Clinical, laboratory, and radiological predictors of difficult laparoscopic cholecystectomy: A case control study

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Abstract:

Background: Laparoscopic cholecystectomy is widely accepted as the gold standard surgical treatment for gall stone disease. However, owing to technical difficulties during surgery, complications or conversion to open surgery may be needed leading to undesired trouble for both surgeon and patient.

Objectives: To evaluate predictors of a difficult laparoscopic cholecystectomy by pre-operative assessment of the clinical, laboratory, ultrasonographic (USG), and computed tomographic (CT) variables.

Patients and methods: This was a retrospective observational study done in patients undergoing laparoscopic cholecystectomy during a period of 1 year at a tertiary care medical institute in Northern India which comprised 32 patients of difficult laparoscopic cholecystectomy (surgery duration of more than 60 minutes or any major complications) and a control group of 32 patients undergoing easy laparoscopic cholecystectomy during the same time interval. Multiple clinical, laboratory & radiological parameters were assessed in cases and controls by analysis of hospital data and imaging records.

Results: Male gender, fever with raised inflammatory markers, impacted calculus with palpable gallbladder (GB), and signs of inflammation on USG and CT including GB wall thickness and pericholecystic fluid/stranding were major predictors of a tough laparoscopic surgery.

Conclusion: A well-defined clinical, laboratory & radiological assessment pre-operatively has the potential to prevent an arduous laparoscopic experience for both surgeon and the patient & provide a directive to take a better informed and planned surgical approach. Inflammatory markers and previous attacks are the strongest predictors of an upcoming difficulty. Both USG and CT have independent roles in paving the path for pre-operative diagnosis for the surgeon.

Keywords: Cholelithiasis; Complicated Surgery; Conversion to Open Cholecystectomy.

Introduction

Laparoscopic removal of gall bladder is widely accepted as the gold standard treatment for gall stone disease (**Olsen, 2004; Chand et al., 2019**). Reasons of wide acceptance over open cholecystectomy include minimally invasive technique, lesser morbidity, faster recovery and better cosmetic results (**Alponat et al., 1997**). However, up to 15% of laparoscopic cholecystectomies are converted into open procedure due to various factors contributing to on- table difficulties faced by the surgeon (**Rosen et al., 2002; Ibrahim et al., 2006**).

Even though the conversion is meant for the safety of the patient, it is sometimes necessary to take the decision of taking an open surgical route primarily rather than converting a complicated laparoscopic surgery (**Mannino et al., 2019**).

A difficult laparoscopic surgery includes many reasons, some of them being inflammation in the peri-cholecystic region and Calot's triangle which inhibit smooth tissue dissection, anatomical variants or anomalies in gall bladder or biliary tree & adhesions in the operative bed due to multiple prior attacks of cholecystitis. These variables can be assessed by multiple clinical, laboratory as well as radiological parameters in pre-operative assessment of the patient and a potential module can be obtained to predict the difficulty in laparoscopic cholecystectomy, thereby, guiding the surgeon better in making decisions regarding the operative route (**Bourgouin et al., 2016; Di Buono et al., 2021**).

The present study aims to evaluate the independent as well as combined predictors of a difficult laparoscopic cholecystectomy by pre-operative assessment of the clinical, laboratory, ultrasonographic (USG) and computed tomographic (CT) variables.

Patients and methods

This was a retrospective observational study done on hospital data & imaging records of patients who had laparoscopic cholecystectomy during a period of 1 years at a tertiary care medical institute in Northern India. The study group comprised of 32 patients of difficult laparoscopic cholecystectomy and a control group of 32 patients who had easy laparoscopic cholecystectomy during the same time interval. For the purpose of the study, difficult laparoscopic cholecystectomy was defined with the following criteria: operation duration > 60 minutes, bile leak, arterial leak and conversion to open cholecystectomy (**Siddiqui et al., 2017**).

All procedures performed in study involving human participants were in accordance to the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Inclusion criteria

Patients of cholelithiasis, who underwent laparoscopic cholecystectomy, and whose pre-operative laboratory, ultrasonographic

and CT scan imaging records, were accessible at the time of study.

Exclusion criteria

Conversion to open cholecystectomy due to non-surgical reasons, which included co-morbidities, anesthesia complications, and mechanical/equipment issues, among others.

The following parameters were taken into consideration for the study,

A) **Clinical and laboratory parameters:** Age, gender, pain, fever, vomiting, number (No.) of previous acute attacks (<2 / >2), palpable gallbladder, WBC count (4-11000 / >11000 per microliter), and C- reactive protein (<10 / >10mg/L).

