ORIGINAL RESEARCH KERALA MEDICAL JOURNAL

Multivariate Analysis for Preoperative Prediction on Intraoperative Conversion of Laparoscopic Cholecystectomy to Open Cholecystectomy

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Published on 27th September 2017

ABSTRACT

Background: Intraoperative conversion of laparoscopic cholecystectomy (LC) to open cholecystectomy (OC) to avoid biliovascular injury is considered a strategy, not a failure. But conversion from LC to OC causes significant postoperative morbidity. Preoperative prediction of conversion, using clinical, laboratory and imaging parameters, can help the patient and the surgeon for better preoperative preparations.

Objective: To identify preoperative predictors for intraoperative conversion of LC to OC by multivariate analysis of clinical, laboratory and imaging parameters.

Methods: Single centre retrospective comparative study was done using the database in the Department of Surgical Gastroenterology, Medical College, Trivandrum; on patients taken up for LC during the period from 01/01/2010 to 30/09/2016. Inclusion criteria were symptomatic gall stone patients confirmed by imaging whose surgical treatment is planned as LC. Exclusion criteria were LC-converted-OC before dissection (suspected carcinoma / hemodynamic instability / technical problems). Data collection was done using a proforma structured for prediction analysis using clinical, laboratory and imaging parameters. Statistical analysis was done by stratifying the patients as Group-I (LC) and Group II (LC-converted-OC). Univariate analysis (Chi- squared test) was done for factors favouring conversion, with which multivariate logistic regression analysis performed for OR and 95% CI (SPSS; statistical significance=p<0.05).

Results: Total 502 patients were enrolled (Group-I=428; Group-II=74). Age range was 13-78 years (mean age, Group-I=43.4; Group-II=52.6 (p<0.001). 79.9% males in Group-I; 20.1% in Group-II (p=0.008). Among diabetics; Group-I=76.7%; Group-II=23.3% (p<0.05). Jaundice was 61.7% Group-I and 38.3% Group-II (p<0.001). Pre-operative biliary stenting was done in 62.7% Group-I; 37.3% Group-II (P<0.001). Stone size of >20 mm observed in 66.7% Group-I; 33.3% Group-II (p<0.001). Serum alkaline phosphatase was >120 in 72.7% Group-I; 27.3% Group-II (p<0.05). 18.9% LC done by consultants and 6.5% LC by residents under supervision of consultants were converted to OC. Logistic regression analysis showed significant correlation regarding prediction of conversion to OC with male gender (OR 3.826;95%CI0.419-1.313), age>40 (OR3.826;95%CI1.869-7.831), diabetes (OR1.223;95%CI0.628-2.383), jaundice (OR4.954; 95%CI0.905-7.113), biliary stenting (OR2.684;95%CI0.254-8.382), interval after stenting >8 weeks (OR0.482;95%CI0.078-2.979) and single large stone (OR 2.540; 95%CI1.634-3.947). Among these age >40 years, jaundice and single large stone are observed as the most correlating factors.

Conclusion: Logistic regression analysis showed significant correlation between converted laparoscopic cholecystectomy and parameters including male gender, age above 40 years, diabetes, jaundice, biliary stenting, interval after biliary stenting >8 weeks and single large stone. These could be further utilised for formulating a simple bedside numerical prediction score using statistical software.

Keywords: Laparoscopic cholecystectomy, Intraoperative conversion, Multivariate analysis, Preoperative prediction

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BACKGROUND AND RATIONALE

Cholelithiasis is one of the most common diseases affecting the gastrointestinal tract. When a patient presents with symptomatic cholelithiasis, cholecystectomy becomes the treatment of choice. Diagnosis of symptomatic cholelithiasis is based on the clinical presentation and evidence of gall bladder stones on diagnostic imaging. Since the National Institutes of Health Consensus Conference in 1993 laparoscopic cholecystectomy is considered as the gold standard treatment for symptomatic cholelithiasis.[1] The first cholecystec-

Cite this article as: ---

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tomy was done by Langenbach in 1892.[2] The first successful laparoscopic cholecystectomy was done by Eric Muhe in 1985.[3] Presently, about 90% of cholecystectomies are performed by the laparoscopic approach.[4]

