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Research Article

Laparoscopic Cholecystectomy in Cirrhotic Patients

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Abstract: The aim of this study was to value in a cohort of cirrhotic patients undergoing cholecystectomy, the safety of laparoscopic approach. In the period 2002-2012 we treated 65 patients with cirrhosis who underwent a cholecystectomy: 28 males, 37 females; mean age 58.4 years (range 27-83 y). we evaluated a in this cirrhotic group the results between laparoscopic, converted to open and open approach. The choice of the approach was made on the basis of clinical evaluation of each patient. We also compared the results with a control group of non cirrhotic patients. Statistical analysis was completed using the Student t test as appropriate. Sixty-five procedure were performed. Subdivision according Child-Pugh score was: Class A 66.2%; Class B 29.2%; Class C 4.6%. Six patients in the cirrhotic cohort underwent OC, the remainder LC with 12 converted to OC (conversion rate 20.3%). Conversion rate in non-cirrhotic group was 3.7%.No mortality in our series. In cirrhotic group in all were 17 (26.15%) blood or blood products transfusion; none in non cirrhotic group. Postoperative morbidity was 10.8% in cirrhotics, whereas was 2.46% in non cirrhotic group. The changes of LFTs between pre and postoperative control was not statistically significant in cirrhotics. The mean hospital stay with laparoscopic approach was 4.8 days vs 9.1 days in cirrhotic series. Cirrhotic patients with symptomatic cholelithiasis have increased hospital stay, operative time and postoperative morbidity with open cholecystectomy versus laparoscopic approach; therefore minimally invasive surgery should be the preferred initial choice in cirrhotics.
Keywords: Cirrhosis, Laparoscopic Cholecystectomy, Cholelithiasis, Morbidity, Liver function tests

INTRODUCTION

Cholelithiasis is twice as prevalent in patients with cirrhosis as compared with the general population with a reported incidence of 9.5% to 13.7% versus 5.2% in patients with no cirrhosis[1-6]. Moreover, cholecystectomy in cirrhotic patients is associated with a high rate of morbidity and mortality, due to blood loss, postoperative liver failure and sepsis. With the introduction of video laparoscopy in the treatment of cholelithiasis, the question as to whether cirrhotic patients will benefit from this technique is increasingly raised[7]. As surgeons gain experience and confidence in using the new equipment and techniques required by this procedure[8-10], absolute and relative contra-indications are gradually being eroded. In keeping with this scenario, the goal of this retrospective observational study is to assess the safety and usefulness of the laparoscopic approach in cirrhotic patients undergoing a cholecystectomy, including comparison with similar results in a control group of non-cirrhotic patients.

EXPERIMENTAL SECTION

We performed some 997 cholecystectomies over the last decade (precisely in the 2002-2012 period) of which 732 were laparoscopic cholecystectomies (LC) and 265 open cholecystectomies (OC). They included 65 patients with hepatic cirrhosis and symptomatic gallstone disease. There were 37 women and 28 men in the cohort, with a mean age of 58.4 years (range 27-83 years). We included in the study all cirrhotic patients undergone to cholecystectomy in the period 2002-2012. No exclusion criteria were adopted. The study regards the outcomes in this cohort of cirrhotics referred to different approach: laparoscopic, open, converted to open. The choice of the approach was made (along the whole period) on the basis of clinical evaluation of each patients. We also compared these results of the cirrhotic group with a cohort of our non cirrhotic patients undergone cholecystectomy in the period October 2011-May 2012. In the control group there were 81 non cirrhotic patients with no significant comorbidity. This cohort included 27 men and 54 women, with a mean age of 52±17 years. The indications for surgery in this group were symptomatic cholelithiasis in 60 patients, gallbladder adenoma in 2 patients, acute biliary pancreatitis in 8 patients, and acute cholecystitis in 11 patients. No significant differences in demographic data (sex, age and lithiasic pathology) emerge from the cirrhotic and control cohorts. All cholecystectomies in our department were performed using the anterograde technique (fundus first) and were followed up by a liver biopsy for histological confirmation of chronic liver disease. A subhepatic drain was kept in place in all cases. No emergency operation was performed, but all cirrhotic patients were compensated before undergoing surgery. Regarding the anesthetic techniques, all patients enrolled in our study underwent a general balanced anesthesia technique, in particular our protocol provides during the induction phase the infusion of three drugs: propofol (2 mg/Kg), cisatracurium (0.2 mg/Kg) and fentanyl (2-3 mg/Kg); manteinance phase is obtained by a bolus cisatracurium