B) **Ultrasonographic Criteria:** GB wall thickness (<4 mm / >4 mm), number of calculi, impacted calculus (i), pericholecystic fluid, common bile duct (CBD) width (>6 mm / < 6 mm) and hydrops of GB (4x9 cm with convex margins).

C) **CT Criteria:** GB wall thickness (<4mm / >4mm), presence of intraluminal gas, irregular GB wall, peri-cholecystic inflammation, CBD width (>6 mm / <6 mm) and hydrops of GB (4x9 cm with convex margins) **(Sebastian et al., 2013).**

All parameters were assessed in cases and controls by analysis of hospital data and imaging records with the aim of finding statistically significant preoperative predictors of difficult laparoscopic cholecystectomy.

Statistical analysis

Continuous variables were analyzed in mean and frequency. Categorical variables were made dichotomous and association of each parameter with difficult cholecystectomy was analyzed by Chi Square / Fisher Exact Tests. Linear regression analysis was done to test the strength of association of variables with difficult surgery. Multiple regression analysis was done to obtain the most significant group of variables which can predict a difficult surgery. Intermodality agreement between various USG and CT findings were analyzed by Cohen's Kappa coefficient. P value <0.05 was considered significant. All statistical analysis was done by using Graph pad prism software Version (9.4.0).

Results

Out of total 64 cases of laparoscopic cholecystectomy, three patients had to be converted to open, giving a conversion rate of 4.68% for the study population. The study population included cases between 19 to 65 years of age while the control group consisted of patients between 21 to 63 years of age. The mean age for cases was 40.26 years while for controls was 39.38 years.

There was a definite male preponderance in the study group comprising 78.12 % males (n=25), while in the control group, females were more common with a 53.12% (n=15) presence. The male gender was significantly associated with difficult surgery in the present study (P=0.0098), (**Table .1**).

While analyzing clinical features, pain was the most common presenting feature in the study group (n=28, 87.5%) followed by fever (n=19, 59.37%) and vomiting (n=12, 37.5%). While pain (n=30, 93.75%) and vomiting (n=13, 40.26%) were common, fever was an uncommon presentation in the control group (n=6, 18.7%). Fever was thus significantly associated with difficult cholecystectomy (P=0.0008), (**Table .1**).

Previous attacks of cholecystitis were assessed from patient history and it was observed that while 15 out of 32 patients (46.87%) of the study group and six (18.75%) out of 32 patients from the control group had more than 2 attacks previously (P=0.0165). On examination, a palpable gall bladder was found in six cases (18.75%) and only in one (4.12%) among control patients (P=0.0242), (**Table .1**).

While assessing the laboratory parameters, both increased WBC count (cases: 17, controls: 4, P=0.0011) and C Reactive Protein (cases: 20, controls: 8, P= 0.001) were found to be significantly present in cases of difficult surgery (**Table .1**).

Table1. Clinical and laboratory parameters in cases of difficult laparoscopic cholecystectomy in comparison to controls

Variables	Cases (n=32)	Controls (n=32)	P value
Age in Years (Mean)	40.26 ± 3.26	39.38 ± 2.74	
Gender			
• Male	25	15	0.0098
• Female	7	17	
Gall Bladder			
• Palpable	6	1	0.0242
• Not palpable	26	31	
Number of Previous Attacks			
• <2	17	20	0.0165
• >2	15	6	
Pain			
• Yes	28	30	0.6719
• No	4	2	
Fever(>38'C)			
• Yes	19	6	0.0008
• No	13	26	
Vomiting			
• Yes	12	13	0.7977
• No	20	19	
WBC Count			
• 4000-11000/cmm	15	28	0.0011
• >11000/cmm	17	4	
CRP			
• >10 mg/L	20	8	0.001

• <10 mg/L	12	24	

The USG parameters significantly associated with difficult surgery were GB wall thickness >4mm, impacted calculus / calculi & peri-cholecystic fluid. Number of calculi, CBD width and hydrops on USG were not significantly associated with operative difficulty in the present study (**Table .2**).

