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Original Research Article

Validation of A Preoperative Scoring System to Predict Difficult Laparoscopic Cholecystectomy: A Nepalese Perspective

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ABSTRACT:

Introduction: Preoperative prediction of the factors leading to difficulty or conversion in cholecystectomy could help plan the surgical strategies and possible outcomes beforehand. The present study aimed to predict and analyze risk factors using a scoring system deemed responsible for surgical difficulties in patients undergoing cholecystectomy for symptomatic cholelithiasis. **Methods:** This hospital based prospective study was conducted at Department of Surgery, Lumbini Medical College and Teaching Hospital, Nepal. Various factors considered preoperatively were gender, age, previous history of hospitalization, impacted stone, obesity, gall bladder wall thickness, pericholecystic collection, previous abdominal scar and palpable gall bladder. **Results:** Among 177 cases operated, the mean age ±SD of the patients was 47.72±17.54 years. Conversion rate was 7.9 %. At preoperative score of 5; sensitivity, specificity, positive predictive value and negative predictive value were 89.40% (CI: 83.36%-93.82%), 69.23% (CI: 48.21 %-85.67%), 94.41%(CI: 90.44%-96.79%) and 52.94% (CI: 39.85%-65.64%) respectively{Area under curve– 0.74, p=0.0001, CI (0.637-0.846)}. Multivariate analysis showed abdominal scar {p=0.02, OR (CI): 5.2 (1.2-21.8)}, previous hospitalization {p=0.001, OR(CI): 6.8(2.2-20.8)} and thickened gall bladder wall {p= 0.03, OR(CI): 3.6(1.1-11.5)} to be statistically significant risk factors. **Conclusion:** With possible prediction beforehand, high risk group of patients can be identified and dealt accordingly to generate good surgical outcome avoiding complications.

Key Words: **Conversion, Laparoscopic cholecystectomy, Preoperative prediction**

INTRODUCTION:

Laparoscopic Cholecystectomy(LC) is one of the most common surgical procedures performed worldwide and is the procedure of choice for the management of symptomatic gall stones.[1] Though this has been considered one of the safest surgeries to begin with laparoscopy, it requires meticulous dissection and good exposure of Calot's triangle in order to prevent bile duct injuries.[2] Dense adhesions at Calot's triangle and patients presenting with chronic cholecystitis with fibrotic and contracted gall bladder sometimes make surgery difficult and chances of conversion remains.[3] Various preoperative risk factors include male sex, old age, features of acute cholecystitis with fever and leukocytosis, obesity, previous surgery leading to abdominal scar, ultrasonographic findings like thickened gall bladder wall more than 4 mm, distended gall bladder, pericholecystic collection, impacted stone etc. which make laparoscopic surgery difficult.[4]

Preoperative prediction of difficulty in laparoscopic surgery and grading scales have widely been studied.[3,5,6] They have an advantage for the

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operating surgeon regarding quantifying the high-risk cases, managing operation room schedules, and counselling the relatives before the surgery about the potential complications. Also, the surgeons can prepare themselves for the adverse outcomes like arranging logistics and facilities, seeking help from seniors and colleagues. The present study aimed to utilize a preoperative scoring system and validate its applicability in a tertiary hospital of a developing country.

METHODS:

This was a prospective cross-sectional study conducted in the Department of Surgery, Lumbini Medical College Teaching Hospital after the approval from Institutional Review Committee (IRC-LMC 02-E/019). The study commenced from 15th July 2019 to 14th March 2020 for a period of eight months. Proper history and physical examination were carried out along with abdominal ultrasonography (USG). Laboratory parameters like Complete Blood Count (CBC), Liver Function Test (LFT) and preoperative laboratory assessment were carried out regarding fitness for surgery. All the patients with symptomatic gall stone disease including acute calculus cholecystitis were included in the study. Those patients who were unfit for general anesthesia, acute calculus cholecystitis managed conservatively, and those with chronic liver disease, choledocholithiasis and features of obstructive jaundice were excluded. A preoperative difficulty scoring system developed by Randhawa et al. was used in the present study. [7] The patients were assigned their difficulty level according to history, clinical parameters and USG findings (Table 1). History included variables like age, sex and past history of hospital admission for acute cholecystitis. Clinical parameters included Body Mass Index (BMI) which was designated 18.5-24.9 kg/m^2 being normal weight as per WHO classification[8] and more than 25 kg/m^2 was taken as risk factors which was splitted to 25-27.5 kg/m^2 and more than 27.5 kg/m^2 to corroborate with the scoring system, abdominal scar following previous abdominal surgery, and presence of clinically palpable gall bladder. A performa was filled up by the operating surgeons before attending surgery. The patients were admitted a day before the procedure, evaluated for the surgical fitness and posted for surgery the next day as electives which applies for acute calculus cholecystitis cases too. All the surgeries were performed by experienced surgeons.

