

Laparoscopic Cholecystectomy in Cirrhotic Patients: A Retrospective Study

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Rezumat

Colecistectomia laparoscopică la pacientul cirotic: un studiu retrospectiv

Introducere: Ciroza reprezintă o cauză importantă de mortalitate și morbiditate la nivel global. Deși pacientul cu ciroză prezintă riscuri crescute în cazul intervențiilor chirurgicale, anumite afecțiuni, cum ar fi colecistita litiazică nu pot fi tratate altfel. Scopul acestui studiu este reprezentat de evaluarea parametrilor preoperatori ai pacienților cirolici cu colecistită litiazică și a unei posibile corelații între acestea și complicațiile postoperatorii estimate prin clasificarea Dindo-Clavien.

Materiale și Metode: Acesta este un studiu retrospectiv. Cazurile au fost selectate din baza de date a Departamentului de Chirurgie Generală din cadrul Institutului Clinic Fundeni, în perioada 2014-2018, utilizând ca și cuvinte cheie următoarea asocieră: „ciroza” și „colecistita”. Din 57 de cazuri inițiale au fost excluse 3 datorită rezecțiilor asociate.

Rezultate: Studiul a identificat o corelație pozitivă între clasificarea Dindo-Clavien și următoarele variabile: abordul deschis (0.405, $p=0.002$), intervenția chirurgicală de urgență (0.599, $p=0.000$), colecistita acută (.476, $p=0.000$), scorul MELD (0.291, $p=0.008$) și scorul Child (0.346, $p=0.007$), bilirubina totală (0.220, $p=0.047$), INR (0.286, $p=0.010$), prezența lichidului de ascită (0.303, $p=0.022$) și a semnelor de hipertensiune portală (0.266, $p=0.044$); de asemenea s-a identificat o corelație negativă între morbiditate și valoarea preoperatorie a hemoglobinei (-0.295 , $p=0.044$).

Concluzii: Estimarea adecvată a morbidității și mortalității perioperatorii este în general limitată de natura retrospectivă a

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majorității studiilor existente și de criteriile de selecție ale pacienților. Chirurgia de urgență, diagnosticul de colecistită acută și abordul deschis prezintă risc de morbiditate și mortalitate post-operatorii crescute.

Cuvinte cheie: ciroză, colecistită, laparoscopie, Child-Pugh, MELD

Abstract

Introduction: Cirrhosis is a leading cause of morbidity and mortality around the world. Although cirrhotic patients are considered to have a higher risk for surgical procedures than non-cirrhotic ones, there are certain pathologies such as gallstones cholecystitis that cannot be treated otherwise. The focus of this study is to evaluate the main characteristics of the patients with lithiasic cholecystitis and liver cirrhosis and to assess if there is a correlation between them and post-operative morbidity evaluated with Dindo-Clavien classification.

Material and methods: This is a retrospective study. The database from General Surgery Department of Fundeni Clinical Institute was queried between 2014-2018 using as key words "cirrhosis" and "cholecystitis". The initial interrogation revealed 57 cases out of which 3 were excluded since other resections were associated.

Results: This study identified that Dindo-Clavien classification positively correlates with the open approach (0.405, $p=0.002$), emergency surgery (0.599, $p=0.000$), acute cholecystitis (0.476, $p=0.000$), high MELD score (0.291, $p=0.008$) and Child score (0.346, $p=0.007$) and furthermore with high levels of total bilirubin (0.220, $p=0.047$), high INR (0.286, $p=0.010$), the presence of ascites (0.303, $p=0.022$) and portal hypertension (0.266, $p=0.044$). It also correlates negatively with the levels of hemoglobin (-0.295, $p=0.044$).

Conclusion: Adequate estimation of perioperative mortality and morbidity is generally limited by the retrospective nature of most studies and the patient's selection criteria. Emergency surgery, acute cholecystitis and the open approach carry the highest risk for unfavorable results of cholecystectomy in cirrhotic patients.