(1/3 of the initial dose), sevoflurane inhalation and continuous infusion of remifentanil. Twenty minutes before the emergency all patients received an antalgic bolus of 0.05 mg/ kg sulfate morphine. We also compared, in cirrhotic patients, the pre- and post-operative changes (1 day before and 3 day after) in liver function tests (LFT's). All patients underwent antibiotic prophylaxis with single intravenous infusion of cefazolin 2 gr one hour before surgical incision. Statistical analysis was performed with Student T test as appropriate.

RESULTS AND DISCUSSION

Preoperative data of the patients

Demographic data, comorbidities and laboratory tests of the patients are reported in the Table 1: 38 patients (58.5%) had at least one comorbid medical condition, most commonly hypertension (35.9%), diabetes mellitus (30.8%) and cardiac disease (23.1%). Preoperative laboratory abnormalities were frequent and included hyperbilirubinaemia (>1 mg/dL) in 34 patients (52.3%), hypoalbuminaemia (<4 g/dL) in 41 (63.1%), thrombocytopaenia (<160,000/μL) in 22 (33.8%), coagulation deficit (PT <70sec) in 17 (26.1%).

Table 1 Demographic data, comorbidities, laboratory tests

Male/Female	28/37
Age (years)	58.4
Patients with ≥ 1 comorbid conditions	38
Patients with ≥ 2 comorbid conditions	14
Hypertension	14
Cardiac disease	9
Ischaemic heart disease/Cardiomyopathy	6
Dysrhythmia	2
Valve disease	3
Diabetes mellitus	12
COPD/Asthma	8
Peripheral vascular disease	1
Cerebral vascular disease	4
Other	11
Preoperative tests	
Bilirubin	
>1 mg/dl	34
>2 mg/dl	16
>10 mg/dl	1
Albumin	
<4 g/dl	41
<3.5 g/dl	20
Platelets	
<160000/μl	22
<100000/μl	9
Coagulation deficit (PT)	
<70 sec.	17
<60 sec.	10

The diagnosis of cirrhosis was determined according to clinical history and laboratory data. A diagnosis of liver cirrhosis was clearly known preoperatively only in 24 patients (36.9%). In the remaining 41 patients (63.1%), liver cirrhosis was diagnosed during hospitalization, in relation to: alcohol abuse history; previous hepatic infections; laboratory tests and ultrasound evaluation. Cirrhosis was cause by hepatitis B in 17 patients (26.1%), hepatitis C in 12 patients (18.4%), hepatitis B and C in 11 patients (16.9%), alcohol abuse in 7 patients (10.7%), hepatitis C and alcohol abuse in 2 patients (3.1%), metabolic hepatitis in 6 patients (9.2%), and CMV hepatitis in 4 patients (6.1%). As figure 1 shows, we applied the Child-Pugh classification to the cohort with the following findings: 43 patients had a Child-Pugh A score (66.2%), 19 patients a B score (29.2%), and 3 patients a C score (4.6%). In the preoperative time the 3 Child-Pugh Class C patients were medically treated and reclassified as Child-Pugh B8 because the improvement of ascites and prothrombin time.