Table 1. Scoring factors used for grading the patient parameters

Patient Characteristics (N= 177)		Score
Age (years)	<50	0
	≥50	1
Sex	Male	1
	Female	0
History of hospitalization for acute cholecystitis	Yes	4
	No	0
BMI	<25	0
	25-27.5	1
	>27.5	2
Abdominal scar	Infra-umbilical	1
	Supra-umbilical	2
	No	0
Palpable gall bladder	Yes	1
	No	0
Thick gall bladder wall	≥4 mm	2
	<4mm	1
Pericholecystic collection	Yes	1
	No	0
Impacted stone	Yes	1
	No	0

Score: 0-5: Easy 6-10: Difficult 11-15: Very Difficult

Surgery was conducted creating CO_2 pneumoperitoneum through open Hasson method. The 4-port technique was used with umbilical as camera port, epigastric as working port, and two 5mm ports on mid clavicular and anterior axillary line. Attaining a critical view of safety was the major goal, starting the dissection posteriorly and artery first clipping followed by cystic duct was the method we follow. However, Intraoperative Cholangiogram (IOC) was not done because of lack of feasibility and assets. Open conversion was done if critical view of safety was not attainable along with reconstituting subtotal cholecystectomy in cases of frozen calot's triangle where complete removal of gall bladder was deemed impossible. Total duration of surgery was the time after the commencement of skin incision and layer by layer closure after the procedure. All intraoperative events like bile spillage, bile duct injury or open conversion were recorded. The preoperative scores were compared with the

intraoperative assessment (Table 2).

Table 2. Showing the parameters and scoring/ grading on the basis of intraoperative assessment.

Parameters	Score	Grading
Time taken <60 minutes and No Bile Spillage and No injury to duct	0-5	Easy
Time taken 60-120 minutes and/or bile or stone spillage and/or injury to duct	6-10	Difficult
Time taken > 120 minutes or conversion	11-15	Very Difficult

Statistical analysis was performed with Statistical Package for Social Sciences (SPSS™) software version 20. Chi-square test/ Fisher exact test was used to find significance of association between preoperative and intraoperative findings for categorical variables whilst student-t test was used for continuous variables. Univariate and multivariate analysis were done to predict the risk factors for difficulty in surgery using binary logistic regression on the basis of intraoperative outcome as easy or difficult. Area under the Receiver Operating Characteristic (ROC) curve was used to find the diagnostic and predictive value of preoperative score for predicting the intraoperative outcome. Similarly, sensitivity and specificity of the proposed preoperative scoring system at our setting were also determined. P value <0.05 was considered statistically significant.

RESULTS:

There were 190 patients with symptomatic cholelithiasis during the study period. However, 13 of them did not fulfill the inclusion criteria. One hundred and seventy-seven patients under went laparoscopic cholecystectomy which included 36 males and 141 females. The mean age±SD of the patient was 47.72 ± 17.54 years. Twenty-four patients had past history of hospitalization for acute calculus cholecystitis while 12 had prior history of surgery with abdominal scar mostly midline. Gall bladder was palpable clinically in 27 patients. Seventeen patients had thickened gall bladder wall more than 4 mm. Pericholecystic collection was seen in 15 patients while impacted stone was observed in 16 cases. Fourteen patients needed conversion to open cholecystectomy with conversion rate of 7.9% (Table 3). Conversion occurred due to difficulty in dissection owing to dense adhesions rather than biliary spillage or uncontrolled intraoperative bleeding. Mean operative time was 51.16 ± 15.27 minutes for easy cases and 62.79 ± 16.66 minutes for difficult cases.