Key words: cirrhosis, cholecystitis, laparoscopy, Child-Pugh, MELD

Introduction

Cirrhosis is a leading cause of morbidity and mortality around the world, the annual death rate from liver cirrhosis in Europe being around 170,000 (1,2). Although cirrhotic patients are considered to have a higher surgical risk than non-cirrhotic ones, there are certain pathologies that cannot be treated otherwise. Gallstone prevalence in patients with liver cirrhosis is at least twice that in the general population, ranging between 25% and 30%, and it usually develops after a longer duration of cirrhosis (3). Therefore, cholecystectomy is the most

common surgical procedure performed on cirrhotic patients, with known complications such as perioperative bleeding, hepatic failure, kidney failure, postoperative infection, and impaired wound closure (2). Consequently, there is a consensus that only patients with symptomatic gallstones should undergo surgery (4). Laparoscopic cholecystectomy appears to be an effective and safe procedure for patients with Child-Pugh class A or B, with shorter operative time, reduced complication rates and shorter hospital stay, but there are few data regarding patients with Child-Pugh class C cirrhosis (5-7). The focus of this study is to assess the main characteristics of the

patients with lithiasic cholecystitis and cirrhosis and to evaluate if there is a correlation between some variables and postoperative morbidity evaluated with Dindo-Clavien classification.

Material and Methods

Data Source and Patient Selection

This is a retrospective study. The database from General Surgery Department, Fundeni Clinical Institute was queried between 2014-2018 using as key words "cirrhosis" and "cholecystitis". The initial interrogation revealed 57 cases out of which 3 were excluded since other resections were associated. The following parameters were evaluated: age, gender, comorbidities, the etiology of the cirrhosis, number of days to surgery and postoperative in hospital stay, ASA score, grade of urgency, the type of cholecystitis (acute or chronic), the type of approach (open or laparoscopic), if choledocholithiasis was associated, Child-Pugh score, MELD score, if dialysis is performed, presence of portal hypertension. Assessed bioumoral markers included: total bilirubin, albumin, fibrinogen, INR, aPTT, GGT, ALT, AST, Na, K, Cl, Ca, creatinine, leukocyte, hemoglobin and thrombocytes.

Statistical Analysis

The statistical analysis was performed with IBM SPSS Statistics for Windows (version 23.0, IBM, Chicago, IL) and Microsoft Excel. Continuous variables were presented as mean \pm standard deviation or median and range after checking for normality. Categorical variables were described in frequencies and percentages. Kendall's tau_b Correlation Coefficient and Spearman's Rho was used to assess correlations between different variables. For all analyses, p-values less than 0.05 were considered statistically significant.

Results

The mean age was of 58 years old with a minimum of 46 and maximum of 80 years. In what concerns the gender distribution, the

study shows that 49% of the patients were males. Only 23% had no known comorbidities, except cirrhosis.

Evaluating the etiology of the cirrhosis, the study concludes, as described in *Fig. 1*, that predominantly 41% of the cases were hepatitis C virus (VHC), followed by chronic alcohol abuse (TN) 30% and hepatitis B virus (VHB) 11%. Other causes of cirrhosis were the association between VHB and hepatitis D virus (VHD) 8%, cryptogenic 6% and in 4% of cases VHB and VHC.

Within the studied group, the ASA score varies between 2 and 4, most patients having a score of 3 (43%), while the rest are divided equally between ASA 2 and 4, each comprising 28% of the patients.

Assessment of cirrhosis severity was performed using the Child-Pugh and MELD score. 72% of patients were in class A of Child-Pugh score, 21% in Child-Pugh B and only 8% in C. The average value of the MELD score was 10.9 with a minimum of 1.05 and a maximum of 25.5.

32% of patients showed signs of portal hypertension, of which 19% associated ascites at the time of diagnosis. These patients required preoperative treatment to optimize hemodynamics and metabolic derangements. Only one patient was on dialysis and there were no patients with encephalopathy at the moment of diagnosis.

