Research Article

Difficult Laparoscopic Cholecystectomy: Could It be Anticipated Preoperatively? A Prospective Study of the Predicting Surrogates.

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Abstract

Background: Laparoscopic cholecystectomy (LC) represents the gold standard surgical treatment for gallstones. Several predictive factors have been proposed to affect the conversion rate from LC to open cholecystectomy (OC). A literature review showed highly contradictory results. In this prospective trial, we tried to evaluate the proposed factors in order to reach a conclusion. **Materials:** From January 2016 to March 2018, a prospective study has been conducted at Abha Private Hospital, Abha, Saudi Arabia on 387 patients who had a LC for gallstone disease. All patients were scheduled for LC. Ten variables were tested in order to determine their predictive value; age, gender, BMI, DM, previous abdominal surgery, acute pancreatitis, TLC, CRP, gallbladder wall thickness and pericholecystic collection. **Results:** During the defined period of study, 387 patients had undergone LC; 240 females (62.01%) and 147 males (37.9%), with a mean age of 48.6 ±11.3 years (range 18.7-78.6 years). Twenty-nine patients required conversions to OC with an overall rate of 7.49%. The commonest cause of conversion was severe inflammation in the hepatocystic triangle. Other causes of conversion included adhesions, a huge stone, bile duct Injury (BDI), intractable bleeding. **Conclusion:** It was shown that age> 60 years, male gender, DM, TLC>11,000 c/mm^3, CRP> 200 mg/dl, gallbladder wall thickness>4 mm and pericholecystic collection can increase the conversion rate to OC, whereas obesity, previous abdominal surgery, and acute pancreatitis seems not to significantly affect the conversion risk.
Keywords: cholecystectomy, treatment, gallbladder

Introduction

Gallstone disease is a common disease worldwide, for which LC represents the gold standard surgical approach[1,2]. In comparison to the OC, LC offers less pain, more rapid recovery, and better cosmetic appearance. However, these advantages could not be obtained in 1-15% of patients in whom the conversion to OC is the inevitable fate [3-5].

Several predictive factors have been proposed to affect the conversion rate and were accordingly, in the focus of the scientific research in the present era. Yet, these studies yielded contradictory results regarding these factors. In spite of the growing surgeons' experience with this common procedure, the rate of the conversion to OC is still unacceptably high.

Identification of factors predicting the risk of the conversion is of utmost importance. Low-risk patients could have their operation carried out as one-day surgery and even could be done by junior surgeons. On the contrary, patients with high risk should be appropriately informed about possible complications and the operation should be carried out by an experienced staff [6]. Such a dilemmatic issue is considered to be extremely important in the teaching hospitals and from the economic point of view, alike.

Some experts have been trying to gather these predicting factors and incorporate them in form of a scoring model [*such as CLOC score*[2]*, RSCLO score* [7] *and the prediction nomogram*[8]]. However, practically nobody, it seems, is convinced of these scores. In the present

prospective trial, we tried to evaluate the proposed factors which can influence the risk of conversion of LC.

Materials and Methods
Study Design:
Upon approval of the Institutional Review Board, a prospective study has been conducted at Abha private hospital, Abha, Saudi Arabia, on 387 patients who had a LC for gallstone disease in the period from January 2016 to March 2018. Patients of either gender, aged from 15 to 85 years with an established diagnosis of gallstones were included. Exclusion criteria were bleeding disorders, psychiatric disorders, history of malignancy, CBD stones and those with high anesthetic risk.

Patients were evaluated using some blood tests (including TLC and CRP), and by conducting an Ultrasound (U/S) study (*iU 22 scanner, xMATRIX, Philips Medical Systems, Bothell, Washington, USA*). The stones are defined by having a characteristic bright white echo with a posterior acoustic shadow beyond them, in addition to their mobility with the change of patient position. The GB wall thickness was estimated by measuring the maximum thickness of the anterior wall (which is adjacent to the liver). A wall thickness equal to or more than 4 mm was set as a cut-off. The acute cholecystitis was diagnosed according to the Tokyo Guidelines[9]. All the enrolled patients signed a preoperative written informed consent and were scheduled for LC (either elective or emergency).

The LC was performed using a standard four-port technique. However, in some cases, laparoscopic subtotal cholecystectomy was done through resecting both the posterior and anterior walls of the gallbladder followed by closing the remnant at the level of the gallbladder's neck.