Table 3: Distribution of Parameters.

Patient Characteristics (N= 177)		Frequency
Age (years)	<50	96
	>50	81
Sex	Male	36
	Female	141
History of hospitalization for acute cholecystitis	Yes	24
	No	153
BMI	<25	108
	25-27.5	42
	>27.5	27
Abdominal scar	Yes	12
	No	165
Palpable gall bladder	Yes	27
	No	150
Thick gall bladder wall	Yes	17
	No	160
Pericholecystic collection	Yes	15
	No	162
Impacted stone	Yes	16
	No	161
Conversion		14

Table 4: Preoperative Score and the outcome

Pre-operative Score	Easy	Difficult	Very Difficult	Total
0-5	135	14	2	151
6-10	8	6	12	26
11-15	-	-	-	-
Total	143	20	14	177

Most of the patients had preoperative score of 0-5 and most were easy. None of the patients had score above 10 pre-operatively (Table 4). However, 14 patients were labelled very difficult according to intraoperative assessment. Considering preoperative score of 5; sensitivity, specificity,

Positive PredictiveValue (PPV) and Negative Predictive Value (NPV) were 89.40% (CI: 83.36%-93.82%), 69.23%(CI: 48.21 %-85.67%), 94.41%(CI: 90.44%-96.79%) and 52.94% (CI: 39.85%-65.64%) respectively.Area under the Receiver Operating Characteristic (ROC) curve was 0.74{p value – 0.0001, CI: (0.637-0.846} (Figure 1).

Univariate analysis of intraoperative outcome with risk factors showed abdominal scar due to previous surgery, previous hospitalization for acute calculus cholecystitis managed conservatively during previous episode, thickened gall bladder wall more than 4 mm and impacted gall bladder stone to be statistically significant (p value <0.05). Multivariate analysis depicted abdominal scar {p=0.02, OR(CI) 5.2 (1.2-21.8)}, previous hospitalization {p=0.001, OR(CI):6.8(2.2-20.8)} and thickened gall bladder wall {p= 0.03, OR(CI):3.6(1.1-11.5)} to be statistically significant risk factors (Table 5).

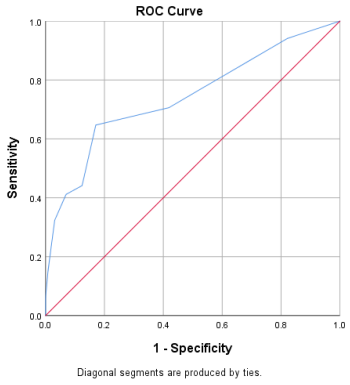

Fig. 1. Receiver Operating Characteristic (ROC) curve and Area Under the Curve (AUC) for prediction of intra-operative outcome based on preoperative scores.

Table 5: Predictive association of risk factors with intraoperative outcome

Risk Factors	Level	Intra-Operative Outcome		Univariate (OR-CI)	Multivariate (OR-CI)
		Easy	Difficult		
Age	<50	70	14		
	≥50	59	20	p=0.177 OR=1.7(0.78-3.6)	
Sex	Female	108	24		
	Male	21	10	p=0.08 OR=2.1(0.89-5.1)	
BMI	<25	92	19		
	25-27.5	25	11	p=0.08 OR=2.1(0.89-5.0)	
	>27.5	12	4	p=0.44 OR=1.6(0.47-5.5)	
Abdominal Scar	No	124	29		
	Yes	5	5	**p=0.02 OR=4.2 (1.1-15.7)**	**p=0.02 OR= 5.2 (1.2-21.8)**
Previous hospitalization for acute calculus cholecystitis	No	121	22		
	Yes	8	12	**p=0.0001 OR=8.2 (3.0-22.5)**	**p=0.001 OR= 6.8 (2.2-20.8)**
Palpable gall bladder	No	116	27		
	Yes	13	7	p= 0.104 OR=2.3 (0.84-6.3)	
Thick Wall ≥ 4mm	No	120	26		
	Yes	9	8	**p=0.008 OR= 4.1 (1.4-11.6)**	**p=0.03 OR= 3.6 (1.1-11.5)**
Pericholecystic Collection	No	119	32		
	Yes	10	2	p=0.711 OR= 10.7(0.15-3.5)	
Impacted Stone	No	124	26		
	Yes	5	8	**p=0.001 OR=7.6 (2.3-25.2)**	