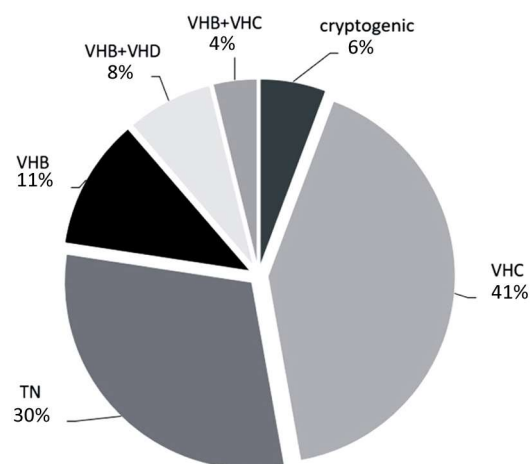


Figure 1. Percentage of cases according to cirrhosis etiology

28% of patients underwent emergency surgery, although 42% were diagnosed with a form of acute cholecystitis. The minimally invasive approach was preferred by most surgeons (72%) with a conversion rate of 7%. Only two patients (4%) associated choledocholithiasis for which endoscopic retrograde cholangiopancreatography (ERCP) with stone extraction was performed preoperatively.

Postoperative complications were evaluated using Dindo-Clavien classification. No reoperation was recorded, and 64% of patients had an uneventful course. 23% developed minor complications Dindo-Clavien 1 and 2, which were mostly conservatively managed; only two patients (4%) required percutaneous drainage of intra-abdominal collections. Five patients (2 Child B, 2 Child C and one Child A), representing 9% of the cases, died. All were diagnosed with acute cholecystitis and had other important comorbidities (neoplasia, decompensated cardiovascular diseases, etc.).

The mean preoperative number of days was 4.7 days varying between 0 and 14 days. Postoperative hospitalization was on average 7 days with a minimum of 3 and a maximum of 15 days.

Discussions

The vast majority of the studies evaluating biliary surgery in cirrhotic patients focus on lithiasic cholecystitis. The incidence of cholelithiasis in cirrhotic patients is twice as high as in patients without cirrhosis (8,9). Among the pathogenic factors responsible for lithogenesis in this particular group are implicated: hemolysis, hypersplenism, decreased concentration of bile acids, metabolic liver failure which leads to an increased unconjugated bilirubin blood level and dysregulation of gallbladder function (10). Surgery in the cirrhotic patient has always been a controversial topic, with limited indications due to increased risk of intraoperative accidents and postoperative complications. The surgical decision for cholecystectomy in cirrhotic patients should be carefully evaluated due to the risks of

liver failure and severe bleeding, especially in those with overt clinical portal hypertension syndrome. Moreover, cirrhosis is the leading cause of death after biliary tract surgery (11) with a mortality after open surgery that can reach 7-15% (12) in contrast to the mortality of normal patients of 0.5-1% (9). The mortality recorded in this study is of 9.4% within the data reported in the literature.

Initial literature data showed high rates of morbidity and mortality after laparoscopic cholecystectomy (13-15). Subsequently, a meta-analysis based on 25 previous publications established the superiority of laparoscopic approach in terms of operative time, intraoperative bleeding, and postoperative hospitalization in patients with Child A and B cirrhosis. Cirrhotic patients were more frequently treated in the emergency department (47% with acute cholecystitis compared to 17.7% in non-cirrhotic patients) and had higher morbidity rates (20.86% versus 7.99%). 28% of patients in the evaluated group underwent emergency surgery. Child C patients ought to undergo conservative treatment, or if necessary, percutaneous cholecystostomy may be considered (16). These data are consistent with the results published by Curro et al which reports a morbidity of 75% and mortality of 50% in Child C patients (17). The ASA score positively correlate with Dindo-Clavien classification and the number of postoperative days as showed in *Table 1*.