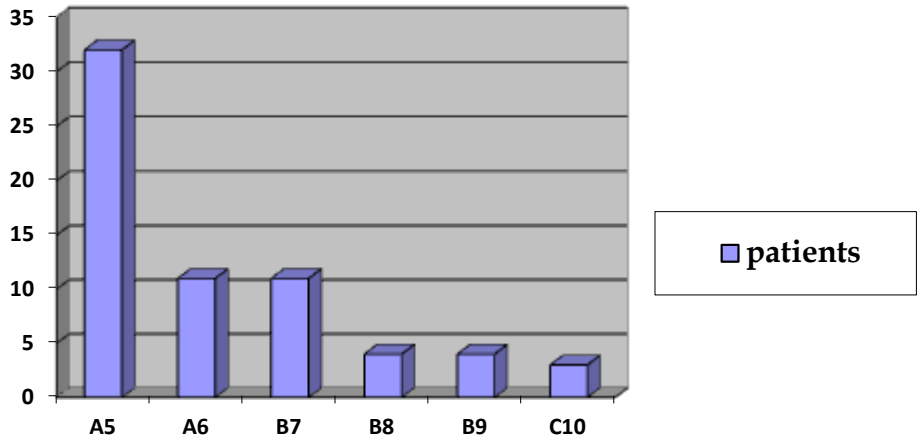

Figure 1 Patients distribution according to Child-Pugh classification grades

The diagnosis of cholelithiasis was confirmed in all patients by ultrasonography. Patients with jaundice also underwent MRI and additionally ERCP, when choledocholitiasis was confirmed. The indications for surgery were symptomatic cholelithiasis in 37 patients, acute biliary pancreatitis in 5 patients, gallbladder and common bile duct stones in 5 patients, acute cholecystitis with cholangitis in 1 patient, acute cholecystitis in 17 patients; in the case of acute cholecystitis, gallbladder hydrops were found in 3 patients, gallbladder empyema in 2 patients, perforated gangrenous cholecystitis in 3 patients.

Surgical Procedures

Six patients in the cirrhotic cohort underwent OC, the remainder LC, with 12 patients converted from LC to OC (conversion rate 20.3%). The 20.3% rate was higher than the conversion rate in non-cirrhotic patients (3.7%), due to presence of adherences in 10 patients: 3 patients had undergone previous laparotomies, 4 patients had acute cholecystitis (2 with gallbladder perforation), 2 patients had acute pancreatitis, 1 patient needed intraoperative cholangiography (difficulties due to adherences). Conversion to laparotomy was due in 2 patients to a hypertrophic left hepatic lobe. In the control group 78 patients (96.3%) underwent LC. The mean operative time in cirrhotic patients was 88.9 min in LC, 159 min in converted cholecystectomies and 141 min in OC. The mean operating time in non-cirrhotic patients was 83.4 min. Mean hospital postoperative stay in cirrhotic patients was 4.8 days in LC, 8.1 days in converted LC and 9.1 days in OC; in non-cirrhotic patients it was 3 days (Table 2). The results of the comparison between LC versus OC and LC versus OC+ converted , in the cirrhotic group, regarding both mean hospital stay and surgical time are statistically significant.

Table 2 Surgical Procedures

	CIRRHOTIC (65)					**NON CIRRHOTIC (81)**
	LC (47)	OPEN (6)	CONVERTED (12)	p value (LC vs OC)	p value (LC vs OC+conv.)	
SURGERY TIME (minutes)	88.9	141	149	0.0207	0	85
HOSPITAL STAY (days)	4.8	9.1	8.1	0,0004	0,0008	3.2
CONVERSION RATE	20.34%					3 (3.7%)