DISCUSSION:

Laparoscopic Cholecystectomy (LC) is one of the most commonly performed surgeries worldwide and has been considered gold standard for the treatment of symptomatic gall stones. Because of the propensity of lesser post-operative pain, cosmesis, shorter hospital stay and disability from work, this has been the choice of procedure for maximum patients worldwide.[9,10] However, post-operative complication rates have been found higher in minimal invasive procedures like LC in comparison to open surgeries.[11] Safe laparoscopic surgery has become one of the most important topics discussed and various studies are ongoing regarding well-being of the patient and surgeon himself. Intraoperative findings may not be similar in every case and these greatly vary upon clinical presentation and surgical challenges might arise for the operating surgeon. If the prediction of safety of surgery could be made beforehand, surgeon will have a range of benefits like planning for surgery, patient counselling, operating room preparation and scheduling, and prepare for help from seniors and colleagues if needed.[12]

Increasing age or elderly population tend to be an important risk factor for difficulty in surgery as they are likely to have more longstanding disease with higher likelihood of complicated biliary tract disease which gets superimposed by various co-morbidities.[13] Various studies have concluded that older age is one of the significant risk factors.[7, 14] However, our study could not corroborate with their findings which other studies did too (p=0.177). [3,15] This could be due to cut off of age group as more than 50 years as some studies predicted using the cut off of 40 years.[12] The role of gender has also been mentioned in literatures as male population showed trends of high risk of conversion and surgical difficulty.[7,12,16,17] However, in our study, gender was not related to high risk of conversion. There was not any significant association between gender as male patients showing difficult surgeries or conversion rates (p= 0.08) which was also seen in study by Gupta et al.[3] This could be due to less sample population of males who were operated in comparison to female groups.

Previous history of hospitalization for acute cholecystitis managed conservatively is one of the risk factors for difficulty in surgery which has been clarified by our study too (p=0.001, OR=6.8). This can be explained as the chances of difficulty that may lead to conversion are about six times higher than those groups of people who have not been previously admitted or treated conservatively for acute cholecystitis. The absence of previous repeated attacks of cholecystitis and hospitalizations has been clarified to determine safe surgery in a study from Montenegro.[18] Pathogenesis could be repeated scarring and fibrosis of gall bladder due to multiple colic. Obesity or high BMI also has been considered the risk factor for conversion in another study.[19] However, this was not statistically significant in our study. Abdominal scar due to previous surgery may develop adhesions of viscera to the anterior abdominal wall and chances of conversion remains as risk of injury to bowel or other visceral structures are prudent during insertion of trocars.[20] Our study concluded the same (p= 0.02, OR = 5.2). This suggests the chances of difficulty are five times in patients with past history of surgery leading to abdominal scar. Thickened gall bladder wall more than 4 mm is one of the sonological criteria for diagnosis of acute cholecystitis and this has been attributed to difficulty in surgery or chances of conversion in various studies. [21,22] Palpable gall bladder due to development of mucocele or cholecystitis leading to empyema could render surgery difficult due to inability to grasp the fundus of the gall bladder leading to perforation and spillage of bile or pus along with gall stones in the peritoneal cavity. A study by Randhawa et al.[7] has correlated the significant association of palpable gall bladder with intraoperative difficulty which is also supported by Gupta et al.[3]

Pericholecystic collection was seen in 12 patients in our study. However, no significant association was seen with difficulty in laparoscopy (p= 0.71) which was consistent with that observed in studies from Delhi and Banglore, India.[3,7] Impacted stone was significantly associated with difficulty in laparoscopic cholecystectomy which has been concluded in other studies too.[3,5]

Preoperative difficulty scores seem not coordinating with intraoperative scoring at score level of 6-10 in difficult surgeries. Difficult numbers are small however we could see increased very difficult cases that corroborates the preoperative level of difficulty. This could be due to selection bias; a smaller number of sample size and the intraoperative scoring system could be merged as very difficult level to difficult considering only two intraoperative variables modifying the scoring system. Also, none of the samples attained very difficult score

preoperatively which could be removed.