The data of a study conducted over a period of 16 years (1994-2011) indicates superior results to those previous published; they could be due, on one hand to the technological progress and the use of hemostatic materials and on the other hand to subtotal cholecystectomy performed in patients with difficult dissection and high risk of bleeding. The overall conversion rate was 4.58%, morbidity 17% and mortality 0.45% (18). This study reports a conversion rate of 7.4%, morbidity 35.8% and mortality of 9.4%.

Delis S. et al evaluated a possible correlation of Child score and MELD score with the

Table 1. Kendall's tau_b Correlation Coefficient for ASA Score

Kendall's tau_b		Post operative days	Dindo Clavien Classif.	Surgical approach	Elective/Emergency surgery	MELD	Child	Age	Albumin (g/dl)	INR	Ascites	Hb (g/dl)
ASA Score	Correlation Coefficient	.306**	.370**	.316*	.368**	.291**	.378**	.258*	-.368**	.253*	.303*	.259*
	p-value	.006	.003	.016	.005	.007	.003	.018	.006	.021	.021	.018
N					53				37	52		53

** . Correlation is significant at the 0.01 level (2-tailed)

* . Correlation is significant at the 0.05 level (2-tailed)

morbidity, identified as 19% in the study (bleeding, wound suppuration, and intra-abdominal abscess- all treated conservatively). The reported conversion rate was 5.45%. Patients who developed postoperative complications had predominantly a postoperative MELD score greater than 13. Apparently, the Child-Pugh score was not significantly correlated with the morbidity, but prospective large cohorts' studies are needed to achieve high statistical significance.

The postoperative in hospital stay, as described in *Table 2*, positively correlates with Dindo-Clavien classification, open approach emergency surgery, conversion rate, acute cholecystitis, MELD score and the level of total bilirubin, fibrinogen, leucocytes and; it also negatively correlates with the levels of albumin.

Child A and B patients are generally good candidates for laparoscopic cholecystectomy Child C patients should be converted preoperatively to Child B (10), if possible, or surgery should be avoided, and non-surgical alternatives sought.

Overt portal hypertension syndrome is an absolute contraindication for laparoscopic

cholecystectomy (19). An overdeveloped collateral venous circulation is a major problem for the biliary tract surgery in cirrhotic patients, being the most common cause of intra- and post- operative complications. Therefore, when this situation is encountered intraoperatively, most authors recommend conversion to open surgery (13,20). As for the type of approach, cholecystectomy performed in cirrhotic patients, whether open or laparoscopic becomes a difficult procedure (19,21).

In the Department of General Surgery of Fundeni Clinical Institute the preferred approach by most surgeons was laparoscopy, 71.7%, with a conversion rate of 7.4%. This is also due to the vast experience in minimally invasive surgery, being a renowned tertiary center, including minimally invasive surgery for neoplastic pathologies.

Open surgery in cirrhotic patients is associated with high morbidity rates (5-20%), even in this study it is observed a significant statistical correlation between the type of approach and postoperative complications. The main postoperative complications of open surgery are hemorrhage, decompensa-

Table 2. Kendall's tau_b Correlation Coefficient for Postoperative Days

Kendall's tau_b		Dindo Clavien Classif.	Surgical approach	Elective/Emergency surgery	Conversion	Acute /Chronic	MELD	Total Bilirubin (mg/dl)	Albumin (g/dl)	Fibrinogen (mg/dl)	Leukocytes (x10 ⁹ /ul)
Postoperative Days	Correlation Coefficient	.430**	.398*	.421**	.310*	.412**	.352**	.262**	-.247**	.208*	.216*
	p-value	.000	.001	.000	0.30	.001	.000	.008	.040	.050	.028
N			53		38		53		37	46	53

** . Correlation is significant at the 0.01 level (2-tailed)

* . Correlation is significant at the 0.05 level (2-tailed)

tion of cirrhosis with ascites and upper digestive hemorrhage, and wound infections (22). Open cholecystectomy was considered a contra-indication for this fragile group of patients. However, careful assessment of the risk factors and adequate preoperative management may extend these indications. Laparoscopic surgery has indisputable advantages over the classical approach, a fact demonstrated by the literature data (23,24). Thus, laparoscopic cholecystectomy has a better postoperative evolution, with minimal pain, early mobilization, faster resumption of the digestive tolerance and intestinal transit. Postoperative morbidity is lower, with postoperative liver failure much less frequently encountered. In addition, the absence of laparotomy greatly shortens the period of postoperative convalescence, related complications are avoided (hemorrhage, hematomas, infections, eventrations and eviscerations) and minimizes the risk of infected ascites.