Laparoscopic cholecystectomy (LC) has shown to have several advantages over open cholecystectomy (OC); including faster recovery, less post-operative pain, shorter hospital stay and better cosmoses.[5] But laparoscopic cholecystectomy also has got complications; those related to anesthesia, peritoneal access (vascular injury, visceral injury and port-site hernia), side effects of pneumoperitoneum (cardiac or pulmonary complications) and thrombo-embolism. Specific complications related to laparoscopic cholecystectomy are vascular injury, gall bladder perforation, biliary injury, biliary fistula, bile collections, sepsis and foreign body entrapment.[6]

Conversion to OC is reported in 2% to 15% of patients undergoing LC.[7] Conversion of LC to OC sometimes become necessary to avoid or repair a biliary injury or to manage some intraoperative adverse situations like a difficult biliovascular anatomy, bleeding, biliary injury or an associated condition. Meanwhile, conversion to OC results in a significant change in the postoperative outcome because of the higher rate of postoperative morbidity and the longer hospital stay.[8,9,10,11] This study focuses on pre-operative prediction of a difficult LC and the risk for conversion, from the pre-operative data on clinical and laboratory parameters and imaging details, which could help the patient and the surgeon by better preoperative preparation for an open cholecystectomy.

OBJECTIVES

To identify pre-operative predictors for intra-operative conversion of laparoscopic cholecystectomy to open cholecystectomy by multivariate analysis of clinical, laboratory and imaging parameters.

METHODS

A single centre, retrospective comparative study was done in the Department of Surgical Gastroenterology, Government Medical College, Trivandrum; based on the prospectively maintained database on the consecutive cases taken up for laparoscopic cholecystectomy. The study was done over a period from 01/01/2010 to 30/09/2016. Inclusion criteria were symptomatic gall stone disease patients confirmed by imaging, whose surgical treatment was planned as laparoscopic cholecystectomy. Those cases of laparoscopic cholecystectomy converted to open by a diagnostic laparoscopy before starting dissection, due to precluding factors including suspicion of carcinoma gall bladder, hemodynamic instability or technical problems were excluded from the study. Retrospective data collection was done from the department database on operated cases, using a pre-structured proforma for preoperative prediction analysis of clinical, laboratory and imaging variables. The continuous and categorical variables studied included; age, gender, presenting symptom, duration of the symptom, comorbidities (including diabetes mellitus and obstructive jaundice), total count, liver function tests, preoperative biliary stenting status, time interval after biliary stenting, preoperative diagnosis, indication for intraoperative conversion, number of stones, size of stone (mm), status of gall bladder, gall bladder wall thickness (mm), and the experience of the surgeon (consultant or resident under direct supervision of the consultant).

Statistical Analysis

The patients enrolled were stratified as two groups; Group-I (laparoscopic cholecystectomy) and Group-II laparoscopy converted to open cholecystectomy. Statistical significance of differences in the variables between these two groups was analysed using the chi- squared test to determine the factors associated with conversion of LC to OC. Then a stepwise logistic regression analysis were performed using the significant variables. Odds ratios (OR) and their 95% confidence intervals (CI) were calculated using univariate analysis followed by multivariate logistic regression analysis. From the observations a formulation for calculation of probability of conversion from LC to OC in an individual patient was explored. The statistical analysis was done using the SPSS (version 13) and a p-value < 0.05 was considered as statistically significant.

RESULTS

In the present study total 502 patients were enrolled. Among them, those who had laparoscopic cholecystectomy (LC) taken as Group-I were 428 (85.3%) and those who were converted to open cholecystectomy (OC) taken as Group-II were 74 (14.7%).