Our study could conclude sensitivity of around 90% and specificity of around 70% which can be correlated with findings from Gupta et al. who mentioned sensitivity of 95% and specificity of around 74% in his validation study.[3]Similarly, conversion rate in our case was 7.9% which is comparable to a national conversion rate in United states which was 5-10% in a nationwide study conducted on 2004 collecting sample operated from 1998 to 2001.[23]Ghnnam et al. showed the conversion of 5% at Khamis General Hospital, Saudi Arabia where he analyzed retrospectively 340 patients.[24] However, males constituted about 20%(N=36) of total operated cases and conversion rate was as high as 25 % which could be due to less sample size . Females had conversion of 3.5% in our study.

CONCLUSION:

The scoring system can be used clinically to predict and guide the surgeons regarding safe surgical practice and anticipate the outcomes beforehand. However, larger sample sizes and multi center studies may be required in order to validate statistically and purposeful wide spread applicability in daily schedules.

Conflict of interest: Authors declare that no competing interest exists.

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REFERENCES:

1. Acar T, Kamer E, Acar N, Atahan K, Bağ H, Hacıyanlı M, et al. Laparoscopic cholecystectomy in the treatment of acute cholecystitis: comparison of results between early and late cholecystectomy. Pan Afr Med J. 2017;26:49.PMID: 28451027DOI: 10.11604/pamj.2017.26.49.8359
2. Suliman E, Palade RȘ, Suliman E. Importance of cystic pedicle dissection in laparoscopic cholecystectomy in order to avoid the common bile duct injuries. J Med Life. 2016;9(1):44-48. PMID: 27974912
3. Gupta N, Ranjan G, Arora MP, Goswami B, Chaudhary P, Kapur A, et al. Validation of a scoring system to predict difficult laparoscopic cholecystectomy. Int J Surg. 2013;11(9):1002-1006. PMID: 23751733 DOI: 10.1016/j.ijsu.2013.05.037
4. Abdel Baki NA, Motawei MA, Soliman KE, Farouk AM.Pre-operative prediction of difficult laparoscopic cholecystectomy using clinical and ultrasonographic parameters. JMRI. 2006;27(3):102-107.
5. Agrawal N, Singh S, Khichy S. Preoperative Prediction of Difficult Laparoscopic Cholecystectomy: A Scoring Method. Niger J Surg. 2015;21(2):130-133. PMID: 26425067 DOI: 10.4103/1117-6806.162567.
6. Hayama S, Ohtaka K, Shoji Y, Ichimura T, Fujita M, Senmaru N, et al. Risk Factors for Difficult Laparoscopic Cholecystectomy in Acute Cholecystitis. JSLS. 2016;20(4):e2016.00065. PMID: 27807397 DOI: 10.4293/JSLS.2016.00065.
7. Randhawa JS, Pujahari AK. Preoperative prediction of difficult lap chole: a scoring method. Indian J Surg. 2009;71(4):198-201. PMID: 23133154 DOI: 10.1007/s12262-009-0055-y
8. Lim JU, Lee JH, Kim JS, Hwang YI, Kim TH, Lim SY. Comparison of World Health Organization and Asia-Pacific body mass index classifications in COPD patients. Int J Chron Obstruct Pulmon Dis. 2017;12:2465-2475. PMID: 28860741 DOI: 10.2147/COPD.S141295.
9. Chesney T, Acuna SA. Do elderly patients have the most to gain from laparoscopic surgery? Ann Med Surg (Lond). 2015;4(3):321-323. PMID: 26557989 DOI: 10.1016/j.amsu.2015.09.007.
10. Yamashita Y, Takada T, Kawarada Y, Nimura Y,

Hirota M, Miura F, et al. Surgical treatment of patients with acute cholecystitis: Tokyo Guidelines. J Hepatobiliary Pancreat Surg. 2007;14(1):91-97.PMID: 17252302 DOI: 10.1007/s00534-006-1161-x