$p < 0.05$; CI 95%

Perioperative transfusions

None of the control group patients required transfusion whereas 17 patients in the cirrhotic group (26.1%) required blood product transfusion in perioperative time as follows: intraoperative platelet transfusion (2 pts.); intraoperative blood and plasma transfusion and postoperative blood transfusion (1 pt.); intraoperative platelet transfusion and postoperative plasma and platelet transfusion (5 pt.); intraoperative platelet transfusion and postoperative blood and plasma

transfusion (1 pt.); intraoperative and postoperative plasma transfusion (3 pt.); intraoperative blood transfusion and postoperative platelet transfusion (1 pt.); intraoperative blood transfusion and postoperative blood and platelet transfusion (1 pt.); postoperative platelet transfusion (2 pts.); 1 patient required postoperative blood and platelet transfusion (Table 3). The need for transfusion correlated with both the Child-Pugh classification (Figure 2) and with the type of cholecystectomy approach (Figure 3) was evaluated. The latter figure provides a clear visual illustration of the percentage differences in blood required between open and minimally invasive procedures: LC 19.1% - LC converted 50% - OC 33.3%. The results of the comparison between LC versus OC and LC versus OC+ converted, in the cirrhotic group, regarding blood and blood products transfusions in perioperative time are not statistically significant.

Table 3 Perioperative transfusions

	CIRRHOTIC (65)					**NON CIRRHOTIC (81)**
	LC (47)	OPEN (6)	CONVERTED (12)	p value (LC vs OC)	p value (LC vs OC+Conv.)	
BLOOD TRANSFUSION IN PERI-OPERATIVE TIME	2 (4.2%)	1 (16.6%)	2 (16.6%)	0.87	0.32	-
BLOOD PRODUCTS TRASFUSION IN PERI-OPERATIVE TIME	7 (14.9%)	1 (16.6%)	4 (33.3%)			-

$p < 0.05$; CI 95%

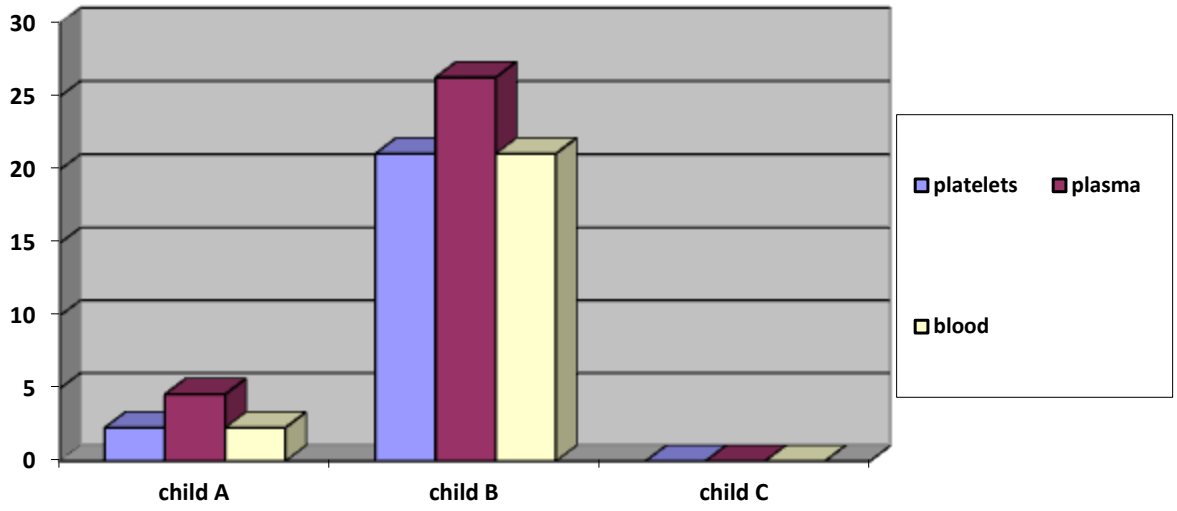

Figure 2 Correlations between transfusion and Child-Pugh Classification (%)