Clinical arameters

The age of the patients ranged from 13 to 78 years (table 1). The mean and standard deviation of the age in Group-I was 43.4 ($\pm$13.5) and in Group-II was 52.6 ($\pm$11.9). 205 patients were <40 years of age of

which 193 (94.1%) had LC and 12 (5.9%) had OC. 297 patients were >40 years of age of which 235 (79.1%) had LC and 62 (20.9%) had OC. Gender also showed a statistically significant association with type of surgery (P<0.01). 80% of the male patients and 88.4% of the females patients underwent LC procedure. Of the total 184 male patients; 147 (79.9%) were in Group-I and 37 (20.1%) were in Group-II. Of the total 318 female patients; 281 (88.4%) were in Group-I and 37 (11.6%) were in Group-II. Conversion to OC has shown an association with the male gender (p 0.008). Presenting symptom was pain in 98.7% cases and jaundice was there in 23 (5.3%) of LC and 12 (16.21%) of OC. Regarding comorbidities; 90 patients were diabetic of which 69 (76.7%) had LC and 21 (23.3%) had OC. Jaundice was present in 47 patients of which 29 (61.7%) was in the LC group and 18 (38.3%) was in the OC group. 334 cases were done by the consultants and 168 cases were done by the residents under direct supervision of the consultant. 18.9% LC done by consultants and 6.5% LC by residents under supervision of consultants were converted to OC.

Laboratory Parameters

Among those with DM, 76.6% did LC procedure where as those without DM 87% did LC procedure. There was a statistically significant association observed with DM and the procedure selected (p<0.05). In those who had evidence of obstructive jaundice, 61.7% had LC and in those without obstructive jaundice 87% were treated with LC. The association was statistically significant (p<0.001). Serum alkaline phosphatase was below 120 in 18.5% of OC and it was above120 in 27.3% of LC (p<0.05).

Imaging Parameters

On analyzing the stone size and the procedure done; there was a steady increase in conversion to OC with rising stone size, 10.3% if the stone is less than 10 mm, 21.7% if the size is upto 20mm and 33.3% if the size is more than 20mm (p<0.001). Single stone had a higher chance for OC than multiple stones or sludge alone. On analyzing preoperative endoscopic biliary stenting; 37.3% had OC and 62.7% had LC, whereas without biliary stenting only 12.2% had OC and 87.8% had LC (p<0.001). When the duration after endoscopic biliary stenting was more than 8 weeks 34.1% had t undergo OC, and when the duration is less than 8 weeks only 12.9% had OC (p<0.001).

On simple binary logistic regression analysis **(table 2)** parameters which showed statistically significant crude

Table 1. Basic characteristics of the patients undergoing LC or converted to OC (n=502)

Variable	Grouping	LC (n=428)		OC (n=74)		p value
		No	%	No	%	
Age	< 40 Years	193	94.1	12	5.9	<0.001
	Gender	235	79.1	62	20.9	
Gender	Male	147	79.1	37	20.1	<0.05
	Diabetes	281	88.4	37	11.6	
Done by	Consultant	271	81.1	63	18.9	<0.001
	Raised SAP	157	93.5	11	6.5	
Diabetes	No	359	87.1	53	12.9	<0.05
	Biliary stent	69	76.7	21	23.3	
Jaundice	No	399	87.7	56	12.3	<0.001
	Yes	29	61.7	18	38.3	
Raised SAP	< 120	278	81.5	43	18.5	<0.05
	> 120	32	72.7	12	27.3	
Stone size	< 10 mm	270	89.7	31	10.3	<0.001
	11-20 mm	108	78.3	30	21.7	
	> 20 mm	16	66.7	8	33.3	
Biliary stent	No	396	87.8	55	12.2	<0.001
	Yes	32	62.7	19	37.3	
Interval after stenting >8 wk	No	399	87.1	59	12.9	<0.001
	Yes	29	65.9	15	34.1	

OR regarding prediction of conversion of laparoscopic cholecystectectomy to open cholecystectomy included age above 40 years (OR 4.24; 95%CI 2.22-8.10), male gender (OR 1.91; 95%CI 1.16-3.14), diabetes mellitus (OR 2.06; 95%CI 1.17-3.64), obstructive jaundice (OR 4.42; 95%CI 2.31-8.48), serum alkaline phosphatase

Table 2. Odds ratio by Logistic Regression Analysis

Variable	Group	OR	95% CI	p value
Gender	Female	1	--	<0.05
	Male	1.91	1.16-3.14	
Age	<=40 years	1	--	<0.001
	>40 years	4.24	2.22-8.10	
Stone size	<=10mm	1	--	
	11-20mm	2.42	1.40-4.19	<0.01
	>20mm	4.36	1.72-11.00	<0.01
Raised SAP	<=40	1	--	<0.001
	41-120	3.43	0.45-26.20	
	120+	7.87	0.95-65.15	
Diabetes	No	1	--	<0.05
	Yes	2.06	1.17-3.64	
Jaundice	No	1	--	<0.001
	Yes	4.42	2.31-8.48	
Biliary stent	No	1	--	<0.001
	Yes	4.28	2.27-8.06	
Interval after stenting > 8 wks	No	1	--	<0.001
	Yes	3.50	1.77-6.90	