Patients were then allocated to either group A (completed laparoscopic) or group B (converted cases). The relevant data in terms of demographic (as age and gender), anthropo-metric, laboratory results (TLC, CRP), radiological findings as well as intraoperative outcomes were documented in a standard Excel sheet for Windows and were verified checking for its statistical significance.

Statistical analyses
The standard descriptive statistics were used to analyze the demographic and anthropometric data, as well as the surgical operations and outcomes. The quantitative variables with a normal distribution were expressed as the mean ± standard deviation (SD), whereas qualitative data with categorical variables were expressed as frequencies and proportions. The categorical variables were analyzed by the Fisher's exact test or Chi-squared test. On the other hand, the continuous variables were analyzed by the Mann-Whitney U test. The statistical analyses were carried out using the Statistical Package for Social Science Version 22 software package (*SPSS, Inc., Chicago, Illinois, USA*), the significance level was set to 5%.

Results
During the defined period of study, 387 patients had undergone LC; 240 females (62.01%) and 147 males (37.9%) (male: female ratio of 1: 1.6) with a mean age of 48.6 ±11.3 years (range 18.7-78.6 years). Ninety-one cases (23.5%) were admitted on an emergency base, acute pancreatitis was diagnosed in 36 cases (9.3%) and acute cholecystitis was evident in 90 cases (23.25%). 106 cases (27.3%) had previous abdominal surgery (table:1). Twenty-nine patients required conversions to OC with an overall rate of 7.49%, the causes of conversion were clarified in table:3. The statistical analyses showed that the converted cases (group: B) had a Median age of 58±9.4 years and 51.7% of them were female.

Ten variables were tested in order to determine their predictive value; age, gender, BMI, DM, previous abdominal surgery, acute pancreatitis, TLC, CRP, gallbladder wall thickness and pericholecystic collection. The measurable vari-ables were tested with a pre-defined set value to increase the accuracy of the results. The demographic, anthropometric, as well as other variables evaluated from the patient history, were summarized in the table:1, whereas other laboratory and radiological variables were presented in the table:2. These variables were compared between the patients of both groups. There was no mortality in this trial.

Table (1): Statistical evaluation of some risk factors associated with conversion

Variable	No.	Percentage (%)	Conversion (Number)	Conversion (Percentage)	P-value
Age: <60 years	322	83.2%	22	6.8%	0.009
≥60 years	65	16.79%	7	10.76%	
Gender: Male	147	37.9%	14	9.52%	0.031
Female	240	62.01%	15	6.25%	
BMI: <30	267	68.9%	19	7.1%	0.12
≥30	120	31%	10	8.3%	
DM: Present	59	15.2%	6	10.1%	0.043
Absent	328	84.7%	23	7.01%	
Previous abdominal surgery: Present	106	27.3%	9	8.4%	0.32
Absent	281	72.6%	20	7.1%	
Acute Pancreatitis: Occurred	36	9.3%	2	5.5%	0.56
Not occurred	351	90.6%	27	6.9%	

Table (2): The laboratory and radiological risk factors.

Variable	No.	Percentage (%)	Conversion (Number)	Conversion (% of total cases)	P-value
TLC: <11,000 / mm^3	293	75.7%	18	6.14%	0.007
≥11,000/ mm^3	94	24.2	11	11.7%	
CRP: <200 mg/dl.	314	81.13%	16	5%	0.004
≥200 mg/dl	73	18.86%	13	17.8%	
Gallbladder wall Thickness: <5mm	299	77.3%	19	6.35	0.011
≥5mm	88	22.7%	10	11.36	
Pericholecystic collection: Absent	306	79%	20	6.5	0.021
Present	81	21%	9	11.1	

Table (3): Causes of conversion.

Cause of conversion	Number	Percentage
➢ Sever Inflammation hindering the progression of the safe dissection.	17	58.6%
➢ Adhesions in the hepatocystic triangle; 6 cases post bariatric, 2 cases post colectomy, and one case post truncal vagotomy and gastrojejunostomy.	9	31.03%
➢ Huge stone with Mirizzi syndrome (Fig:1).	1	3.44%
➢ BDI: due to a bizarre anatomy of the common bile duct and was treated by immediate reconstruction	1	3.44%
➢ Intractable bleeding from the right hepatic artery controlled after conversion by Pringles maneuver and repaired by polypropylene 5-0.	1	3.44%

Fig. (1): Huge stone in one patient converted to OC

Discussion

Since it was first described in 1985 [10], LC continues to be the gold standard surgical approach for the treatment of the gallstones. It has many advantages in terms of less post-operative pain, less morbidity and shorter hospital stay. However, the completion of the LC in some cases is a major challenge and the conversion to OC is inevitable.