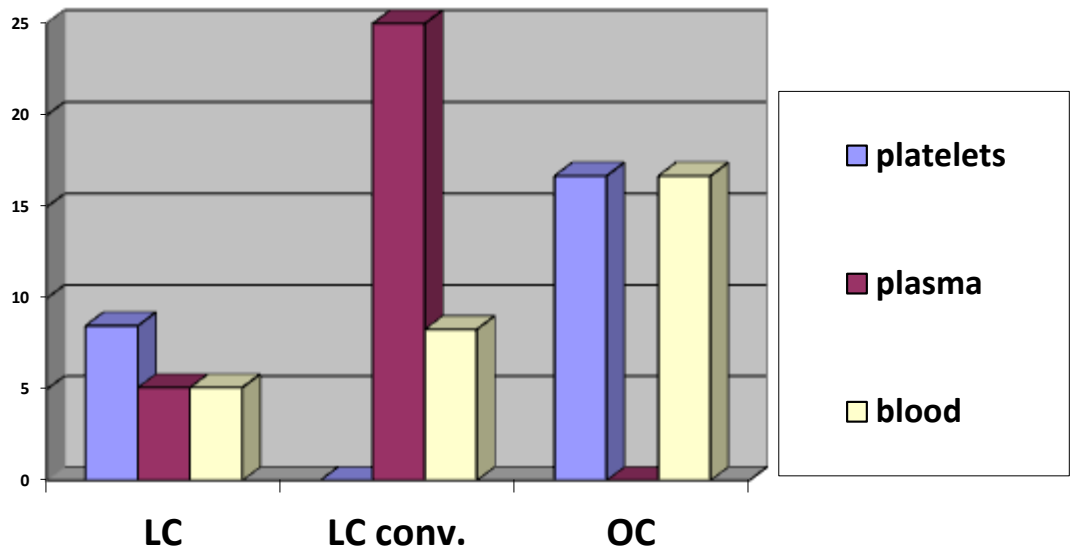

Figure 3 Correlation between type of cholecyctectomy and transfusion (%)

Postoperative morbidity

No postoperative morbidity was observed in non-cirrhotic patients, but was present in 7 cirrhotic patients (10.8%) as follows: presence of blood in drainage (treated only with blood transfusion and medical therapy) (1 pt.); haemoperitoneum (emergency laparotomy showed bleeding from umbilical vein) (1 pt.); pleural effusion (2 pts.); pulmonary infections (1 pt.); acute atrial fibrillation (1 pt.); thrombocytopenia (1 pt.). No operative mortality or intraoperative complications arose in either group. Four cirrhotic patients (8.51%) had postoperative hernia through the umbilical port-site, which appeared some months after laparoscopic cholecystectomy (Table 4). Regarding the global morbidity there are not statistically significant results between LC versus OC; on the contrary the results are statistically significant in the comparison between LC versus OC+ converted.

Table 4 Postoperative morbidity

	CIRRHOTIC (65)					**NON CIRRHOTIC (81)**
	LC (47)	OC (6)	CONVERTED (12)	p value	p value	
EMOPERITONEUM	1 (2.12%)	-	-	(LC vs OC+Conv.)	(LC vs OC)	-
REINTERVENTION	1 (2.12%)	-	-			
PLEURAL EFFUSION	-	-	2 (16.6%)			-
PULMONARY INFECTIONS	-	-	1 (8.33%)			-
TROMBOCYTOPENIA	-	-	1 (8.33%)	0.0459	0.5289	-
ATRIAL FIBRILLATION	-	-	1 (8.33%)			-
MORTALITY	-	-	-			-
LATE INCISIONAL HERNIA ON UMBILICAL PORT SITE	4 (8.51%)	-	-			2 (2.46%)

$p < 0.05$; CI 95%

We also assessed postoperative deterioration in LFT's in cirrhotic patients, comparing total bilirubin, transaminase (AST, ALT), alkaline phosphatase, γ-gt and prothrombin time (PT) levels one day before surgery with those three days after surgery. We used the Kolmogorov-Smirnov test to compare levels before and

after surgery with the following results: total bilirubin p=0.790; AST p=0.437; ALT p=0.790; alkaline phosphatase p=0.010; γ-gt p=0.189; PT p=0.169. These results are not significant, leading to the conclusion that laparoscopic cholecystectomy in cirrhotic patients does not appear to impair LFT's.

