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Role of C - reactive protein as a Predictor of Difficult Laparoscopic Cholecystectomy or Its Conversion to Open Cholecystectomy

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Abstract

Background and Objectives: Laparoscopic cholecystectomy (LC) can be the easiest or the most difficult laparoscopic operation. Conversion to open surgery has been a traditional marker of difficult LC and anticipation of conversion can help in consenting patients and preparing them for longer stay and complications. Though not appreciated widely, difficult LC can have similar implications, as conversion to open operation, in terms of operating time, expertise required for an operation and training of juniors.

Methods: A prospective study on Emergency Laparoscopic Cholecystectomy done for Acute Cholecystitis was undertaken in the Department of General Surgery, ESIC Medical College, Rajajinagar, Bengaluru. A total of 45 cases were studied from January 2018 to June 2019. Association of intra operative difficulty or conversion with pre-operative C - reactive protein values was studied.

Results: Fourty five patients were analyzed of which ten patients underwent difficult laparoscopic cholecystectomy (22%), three underwent laparoscopy converted to open cholecystectomy (7%) and the rest of the patients, and thirty two in number underwent Laparoscopic cholecystectomy that was deemed to be easy. Mean CRP was highest in patients who underwent laparoscopy converted to open cholecystectomy, 453.9mg/L. In patients who underwent difficult laparoscopic cholecystectomy the mean CRP was 111.95mg/L while the patient who underwent easy laparoscopic cholecystectomy had a mean CRP level of 19.77mg/L

Interpretation and Conclusion: C-reactive protein was significantly higher in cases that were noted to have difficult surgery. Hence, high preoperative CRP can be a strong predictor of difficult laparoscopic cholecystectomy or its conversion to open. However, further validation is necessary in larger studies.

Keywords: C-reactive protein; Laparoscopic cholecystectomy.

Introduction

Laparoscopic cholecystectomy (LC) is one of the most common laparoscopic procedures being performed by general surgeons all over the world. Preoperative prediction of the risk of conversion or difficulty of operation is an important aspect of planning laparoscopic surgery.[1]

Laparoscopic cholecystectomy (LC) since its inception in 1987, has dramatically replaced conventional open cholecystectomy. LC has rapidly become the gold standard for routine symptomatic gallstone disease. Management of biliary tract disease has evolved from being a major procedure to a relatively safe and day care procedure today, offering early return to full activity.[2]

LC though safe and effective, yet can be difficult at times. Various problems faced are difficulty in creating pneumo peritoneum, accessing peritoneal cavity, releasing adhesions, identifying anatomy, anatomical variation, dissection of Calot's triangle, avoiding injury to common bile duct and extracting the gall bladder.[2].

Conversion to open cholecystectomy has been associated with increased overall morbidity, surgical site and pulmonary infections, and longer hospital stays. The ability to accurately identify an individual patient's risk for conversion based on preoperative information can result in more meaningful and accurate preoperative counselling, improved operating room scheduling and efficiency, stratification of risk for technical difficulty, may improve patient safety by minimizing time to conversion, and also helps to identify patients in who a planned open cholecystectomy is indicated.[3]

This study is based on the supposition that difficulty can be predicted using a preoperative tool i.e C - reactive protein to decrease post-operative complication and conversion rate.

Methodology

The present study was conducted in the department of General Surgery, ESIC Model hospital attached to ESIC medical college & PGIMSR, Rajajinagar, Bengaluru from January 2018 to June 2019. A total of 45 cases which met the inclusion and exclusion criteria were included in this hospital based prospective study conducted for duration of 18 months. The study population included all patients who underwent emergency Laparoscopic cholecystectomy.

Study Design: Prospective study.

Study Period: From January 2018 to June 2019.

Sample Size: A total of 45 cases.

The sample size for the present study has been calculated by considering the 65% PPV of the C-reactive protein as a predictor of difficult laparoscopic cholecystectomy from the past published literature.[4] The minimum sample size has been calculated as 45 cases with 0.1 as absolute marginal error which at 5% level of significance assuming two tailed hypothesis. Following formula has been used to calculate the sample size:

$$n = \frac{Z^2_{\alpha/2} PQ}{D^2}$$

Where, $Z_{\alpha/2}$ =1.96, P=.50, Q=1-P and D=0.10

Method of Collection of Data

A written informed consent is obtained from patients to be included in the study and data collected on printed proforma including demography, history, lab investigations and radiological investigations.

