., et al.: Risk factors for perioperative complications in patients undergoing laparoscopic cholecystectomy: Analysis of 22,953 consecutive cases from the Swiss Association of Laparoscopic and Thoracoscopic Surgery database. J. Am. Coll. Surg., 203: 723-8, 2006.

4- SHARMA S.K., THAPA P.B., PANDEY A., KAYASTHA B., POUDYAL S., UPRETY K.R., et al.: Predicting difficulties during laparoscopic cholecystectomy by preoperative ultrasound. Kathmandu Univ. Med. J. (KUMJ), 5: 8-11, 2007.

5- TAKEGAMI K., KAWAGUCHI Y., NAKAYAMA H., KUBOTA Y. and NAGAWA H.: Preoperative grading system for predicting operative conditions in laparoscopic cholecystectomy. Surg. Today, 34: 331-6, 2004.

6- CWIK G., SKOCZYLAS T., WYROSLAK-NAJS J. and WALLNER G.: The value of percutaneous ultrasound in predicting conversion from laparoscopic to open cholecystectomy due to acute cholecystitis. Surg. Endosc., 27: 2561-8, 2013.

7- PEPYS M.B. and HIRSCHFIELD G.M.: C-reactive protein: A critical update. J. Clin. Invest., 111: 1805-12, 2003.

8- NASSAR A.H.M., HODSON J., NG H.J., VOHRA R.S., KATBEH T., ZINO S. and GRIFFITHS E.A.: CholeS Study Group, West Midlands Research Collaborative. Surg. Endosc., 34 (10): 4549-4561, 2020.

9- SAKURAMOTO S., SATO S., OKURI T., SATO K., HIKI Y. and KAKITA A.: Preoperative evaluation to predict technical difficulties of laparoscopic cholecystectomy on the basis of histological inflammation findings on resected gallbladder. Am. J. Surg., 179: 114-21, 2000.

10- TECKCHANDANI N., GARG P.K., HADKE N.S., JAIN S.K., KANT R., MANDAL A.K., et al.: Predictive factors for successful early laparoscopic cholecystectomy in acute cholecystitis: A prospective study. Int. J. Surg., 8: 623-7, 2010.

11- RANDHAWA J. S. and PUJAHARI A.K.: Preoperative prediction of difficult lap chole: A scoring method. Indian J. Surg., 71: 198-201, 2009.

12- SAKURAMOTO S., SATO S., OKURI T., SATO K., HIKI Y. and KAKITA A.: Preoperative evaluation to predict technical difficulties of laparoscopic cholecystectomy on the basis of histological inflammation findings on resected gallbladder. Am. J. Surg., 179: 114-21, 2000.

13- SCHÄFER M., KRÄHENBÜHL L. and BÜCHLER M.W.: Predictive factors for the type of surgery in acute cholecystitis. Am. J. Surg., 182: 291-7, 2001.

14- COLE D.S., WATTS A., SCOTT-COOMBES D. and AVADES T.: Clinical utility of perioperative C-reactive protein testing in general surgery. Ann. R. Coll. Surg. Engl., 90: 317-21, 2008.

البروتين سى التفاعلى كعامل تنبؤى لصعوبة استئصال المرارة بالمنظار

خلفية الدراسة: التهاب المرارة الحاد مع الجراحة التنظيرية الصعبة له تأثير على وقت التشغيل وتدريب الصغار. لا يزال التشخيص السريرى لإلتهاب المرارة الحاد المعقد صعباً مع العديد من المعايير المرضية أو الموجات فوق الصوتية المستخدمة لتمييزه عن التهاب المرارة الحاد غير المعقد.

الهدف من الدراسة: تقييم بروتين سى التفاعلى كمعامل يتنبأ بصعوبة استئصال المرارة بالمنظار أو التحويل إلى الجراحة المفتوحة.

المرضى وطرق الدراسة: أجريت تجربة سريرية عشوائية مستقبلية على ١٥٠ عملية استئصال مرارة بالمنظار أجريت من يناير ٢٠١٩ إلى فبراير ٢٠٢٢ فى قسم الجراحة العامة، مستشفيات جامعة الأزهر (القاهرة) مصر. تمت دراسة ارتباط الصعوبات أثناء العملية أو التحويل مع العوامل التالية العمر، الجنس، بروتين سى التفاعلى، وعدد خلايا الدم البيضاء.

نتائج الدراسة: تم تحليل ١٥٠ مريضاً [١٢٤ بالمنظار، ٢٢ اشتئصال المرارة بالمنظار الصعب و ٤ درجات مئوية (التحويل إلى الفتح)]. كان لدى جميع المرضى بروتين سى التفاعلى المسجل. كان متوسط بروتين سى التفاعلى أعلى بالنسبة للمرضى الذين تم تحويلهم (٢٨٠.٥) مقارنة بأولئك الذين لديهم صعوبة فى استئصال المرارة بالمنظار (٦٧.٤٠) أو استئصال المرارة بالمنظار (٧.٠٥). كان ارتفاع بروتين سى التفاعلى قبل الجراحة، وعدد خلايا الدم البيضاء وتصوير البنكرياس والأوعية الصفراوية، عوامل تنبئ بالتحويل. كانت هذه العوامل أفضل بشكل هامشى من بروتين سى التفاعلى وحده فى توقع التحويل.

الاستنتاج: يمكن أن يكون بروتين سى التفاعلى مؤشراً فعالاً لتحويل استئصال المرارة بالمنظار.