With all the technical and tactical progress made over time, and with all the experience gained, laparoscopic cholecystectomy in cirrhotic patients remains one of the difficult laparoscopic surgeries (19) and it can be extremely laborious in acute or scleroatrophic cholecystitis.

Adequate estimation of perioperative mortality and morbidity is generally limited by the retrospective nature of most studies and the patient's selection criteria. The results depend on the severity of the underlying pathologies, the presence of portal hypertension, ascites, and associated comorbidities, but also on the type of approach and the degree of emergency

(25,26). Pre-operative identification and correction of pre-existing imbalances (cardiovascular and nutritional) can reduce the risks and decrease the mortality. Preoperative preparation and close monitoring to detect early complications are essential to improve the prognosis of these patients.

The type of approach should be individualized for each patient and should include a multidisciplinary team to improve the liver function and other comorbidities (27). Assessing the severity of cirrhosis using Child and MELD scores allows for a fairly accurate evaluation of perioperative mortality. The literature data shows a 30-day mortality of 10% for Child A, 30% for Child B and 76-82% for Child C, with no significant improvement over time despite the medical progress made (22,28). Regarding the MELD score, a value lower than 11 correlates with a mortality of 5-10%, 12-25 with a mortality of 25-54% and a value higher than 26 with 90% postoperative mortality (29). Emergency surgery also correlates with an unfavorable prognosis (29-31).

This study identified that Dindo-Clavien classification, as stated in *Table 3*, positively correlates with the open approach, emergency surgery, acute cholecystitis, high MELD score and Child score and furthermore with high levels of total bilirubin, high INR, with the presence of ascites and portal hypertension and low levels of hemoglobin.

Despite these difficulties, laparoscopic cholecystectomy proves to be a well-tolerated procedure in carefully selected cirrhotic patients (23,32,33).

Table 3. Kendall's tau_b Correlation Coefficient for Dindo-Clavien Classification

Kendall's tau_b		Surgical approach	Elective/ Emergency surgery	Acute /Chronic	MELD	Child	Total Bilirubin (mg/dl)	INR	Ascites	Hb (g/dl)	Portal Hypertension
Dindo Clavien Classif.	Correlation Coefficient	-.405**	.599**	.476**	.291**	.346**	.220*	.286**	.303*	-.295**	.266*
	p-value	.002	.000	.000	.008	.007	.047	.010	.022	.007	.044
	N				53			52		53	

** . Correlation is significant at the 0.01 level (2-tailed)

* . Correlation is significant at the 0.05 level (2-tailed)

Conclusion

Patients with Child A cirrhosis without portal hypertension have the same indication for elective cholecystectomy as a non-cirrhotic ones, but with increased risks. Therefore, pre-operative management should be adapted accordingly. Child B or those with portal hypertension require preoperative evaluation and liver function improvement. For Child C patients with limited life expectancy, surgery should be avoided, and non-surgical alternatives sought. Emergency surgery, acute cholecystitis and the open approach carry the highest risk for unfavorable results. Giving the retrospective nature of most studies published with small number of patients, further investigations are needed to achieve statistical significance.

Conflict of Interest

The authors declare no conflicts of interests.

Author's Contributions

Vlad-Costin Ilie and Mohammed Alabed Alhamid share first authorship.

Ethics Approval

Approval from the Review Board was obtained for using patients data in the present study and informed consent was obtained from all the patients who underwent surgery in our institution.

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