The patient after being diagnosed to have acute cholecystitis undergo laparoscopic cholecystectomy**.**

All patients underwent surgical procedure after the following preoperative preparation.

- Informed written consent obtained after explaining the surgical procedure and its results.
- Nil by mouth after 10:00 pm on the previous night of surgery.
- IM Injection tetanus toxoid 0.5ml
- Injection xylocaine test dose.
- Preparation of the parts by shaving

All patients received one dose of preoperative antibiotic, 1gm of 3rd generation cephalosporin immediately after induction of anaesthesia. All patients were operated under general anaesthesia.

Standard four port technique was used. Pneumoperitoneum was created using veress needle technique.

Intraoperative difficulties were assessed and patients were categorized according to following criteria at the end of surgery.

1. Easy

a. Time taken < 60 min, No bile/ calculus spillage, No injury to CBD/cystic artery.

2. Difficult

Time taken >60 min, Bile/ calculus spillage, the presence of circumscribed peritonitis in the right hypochondrium, difficult identification and isolation of the cystic artery and duct, frozen Calot's triangle, inflammation, an abundance of adipose tissue, a short cystic duct, difficult dissection of the gallbladder wall from the hepatic bed.

3. Converted to open

Cases that were converted to open cholecystectomy

Correlation was made between pre-operative C - reactive protein and intra-operative difficulties.

Inclusion Criteria

➢ All the patients aged 18 to 60 years who were diagnosed Acute Cholecystitis using Tokyo Guidelines were included in the study.[5]

Exclusion Criteria

- Patients with high BMI (>35).
- Previous abdominal surgery.
- Patients who have medical illnesses that are known to raise CRP levels (pneumonia, TB, Lupus, Vasculitis, rheumatoid arthritis etc)
- Carcinoma Gall bladder
- Perforated Gall bladder
- Mirizzi's syndrome
- Those with incomplete data.

Statistical Analysis

The data collected were entered into excel spread sheet and it was analyzed using the Statistical Package for Social Sciences (SPSS) version 24. Descriptive and inferential statistics was done. Quantitate data were measured through Mean and Standard Deviation.

The null hypothesis for this test is that the data are normally distributed. Statistical significance was considered at $p < 0.05$ (confidence interval of 95% was taken). If the chosen alpha level is 0.05 and the p-value is less than 0.05, then the null hypothesis that the data are normally distributed is rejected. If the p-value is greater than 0.05, then the null hypothesis has not been rejected. Since the data not violated the assumption of normality in the study Parameteric test was carried out to compare between the study groups.

One way Analysis of Variance (Anova)

One way analyses of variance were used to test the difference between groups. Analysis of Variance is a technique by which the total variation is split into two parts one between groups and the other within the groups. If 'F' value is significant there is a significant, difference between group means.

The formula used:

$$F = \frac{MS_{betweengroups}}{MS_{Withingroups}}$$

Where MS=Mean Sum of Square

Observations and Results

- This study included 45 emergency Laparoscopic cholecystectomies that were studied prospectively over a period of 18 months at ESIC, Rajajinagar, Bengaluru from January 2018 to June 2019.

Distribution of Cases According To Age

Among the 45 patients who underwent laparoscopic cholecystectomy, the age ranged from 19 years to 65 years. The peak incidence of acute cholecystitis was noted in the age group of 41 years to 50 years (33%). The lowest incidence was noted in the 61 years to 65 years age group (8%).

Table 1: Distribution of Cases According To Age

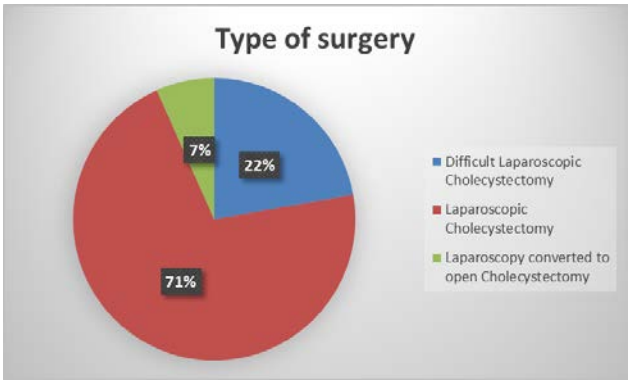
AGE(YRS)	N	%
18-30	9	20
31-40	10	22
41-50	15	33
51-60	7	15
61-65	4	8
Total	100	100

Showing Gender Wise Distribution Of Cholecystitis.