Table 2. Pre-operative USG features of cases of difficult laparoscopic cholecystectomy in comparison to controls

Variables	Cases(n=32)	Controls(n=32)	P value
GB wall thickness			
• > 4mm	21	9	0.0026
• < 4 mm	11	23	
Number of Calculi			
• Single	20	18	0.6107
• More than 1	12	14	
Impacted Calculus/Calculi			
• Yes	9	2	0.0433
• No	23	30	
Pericholecystic fluid			
• Yes	19	6	0.00086
• No	13	26	
CBD width			
• >6mm	3	1	0.6128
• <6mm	29	31	
Hydrops			
• Yes	7	1	0.0539
• No	25	31	

The CT parameters of GB wall > 4mm, pericholecystic inflammation in the form of fluid or stranding and hydrops were found to be significantly associated with difficult surgery. Irregular GB wall, presence of intraluminal gas and CBD width did not have significant association with operative difficulty (**Table .3**).

Table 3. Pre-operative CT features of cases of difficult laparoscopic cholecystectomy in comparison to controls

Variables	Cases (n=32)	Controls (n=32)	P value
GB wall thickness			
• > 4mm	20	7	0.001
• < 4 mm	12	25	
Irregular Wall			
• Yes	3	1	0.6128
• No	29	31	
Presence of intraluminal gas			
• Yes	2	0	0.4921
• No	30	32	

Peri-cholecystic Fluid/Stranding			
• Yes	24	10	0.0453
• No	8	22	
CBD Width			
• >6mm	5	2	0.4258
• <6mm	27	30	
Hydrops			
• Yes	8	1	0.0265
• No	24	31	

The variables showing significant association with surgical difficulty were further assessed by linear regression analysis to test the strength of association and their potential as predictors of difficult surgery. In this analysis for clinical and laboratory parameters, it was assessed that, in descending order, >2 previous acute attacks, male gender and a raised CRP (>10), fever, palpable GB and a raised WBC count, were all significant predictors of surgical difficulty. On ultrasonography, GB wall thickness > 4mm was the strongest predictor of a difficult surgery, followed by impacted calculus and pericholecystic fluid. Similarly, on further analysis of CT parameters, GB wall thickness of > 4 mm and pericholecystic inflammation were significant predictors of a difficult surgery, while the association of hydrops with a difficult surgery was not strong enough for it to be labelled an independent predictor (**Table. 4**).

Table 4. Linear regression analysis for clinical, laboratory, ultrasonographic and CT predictors of difficult laparoscopic cholecystectomy

Variables	R Square	95%CI	P value
Clinical and laboratory variables			
• >2 Previous Attacks	0.2615	0.1494-0.6506	0.0028
• Male Gender	0.2471	0.2095-0.9905	0.0038
• CRP (>10)	0.2000	0.1017-0.6983	0.0103
• Fever	0.1579	0.0439-0.5877	0.0243
• Palpable GB	0.1398	0.0125-0.3208	0.0350
• WBC (>11000)	0.1261	0.0043-0.4663	0.0462
USG variables			
• GB wall >4 mm	0.2050	(0.1139-0.7432)	0.0093
• Impacted Calculus	0.1704	(0.0394-0.4050)	0.0189
• Pericholecystic Fluid	0.1579	(0.0439-0.5877)	0.0243
CT variables			
• GB wall > 4 mm	0.1680	(0.0596-0.6404)	0.0093
• Pericholecystic Inflammation (fluid/stranding)	0.1515	(0.04906-0.7843)	0.0277
• Hydrops	0.0967	(-0.0173-0.2674)	0.0831

Both USG and CT showed good to excellent intermodality agreement as per Cohen's Kappa for various variables (**Table. 5**).

Table 5. Intermodality agreement between USG and CT on various parameters depicted by Cohen's Kappa coefficient

Variables	Cohen's Kappa	% Agreement
GB wall > 4 mm	0.9090	96.42%
Pericholecystic Inflammation	0.6551	84.37%
CBD > 6 mm	0.7168	93.75%
Hydrops	0.9130	96.87%

Multiple regression analysis on these predictors was done to pick up a clinical-radiological group of variables that can predict a difficult surgery and the strongest prediction potential was seen in a patient of male gender with more than > 2 previous acute attacks, raised CRP, having a palpable GB and an impacted calculus on USG with peri-cholecystic inflammation on both USG and CT (Adjusted R2=0.8016, P<0.0001), (**Table. 6**).