The conversion to OC should not be considered as a failure to the surgeon but rather a safe strategic step towards patient's safety[2,4,11]. In this study, the rate of conversion is 7.49%, which is in the range reported by the other studies (2-15%)[7,12]. In addition, a rate of conversion in case of acute cholecystitis is 11.7% which is similar to that reported by other trials (5.6 -32%)[4,13,14,15].

In the present study, the most common reason for conversion to open approach is the severe inflammation hindering the progression of safe dissection (58.6%). This is followed by adhesions in the hepatocystic triangle (31.03%). Other causes include BDI, bleeding and huge stone **(table:3)**.

Besides, Panni & Strasberg[6] found in their landmark systematic review of eleven studies that inflammation and associated adhesions resulting in difficulty of anatomic identification was responsible for conversion in 75- 93% of cases. Steeg et al.,[16] speculated that the most common cause for conversion were acute inflammation (47%) fibrosis of Calot's triangle (30%) and adhesions (27%).

The other Less common causes of conversion include failure of the progression, aberrant anatomy, concern for malignancy, need for bile duct exploration, hypercapnia, choledo-choduodenal fistula, spilled stone as well as colon injury[3,6,11].

There are many factors that were proposed to increase the risk of conversion. Yet, a literature review yielded contradicting results regarding these factors.

Age:

Some authors speculated that age above 40 years [17], 50 years[18], 60 years [19] and 65 years [16] is a risk factor for conversion. On the contrary, others [20,21] did not find any statistical asso-ciation between age and conversion rate when

other variables were adjusted. In this study, we found that the conversion rate in those above 60 years is 10.76% versus only 6.8% in their equivalents below 60 years (P-value 0.009). This could confirm that age above 60 years is a significant factor for conversion of LC to OC. Given that the longer duration of the disease along with the greater number of bouts of inflammation that adds to the gallbladder fibrosis, the LC could be more difficult in those above 60 years [6].

Gender:

Equally important is the male gender which is the single most important predictor of conversion and the only significant predictive factor of operative death in multivariate analysis[23]. In this trial, the conversion rate in males is 9.52% versus only 6.25% in females (P-value 0.031). This is in line with other reports [22-24]. The aforementioned significant association could be attributed to the fact that males have more visceral fat and a higher pain threshold than females. Additionally, men are also less likely to seek medical advice. Therefore, they had a more delayed presentation.

In this context, Buffone et al.,[4] compared, in their Italian retrospective study, the outcomes between early and delayed LC of 100 patients suffered from acute cholecystitis. They stated that male gender, TLC $>18,000/mm^3$ markedly increase the conversion rate. Gangemi et al [17] from the University of Illinois retrospectively revised the medical records of 960 cases. They noted that age above 40 years, male gender, and acute cholecystitis are associated with a significantly higher risk of open conversion in both laparoscopic and robotic cholecystectomy. Surprisingly, some other studies [25] find no significant relation between conversion and male gender.

Obesity:

In spite of the many difficulties that are usually encountered during LC for obese subjects, the actual impact of obesity on the conversion rate is still to be defined. BMI higher than 30 did not appear to increase the conversion rate in this trial (P- value= 0.12). This is similar to that reported by some other studies [2,3,26,27].

DM:

Indeed, it has long been realized that DM is considered as a risk factor for conversion[3,19]. Interestingly, in the present series, we have 59 diabetic patients, the statistical analyses showed that the conversion rate is higher in diabetics than the non-diabetics (10.1% versus 7.01%, P-value= 0.043). DM-induced autonomic neuropathy usually conceals the symptoms of the gallstones; that's why diabetic patients may present late in the course of their disease with a more severe cholecystitis[28]. Moreover, DM increases the risk of gangrenous cholecystitis which in turn increases conversion rate [29,30].

Other Factors:

Seven (8.3%) patients were converted due to adhesions from previous surgeries, but the history of previous abdominal surgeries was not recognized as a risk factor in this study. This is in parallel to another study [24]. In this series, there is no significant association between acute pancreatitis and the risk of conversion to OC. Such a result could confirm Griniatsos et al's [3] points of view.

TLC

Regarding the factors affecting conversion, Panni and Strasberg [6] postulated that their sensitivity and specificity depends mainly on the selected cut-off value. However, the exact value that can accurately predict the conversion is a highly controversial issue as illustrated in **the table:4**.