Table 2: Gender Wise Distribution Of Acute Cholecystitis

Gender	Frequency	Percent
Male	20	33%
Female	40	67%
Total	45	100%

Chart 1: Distribution of Type of Surgery



Value of Mean CRP and Type of Surgery Done

One-way ANOVA was applied to find the value of mean CRP difference and type of surgery done. Table 3 shows, there was significance difference between the types of surgery with the CRP. The mean value of CRP was highest for the Laparoscopy converted to open cholecystectomy, followed by Difficult Laparoscopic Cholecystectomy and least for Laparoscopic Cholecystectomy. ($p<0.001$)

Table 3: Mean Crp And Typr Of Surgery Done

		Mean	Std. Deviation	Std. Error	F value	p-value
CRP	Laparoscopic Cholecystectomy	19.7744	18.71567	3.30849		
	Difficult Laparoscopic Cholecystectomy	111.9550	104.54681	33.06060	12.74	0.001
	Laparoscopy converted to open cholecystectomy	453.9333	208.49835	120.37658		
	Total	69.2029	129.39401	19.28892		

DISCUSSION

- This study was conducted in the Department of General surgery ESIC MC & PGIMSR Rajainagr Bangalore.
- It was conducted over a period of eighteen months from January 2018 to June 2019.
- Forty five patients participated in the single center non randomized prospective, clinical observational study
- The study was aimed at analyzing the feasibility of pre-operative C-Reactive protein levels in predicting intra-operative difficulties in Laparoscopic Cholecystectomy.
- Gall stone diseases are more common in females. Our study group also reflected the same, most of the patients were women (67%) and most of the patients fell in the middle age group i.e between 5th and 6th decade (33% of the patients).
- Díaz-Flores et al in a study concluded that, preoperative C-Reactive Protein with values ≥110 mg/L was associated with the highest odds (OR = 17.9) of presenting as difficult laparoscopic cholecystectomy. This value possesses good sensitivity, specificity, PPV and NPV for predicting difficult laparoscopic cholecystectomy in our population with acute calculous cholecystitis.[6] Our study has similar observations where the mean preoperative C-Reactive Protein of patients' whose surgery was deemed to be difficult was 111.9mg/L. Further on extension we noted that the surgeries that

were converted to open had a mean pre-operative C-reactive protein of 453.9mg/L.