Gallstones are twice as prevalent in patients with cirrhosis as in the general population. Factors implicated are hypersplenism, increased levels of oestrogen, and increased intravascular haemolysis with a reduction in gallbladder emptying and motility. Moreover, increased morbidity associated with symptomatic gallstone disease occurs in cirrhotic patients[3,11-14]. Increased morbidity associated with symptomatic gallbladder disease occurs in cirrhotic patients, with various reports alerting us to the potential morbidity (12.2-23.6%) and mortality (7.5-25.5%) associated with cholecystectomy in cirrhotic patients. In addition, intraoperative transfusion rates ranging from 42.6% to 61.9% have been reported as has the suggestion that the greater the severity of the cirrhosis, the greater the potential for complications[2,3,8,15-17].

The increased risk of bleeding in cirrhotic patients is related to reduced prothrombin time, thrombocytopaenia, and portal hypertension. Patients with less than 50000/mm^3 platelets need to be prepared with platelet infusion, while those with abnormal prothrombin time require fresh frozen plasma[1,18]. In our experience we had global major blood products transfusions in cirrhotic group (26.1% vs none) compared to non cirrhotics in the perioperative period. In the perioperative time, in 12 patients we employed blood products transfusion for treatment and correction of coagulophaty related to abnormal prothrombin time and thrombocytopenia. On the contrary, in 4 patients it was necessary perioperative blood transfusion for compensation of intraoperative blood loss. In the postoperative time we had emergency blood transfusions in 2 patients with emoperitoneum: one patient undergone to reintervention, another treated with conservative therapy and blood transfusions. The blood and blood products transfusion show a correlation with Child-Pugh score and above all with access choiced for intervention. Among the Child A patients 9.3% (4/43) had transfusions, whereas in the Child B patients 59,1% (13/22) required blood or blood products transfusions. In the Child B group are included 3 Child C patients reclassified due to improvement of liver function. The still needed transfusions in perioperative time. In evidence the percentage differences in blood, frozen plasma, platelets transfusions required between miniinvasive approach (19.1%) versus open (33.3%) but the in our experience the results the statistical study are not significant. In this study the morbidity rate in cirrhotic patients was 10.8%. The main complications were postoperative bleedings (3%), there was also pleural effusion, pulmonary infection and incisional hernia in ombelical port-site (8.51%). Our study shows different results between open and laparoscopic approach. With the miniinvasive procedure, minor surgery time and hospital stay are statistically significant. The results of the comparison regarding the postoperative morbidity are stastically significant between LC vs OC + converted. Our results are overlappable with those reported in the literature. From the literature data the comparison with open approach shows that laparoscopic procedure was associated with fewer postoperative complications, shorten hospital stay and quicker resumption of a normal diet[19-22]. The increased risk for postoperative liver failure can be potentially explained by the anaesthetic agent's action, which is known to decrease hepatic arterial blood flow. This hepatic ischemia can be the cause of the release of inflammatory mediators leading to multisystem organ failure. Cirrhotic patients' ability to compensate for this ischaemia is impaired with the result that hepatic dysfunction can develop postoperatively[23,24]. There are some points of interested in cirrhotic patients regarding the anesthetic techniques: it's important to guarantee a deep myoresolution in order to allow low insufflation pressure for pneumoperitoneum (under 12 mmHg), for this reason we use invasive blood pressure monitoring to evaluate the hemodynamic impact of pneumoperitoneum; furthermore in cirrhotic patients , with altered hepatic function, it's useful give drugs with extrahepatic metabolism such as cisatracurium; last point regards the postoperative pain management: nonsteroidal anti-inflammatory drugs should be avoided to avert renal failure and to minimize haemorragic risk, and opiates should be used sparingly, with low and infrequent dosing, to prevent encephalopathy[25] and postoperative opiod respiratory depression. The are also increased risk of infections which also directly correlated with Child-Pugh score. In our study the postoperative infections had little incidence: only 1 patient with pulmonary infection. Considerable postoperative complication in cirrhotics is the ascites[21,26]: several cases are postulated such as leakage of lymphatic vessels interrupted, gallbladder bed lymphatics. This morbidity was absent in our series. The deterioration of liver function is a know postoperative complication in cirrhotics. In our experience the postoperative changes of LFTs with laparoscopic approach were not significant. Identification and correction of reversible altered liver functions by meticulous preoperative definition of aetiology, severity and therapeutic action is the goal before the surgical procedures to prevent severe complications[24]. The mechanisms underlying the advantages of laparoscopic approach can be identified in the minimally invasive technique which means less surgical exposure and dissection. The intraoperative blood loss and duration of surgery are smaller and less hepatic impairment. Minimally invasive approach with the vision is magnified and it reduces the risk of liver injury. Also important to minimize the impairment of liver function is the use of low insufflations pressure for pneumoperitoneum (12 mmHg). In fact, in our