11. Radunovic M, Lazovic R, Popovic N, Magdelinic M, Bulajic M, Radunovic L, et al. Complications of Laparoscopic Cholecystectomy: Our Experience from a Retrospective Analysis. Open Access Maced J Med Sci. 2016;4(4):641-646. PMID: 28028405 DOI: 10.3889/oamjms.2016.128
12. Nassar AHM, Hodson J, Ng HJ, Vohra RS, Katbeh T, Zino S, et al. CholeS Study Group, West Midlands Research Collaborative. Predicting the difficult laparoscopic cholecystectomy: development and validation of a pre-operative risk score using an objective operative difficulty grading system. Surg Endosc. 2019; [Epub ahead of print]. PMID: 31732855 DOI: 10.1007/s00464-019-07244-5.
13. Amin A, Haider MI, Aamir IS, Khan MS, Choudry KU, Amir M,et al. Preoperative and Operative Risk Factors for Conversion of Laparoscopic Cholecystectomy to Open Cholecystectomy in Pakistan. Cureus. 2019;11(8):e5446.PMID: 31637145 DOI: 10.7759/cureus.5446.
14. Terho PM, Leppäniemi AK, Mentula PJ. Laparoscopic cholecystectomy for acute calculous cholecystitis: a retrospective study assessing risk factors for conversion and complications. World J Emerg Surg. 2016 ;11:54. PMID: 27891173 DOI: 10.1186/s13017-016-0111-4
15. Ashfaq A, Ahmadieh K, Shah AA, Chapital AB, Harold KL, Johnson DJ. The difficult gall bladder: Outcomes following laparoscopic cholecystectomy and the need for open conversion. Am J Surg. 2016 ;212(6):1261-1264. PMID: 28340928 DOI: 10.1016/j.amjsurg.2016.09.024
16. Bourgouin S, Mancini J, Monchal T, Calvary R, Bordes J, Balandraud P. How to predict difficult laparoscopic cholecystectomy? Proposal for a simple preoperative scoring system. Am J Surg. 2016 ;212(5):873-881. PMID: 27329073 DOI: 10.1016/j.amjsurg.2016.04.003
17. Kanakala V, Borowski DW, Pellen MG, Dronamraju SS, Woodcock SA, Seymour K, et al. Risk factors in laparoscopic cholecystectomy: a multivariate analysis. Int J Surg. 2011;9(4):318-323. PMID: 21333763 DOI: 10.1016/j.ijsu.2011.02.003
18. Stanisic V, Milicevic M, Kocev N, Stojanovic M, Vlaovic D, Babic I, et al. Prediction of difficulties in laparoscopic cholecystectomy on the base of routinely available parameters in a smaller regional hospital. Eur Rev Med Pharmacol Sci. 2014;18(8):1204-1211. PMID: 24817296
19. Tiong L, Oh J. Safety and efficacy of a laparoscopic cholecystectomy in the morbid and super obese patients. HPB (Oxford). 2015;17(7):600-604. PMID: 25906816 DOI: 10.1111/hpb.12415
20. Geraci G, D'Orazio B, Rizzuto S, Cajozzo M, Modica G. Videolaparoscopic cholecystectomy in patients with previous abdominal surgery. Personal experience and literature review. Clin Ter. 2017;168(6):e357-e360.PMID: 29209684 DOI: 10.7417/T.2017.2034
21. Chand P, Singh R, Singh B, Singla RL, Yadav M. Preoperative Ultrasonography as a Predictor of Difficult Laparoscopic Cholecystectomy that Requires Conversion to Open Procedure. Niger J Surg. 2015;21(2):102-105. PMID: 26425061 DOI: 10.4103/1117-6806.162573
22. Hu ASY, Menon R, Gunnarsson R, de Costa A. Risk factors for conversion of laparoscopic cholecystectomy to open surgery - A systematic literature review of 30 studies. Am J Surg. 2017;214(5):920-930. PMID: 28739121 DOI: 10.1016/j.amjsurg.2017.07.029
23. Livingston EH, Rege RV.A nationwide study of conversion from laparoscopic to open cholecystectomy. Am J Surg. 2004;188(3):205-211.
24. Ghnnam W, Malek J, Shebl E, Elbeshry T, Ibrahim A. Rate of conversion and complications of laparoscopic cholecystectomy in a tertiary care center in Saudi Arabia. Ann Saudi Med. 2010;30(2):145-148. PMID: 20220265 DOI: 10.4103/0256-4947.60521