Table 2. Odds ratio by Logistic Regression Analysis

Variable	Group	OR	95% CI	p value
Gender	Female	1	--	<0.05
	Male	1.91	1.16-3.14	
Age	<=40 years	1	--	<0.001
	>40 years	4.24	2.22-8.10	
Stone size	<=10mm	1	--	
	11-20mm	2.42	1.40-4.19	<0.01
	>20mm	4.36	1.72-11.00	<0.01
Raised SAP	<=40	1	--	<0.001
	41-120	3.43	0.45-26.20	
	120+	7.87	0.95-65.15	
Diabetes	No	1	--	<0.05
	Yes	2.06	1.17-3.64	
Jaundice	No	1	--	<0.001
	Yes	4.42	2.31-8.48	
Biliary stent	No	1	--	<0.001
	Yes	4.28	2.27-8.06	
Interval after stenting > 8 wks	No	1	--	<0.001
	Yes	3.50	1.77-6.90	

above 120 (OR 7.87; 95% CI 0.95-65.15) single large stone (OR 4.36; 95%CI 1.72-11.00), preoperative biliary stenting (OR 4.28; 95%CI 2.27-8.06) and time interval after biliary stenting beyond 8 weeks (OR 3.50; 95%CI 1.77-6.90).

These were included in the multiple binary logistic regression **(table 3)**. There was multicollinearity with independent variables. Final predictor scoring will be formulated by removing some of the variables which are related to each other. The adjusted OR showed statistical significance in age >40 years with AOR 3.83 and 95% CI (1.76-8.32), jaundice with AOR 8.48 and 95% CI (3.50-20.53)and single large stone above 20 mm with AOR 4.83 with 95% CI (1.50-15.57).

DISCUSSION

Cholecystectomy is regarded as one of the easiest or one of the most difficult operations to perform,

Table 3. Multiple binary logistic regression

Variable	Group	OR	95% CI	p value
Jaundice	No	1		<0.001
	Yes	8.48	3.50-20.53	
Age	<=40 years	1		<0.001
	>40 years	3.83	1.76-8.32	
Stone size	<=10mm	1		
	11-20mm	2.36	1.15-4.84	<0.01
	>20mm	4.83	1.50-15.57	<0.001

varying with individual patients. Because, in about 25% of patients, some variation from normal bilio-vascular anatomy is observed, that could cause difficulties during the procedure which could ultimately result in serious postoperative morbidity.[12] Thus conversion from LC to open cholecystectomy is often is a strategy; considered neither as a failure nor as a complication, but as an attempt to avoid complications. The conversion rates of laparoscopic cholecystectomy reported in the literature range from 0–20%.[13] Earlier studies have shown that age, gender, co-morbidities, obesity, history of acute cholecystitis or acute pancreatitis, past history of upper abdominal surgery, gall bladder wall thickness >3 mm and experience of the surgeon are the risk factors for conversion of LC to OC.0[7,14,15] The most frequent reasons for conversion is stated as the intraoperative situation in the form of fibrosis of Calot's triangle or adhesions.[16]

In this study, of the total 502 patients enrolled 85.3% had undergone laparoscopic cholecystectomy and 14.7% underwent open cholecystectomy. There is a considerable difference in number of patients in these two arms analysed. This real time data was accepted as such for the statistical analysis.

On primary analysis of clinical parameters **(table 1)** with the Chi-squared test; the mean age was more among the Group-II patients than the Group-I patients (52.6±11.9 vs 43.4±13.5). Of the 297 patients above 40 years of age, percentage underwent OC was more than the percentage of patients below 40 years of age underwent OC. Thus higher age was found to have a statistically significant association with the conversion to OC. Male gender also showed a statistically significant association with conversion to open cholecystectomy (20.1% vs 11.6%). The commonest presenting symptom was pain which was present in 98.7% cases. Jaundice was more common among those in the OC group than in LC group (16.21% vs 5.3%) which was statistically significant. 18.9% LC done by consultants and 6.5% LC by residents under supervision of consultants were converted to OC. This is due to the factor that the difficult cases were taken over by the consultants by protocol.