- Lee R et al concluded that higher peak serum white blood cell count and levels of C-reactive protein (CRP) was associated with prolonged operative duration. They made an observation that a pre-operative C-reactive protein level of 171±12.4mg/L was suggestive intra operative difficulties causing increased operating time of more than 90 minutes making the laparoscopic cholecystectomy a difficult one.[7] The mean operating time in our study when pre-operative C-Reactive protein is 20mg/L is less than 60 minutes. The mean C-reactive protein of difficult laparoscopic cholecystectomy in our study was 111.9mg/L, the mean duration of surgeries of difficult and laparoscopic converted to open cholecystectomy in our study was 90-141minutes. With a statistically significant p value of 0.003
- Mok KW et al concluded in their study that C-Reactive Protein on its own has been shown to have high predictive value in predicting gangrenous gall bladder. They noted that a low pre-operative C-reactive protein with a mean of 20.6mg/L predicted an easier laparoscopic cholecystectomy.[8] We have made similar observations in our study where when a cholecystectomy was deemed easy, a mean pre-operative C-Reactive protein of 19.7mg/L. The average operating time in such patients with low C-Reactive protein was 47.13 minutes as opposed to the a mean of 89-141.33 minutes in patients who underwent difficult laparoscopic cholecystectomy or conversions to open cholecystectomy.
- In a study done by Bhanu Kuashik et al observed that C-reactive protein level increased significantly with increase difficulty of dissection. Mean CRP was 22.2±18.2 mg/dl for simple cholecystectomy, 46.5±32.0 mg/dl for difficult cholecystectomy and 83.6±22.4 mg/dl for laparoscopic converted to open cholecystectomy, which was statistically significant (p value 0.0002) and that the mean duration of surgery for simple cholecystectomy was 30.6±7.8 minutes while for difficult cholecystectomy it was 54.6±14.6 minutes and highest mean duration of surgery was 84.3±14.2 minutes for laparoscopic converted to open cholecystectomy (p value 0.0003) similar results are seen in our study with a mean pre-operative C-reactive protein of 111.9mg/L in difficult laparoscopic cholecystectomies.[9]
- Jessica Mok KW et al in their study showed a strong association between peak preoperative CRP levels and GB pathology related conversions. They concluded that patients who had laparoscopic cholecystectomies converted to open had a significantly higher C-Reactive protein (P<0.001). A cut-off of pre-operative C-Reactive protein was achieved at a level of 220mg/L above which chances of difficult dissection and chances of conversion to open are the highest.[6] They concluded that C-Reactive protein has high positive as well as NPV. CRP on its own appeared to be a good independent predictor of conversion. Our study also has similar results where lowest C-reactive protein levels were recorded in patients who underwent easy laparoscopic cholecystectomy (Mean 19mg/L)
- Conversion to open cholecystectomy in present study was resorted to in 3 patients (7%) of the total 45 patients undergoing laparoscopic cholecystectomy, which is in accordance to the literature (2% - 11%)[10]

Conclusion

- Laparoscopic cholecystectomy is undoubtedly the gold standard in the management of gall stone disease and its acute presentation.
- Conversion to open cholecystectomy due to intra-operative difficulties is some cases is an inevitability. Predicting the possibility of conversion to open or facing intra-operative difficulty is still a difficult task.
- This study noted that higher pre-operative levels of C-reactive protein is suggestive of higher probability of facing intraoperative difficulties.
- The fact that a pre-operative tool i.e C-Reactive protein has shown to reliably predict intraoperative difficulty during laparoscopic cholecystectomy is promising.
- It can be used to forewarn surgeons of impending difficulty and hence can help surgeons be more prepared, make better decisions and counsel the patients better.
- However larger studies are required to validate the same.

Summary

- A total of 45 cases of acute cholecystitis were studied in the present clinical study done at ESI Medical college and Post Graduate Institute of Medical Science and Research, Bengaluru during a period of one and half years from January 2018 to June 2019.
- Most of the cases were females (67%) and in their 5^{th} to 6^{th} decade of life.
- Of the 45 cases posted for Laparoscopic cholecystectomy. Three cases were converted to open cholecystectomy in view of intraoperative difficulty and inability to continue the surgery laparoscopically. Ten cases were deemed as difficult but laparoscopy cholecystectomy was successfully completed in spite of intra operative difficulties. And the rest of the cases that is thirty two in number were deemed as easy and underwent laparoscopic cholecystectomy successfully without any difficulty.
- The pre-operative C-Reactive Protein of the forty five cases were assessed and it was noted that cases that underwent conversion to open cholecystectomy had a higher level of mean C-Reactive Protein i.e 453.9mg/L. The cases that underwent difficult laparoscopic cholecystectomy also had a high level of mean C-Reactive Protein i.e. 111.95mg/L.
- The cases that underwent laparoscopic cholecystectomy that was deemed to be easy had a low mean C-Reactive Protein level i.e. 19.77mg/L.
- The pre operative CRP levels hence showed a very strong association to GB pathology related conversions of Laparoscopic cholecystectomy to open and increased intra operative difficulty (P value < 0.001).
- Pre operative levels of C-Reactive Protein can be used as a guide in assessing intraoperative difficulty and hence can be used as an important tool in decision making. It can help the surgeon be better prepared in anticipation of intraoperative difficulty, need for delaying surgery or operating at a higher medical facility with better experienced surgeons, propose open cholecystectomy as the first choice and in counselling patients regarding the possibility of open cholecystectomy.
- However, the small sample size may be an impediment in attaining complete statistical validity. We propose large scale, multicentric studies to validate the role of C-Reactive Protein in predicting difficult laparoscopic cholecystectomy and establish is efficacy firmly.

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