Table 6. Multiple regression analysis of clinical, laboratory, ultrasonographic and CT predictors of difficult laparoscopic cholecystectomy

Variables	Adjusted R Square	P value
Male Gender + > 2 Previous Attacks + CRP + Palpable GB	0.4099	0.0005
Male Gender + > 2 Previous Attacks + CRP + Palpable GB + GB Wall > 4mm on USG + Impacted Calculus	0.4656	0.0003
Male Gender + > 2 Previous Attacks + CRP + Palpable GB + GB Wall > 4 mm on USG + Impacted Calculus + Pericholecystic Inflammation on CT	0.8016	<0.0001

Discussion

Laparoscopic cholecystectomy has established itself as treatment of choice in cholelithiasis with excellent results and has lead to drastically reduced morbidity in comparison to open procedure. However, on table difficulties resulting into vascular or biliary injuries, and conversion into open cholecystectomy are also known outcomes of this surgery. To prevent mishaps or unnecessary last minute hiccups in the surgical approach, it is desirable to predict the difficulty level of laparoscopic cholecystectomy at pre-operative stage only. While only clinical parameters do not often suffice to predict a difficult laparoscopy, addition of laboratory and radiological assessment adds to the predictive value of an upcoming difficult surgery. A

constellation of variables that can anticipate an adverse surgical outcome were obtained in the study after evaluation of clinical, laboratory, ultrasonographic and CT parameters (**Joshi et al, 2015; Lal et al., 2002**).

In the present study, male gender was identified as an independent predictor of a difficult laparoscopic cholecystectomy similar to various previous studies by **Lee et al., 2012, Yang et al., 2014, and Agrawal et al., 2015**).

The primary pathophysiological array of fever, raised WBC counts and raised CRP, which indicate acute inflammation suggesting an acute attack of cholecystitis were identified as predictors of difficult laparoscopic cholecystectomy. The inflammatory process as further indicated by a thickened GB wall & pericholecystic fluid and stranding on USG and CT were also associated strongly with a difficult surgery. This is attributed to inflammation in the Calot's triangle precluding smooth dissection, and paving a tougher path where vascular or biliary injury risk is more than in a non-inflamed settings. All these parameters indicated that a laparoscopic cholecystectomy in an acute or emergent setting was definitely tougher for the surgeon. (**Di Buono et al., 2021; Agrawal et al., 2015; Dhanke and Ugane, 2014; Morales-Maza et al., 2021**).

Another compelling clinical parameter of more than two or multiple previous acute attacks of cholecystitis was consistent with an uphill laparoscopy. Repeated attacks

contribute to adhesions in the surgical field, interfere with creation of pneumoperitoneum, and clear dissection during the procedure. (**Gupta et al., 2013; Nidoni et al., 2015**)

Further, an impacted calculus on USG leading to a distended and a clinically palpable GB were also associated with surgical difficulty. However, in the present study, correlation of hydrops with difficult surgery on USG & CT were discordant with only CT diagnosed hydrops showing weak correlation with a difficult surgery (**Agrawal et al., 2015; Gupta et al., 2013; Randhawa and Pujahari, 2009**)

The parameters which did not correlate with surgical difficulty in the present study were pain & vomiting, which were found in both cases and controls in near equal distribution. Radiologically, number of calculi, CBD width, irregular wall enhancement and intraluminal gas bore no significant effect on operative results. This was contrary to the results of **Di Buono et al., 2021and Siddiqui et al., 2017.**

Radiological findings were nearly concordant in both modalities. However, CT was better in diagnosing inflammation beyond the GB wall in the surrounding fat, hydrops, width of CBD and intraluminal gas. Both USG and CT, though complementary, have singular defined roles & form an additive effect in foreseeing the upcoming difficulty.

On regression analysis, the strongest singular predictors of

difficulty were > 2 previous attacks, male gender, impacted calculus; all clinical-radiological parameters suggesting acute inflammation. On multivariate analysis, USG and CT parameters when added to the clinical findings brought strength to the predictive bunch of findings with strongest cluster being: male gender with > 2 previous attacks, raised inflammatory markers, having an impacted calculus with palpable GB & GB Wall > 4 mm on USG with pericholecystic inflammation on CT **(Di Buono et al., 2021; Lee et al., 2012; Yang et al., 2014; Morales-Maza et al., 2021).**

Conclusion

A well-defined clinical, laboratory, and radiological assessment pre-operatively has the potential to prevent an arduous laparoscopic experience for both the surgeon and the patient & provides a directive to take a better informed and planned surgical approach. Along with clinical parameters, both USG and CT have independent roles in paving the path for pre-operative diagnosis for the surgeon, and together, all three, supplement the efficacy of prediction.

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