Laboratory parameters on Chi-squared test have shown that among those with diabetes, there was a statistically significant association observed with DM and OC 23.3% vs 12.95). In those who had evidence of obstructive jaundice, 38.3% had OC where as among those without obstructive jaundice 12.3% had OC which was statistically significant. Serum alkaline phosphatase was below 120 in 18.5% of OC and it was

above120 in 27.3% of OC which was also showed statistical significance.

Chi-squared test of the imaging parameters has shown that there is a direct correlation between conversion to OC and the stone size. Stone size more than 20 mm size had a significant association with conversion to open cholecystectomy. A single large stone had a higher chance for OC than multiple stones or sludge alone. Preoperative endoscopic biliary stenting if prolonged beyond 8 weeks due to any cause had a significantly higher risk for conversion to OC. On logistic regression analysis (table 2); the Odds ratio of the following factors were found significant; age above 40 years (OR 4.24; 95%CI 2.22-8.10), male gender (OR 1.91; 95%CI 1.16-3.14) , diabetes mellitus (OR 2.06; 95%CI 1.17-3.64), obstructive jaundice (OR 4.42; 95%CI 2.31-8.48), serum alkaline phosphatase above 120 (OR 7.87; 95% CI 0.95-65.15) single large stone (OR 4.36; 95%CI 1.72-11.00), preoperative biliary stenting (OR 4.28; 95%CI 2.27-8.06) and time interval after biliary stenting beyond 8 weeks (OR 3.50; 95%CI 1.77-6.90).

On analyzing these significant parameters with multiple binary logistic regression (table 3); adjusted OR showed statistical significance in age >40 years, jaundice and single large stone above 20 mm were observed as the major significant predictors for conversion of laparoscopic cholecystectomy to open cholecystectomy.

CONCLUSION

Logistic regression analysis of the clinical, laboratory and imaging parameters available at the outpatient setting; significant correlation was observed between laparoscopic cholecystectomy and converted open cholecystectomy; regarding those variables including male gender, age above 40 years, diabetes, jaundice, biliary stenting, interval after biliary stenting >8 weeks and single large stone. On multivariate analysis; age above 40 years, obstructive jaundice and single large stone were derived as the factors which could predict the risk for intra-operative conversion of laparoscopic cholecystectomy to open cholecystectomy. These could be further utilised for formulating a simple bedside numerical prediction score using statistical software.

LIMITATIONS OF THE STUDY

The majority of the patients (85.7%) were in the laparoscopic cholecystectomy group and only 14.3% patients were in the laparoscopy converted to open cholecystectomy group. There is a disparity among the two arms regarding the number. This had adversely affected the attempt to construct a numerical scoring system with the present data. Thus a reanalysis with more number of patients enrolled in to the laparoscopy converted to open cholecystectomy group is required to construct a scoring system to predict risk for conversion from laparoscopy to open cholecystectomy for patients diagnosed with symptomatic cholelithiasis.

END NOTE

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Conflict of Interest: None declared

Abbreviations

LC- Laparoscopic Cholecystectomy

OC- Open Cholecystectomy

OR- Odds Ratio

Explanations of Terminologies

1. **Laparoscopy converted to open cholecystectomy:** is a decision taken during surgery due to some technical difficulties in proceeding, to avoid dangerous complications to the patient.
2. **Preoperative endoscopic biliary stenting:** When the patient presents with jaundice and cholelithiasis with or without cholangitis/pancreatitis a cross sectional imaging followed by endoscopic ultrasound is advised. If there is suspected stone or sludge in the bile duct biliary sphincterotomy and stenting is done. Then the patient is advised laparoscopic cholecystectomy after 6 to 8 weeks.

Conflict of Interest: There is no conflict of interests among the authors of this article.

Acknowledgements

We would like to acknowledge our gratitude to the efforts of our faculty and residents of present year and the former years for maintaining the database in a proper manner.

Financial Support: Nil

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