experience with low pressure for pneumoperitoneum, the changes of LFTs in the pre and postoperative time are limited and not statistically significant. Cirrhotic patients may have a gallbladder with a significant intrahepatic component due to the atrophy of the right hepatic lobe and, in addition, a hypertrophic left lobe which sometimes obscures the visual field of the telescope. Further difficulties sometimes arise when inflammatory changes, such as scarring in the *porta hepatis* and hypertrophy of the gallbladder wall, occur, and when adhesions to the omentum and/or intestine are present[8]. In recent reports, the rate of conversion to an open procedure is noted as 0% to 15.7%. Conversion should not be considered as a sign of failure but rather as a means of preventing against more serious complications. Absolute indications for conversion are poorly-controlled laparoscopic bleeding and inability to define the anatomy. A subhepatic drain is used to monitor postoperative bleeding, and is usually removed within 24 to 48 h [1,27]. In a nutshell, when compared with OC, the LC technique is a less invasive procedure, potentially associated with less intraoperative blood loss, less postoperative pain, and more rapid discharge. Cirrhotic patients would appear to benefit from a minimally invasive procedure and from the avoidance of excessive intraoperative bleeding which would prolong operating times and perioperative morbidity[28]. In addition, operating times and length of hospital stay in cirrhotic patients are significantly reduced in LC as compared with OC[28]. Wound-related complications, such as wound infection dehiscence and postoperative hernia, are also significantly reduced in LC in patients with ascites[1].

CONCLUSION

Cirrhotic patients with symptomatic cholelithiasis have increased hospital stay, operative times and postoperative morbidity in open cholecystectomy as compared with the laparoscopic approach. Thus, minimally invasive surgery should be the preferred initial choice in compensated cirrhotic patients with cholelithiasis. Operative intervention for symptomatic cholelithiasis is indicated for Child-Pugh A or B patients before liver function deteriorates to Class C and before emergency intervention becomes necessary[8,15]. Some patients with cirrhosis may be candidates for liver transplantation in the future. Laparoscopic cholecystectomy offers the chance of fewer right upper quadrant postoperative adherences, which may be useful during liver transplantation[1]. In our experience, laparoscopic cholecystectomy morbidity in cirrhotic patients is slightly increased compared to non-cirrhotic patients. The advantages of laparoscopic cholecystectomy in cirrhotic patients are decreases in postoperative infections, haemorrhaging, transfusion rates, liver failure and mortality rates. Minimally-invasive surgery should be the preferred initial choice in compensated cirrhotic patients with cholelithiasis.

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