Table (4): The different cut-off values for TLC level set by different studies.

Study	Cut-off value
Tambyraja et al.,[31]	8×10^3 c/mm^3
Sultan et al.,[32]	9×10^3 c/mm^3
Ibrahim et al.,[33]	10×10^3 c/mm^3
Alponat et al.,[34]	11×10^3 c/mm^3
Domínguez et al.,[35]	12×10^3 c/mm^3
Neylan et al.,[27]	13×10^3 c/mm^3
Rohatgi et al.,[36]	14×10^3 c/mm^3
Bingener et al.,[37]	17×10^3 c/mm^3

Another pertinent factor that could affect the conversion rate is TLC. In this study, TLC greater than 11,000 appears to be a significant risk factor for conversion (11.7% versus 6.14%, P-value= 0.007), which is in accordance with other studies[2,34]. In contrast, other authors [7,8,38,39] speculated that the exact levels of TLC do not alter the conversion risk.

CRP:
CRP as a marker of the severity of inflammation has a superior predictive value than the TLC. Accordingly, it is in the focus of scientific research. Several multivariate analyses considered it as a significant predictor of conversion with different cut-off values from 150 mg/dl to 220 mg/dl (**table: 5**).

Table (5): The different cut-off values for CRP level set by different studies.

Study	Year	Cut-off value
Tehro et al[24]	2016	>150 mg/dl
Wevers et al[28]	2013	>165 mg/dl
Mok et al[40]	2016	>220 mg/dl

In this series, CRP >200 mg/dl proved to have a statistically significant relationship with the conversion rate (P-value= 0.004). Some [41] speculated that a reading over 200 mg/dl is an indication for urgent LC.

U/S:
Similar to most of the predicting factors of conversion, U/S stigmata of acute cholecystitis (such as wall thickness and pericholecystic collection) are considered a matter of debate. Of interest, the findings of this study confirmed a significant association between the pericholecystic collection and the conversion rate (P-value= 0.021). Furthermore, Gallbladder wall Thickness ≥5mm entitles a higher risk for conversion (P-value= 0.011).

Table (6): The different cut-off values for gallbladder wall thickness set by different studies.

Study	Year	Cut-off value
Oymaci et al[42]	2014	>3 mm
Siddiqui et al[11]	2017	>4 mm
Rothman et al[38]	2016	>5 mm
Kania et al[43]	2016	
Izquierdo et al[1]	2018	>6 mm
Domínguez et al[35]	2011	>7 mm

More strikingly, Hu et al in their large-scale systematic review of a total of 30 studies involving data on 57,303 patients was the first to report that an impacted stone in the gallbladder neck is a significant predictor of conversion. Siddiqui et al.,[11] published a standardized U/S-based scoring system in 2017 for preoperative prediction of difficult LC and the conversion to OC. However, the weakness of their study mainly in their exclusion of patients whose LC was done on an emergency base.

In addition, there are some factors that were proposed to have an impact on the conversion risk such as elevated GGT and decreased Serum albumin, frequent biliary colic (> 10 bouts) [3] as well as smoking and drinking [5].

Such a study, in conjunction with similar studies, may provide a framework from which a more meticulous meta-analyses could be designed in order to validate and solidify the existing evidence regarding the predictors of conversion

Finally, the innovation of some new techniques helped in the limitation of the negative impact of some of the previously mentioned factors and eventually could lead to decreasing the

Difficult Laparoscopic Cholecystectomy:
                                      Could It be Anticipated Preoperatively

conversion rate. The use of intraoperative fluorescein can accurately delineate the aberrant anatomy and ultimately can avoid conversion in such cases[6]. Furthermore, the subtotal laparoscopic cholecystectomy is a safer and faster alternative to the classic LC. As might be expected, it enabled surgeons to overcome the potentially hazardous dissection in case of severe inflammation and Mirrizzi syndrome [36,44-46].

Conclusion
By Summarizing the outcomes of this trial, it could be concluded that age> 60 years, male gender, DM, TLC>11,000 c/mm^3, CRP> 200 mg/dl, gallbladder wall thickness>4 mm and pericholecystic collection **can increase** the conversion rate to OC, whereas BMI>30, previous abdominal surgery and acute pancreastitis seems not to affect the conversion risk.

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Difficult Laparoscopic Cholecystectomy: Could It be Anticipated Preoperatively

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