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ORIGINAL ARTICLE

Laparoscopic cholecystectomy is the preferred approach in cirrhosis: a nationwide, population-based study

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Abstract

Background/aim: To assess the impact of open versus laparoscopic surgery in cirrhotic patients undergoing a cholecystectomy using the Nationwide Inpatient Sample (NIS).

Methods: All patients with cirrhosis who underwent a cholecystectomy (open or laparoscopic) between 2003 and 2006 were queried from the NIS. Associated complications including infection, transfusion, reoperation, liver failure and mortality were determined.

Results: A total of 3240 patients with cirrhosis underwent a cholecystectomy: 383 patients underwent an open cholecystectomy (OC) whereas 2857 patients underwent a laparoscopic cholecystectomy (LC), which included 412 patients converted (LCC) from a LC to an OC. Post-operative infection was higher in OC as opposed to a laparoscopic cholecystectomy (TLC) or LCC (3.5% versus 0.7% versus 0.2%, $P <$ 0.0001). The need for a blood transfusion was significantly higher in the OC and LCC groups as compared with the TLC group (19.2% versus 14.4% versus 6.2%, $P < 0.0001$). Reoperation was more frequent after OC or LCC versus TLC (1.5% versus 2.5% versus 0.8%, $P = 0.007$). In-hospital mortality was higher after OC as compared with TLC and LCC (8.3% versus 1.3% versus 1.4%, $P < 0.0001$).

Conclusion: Patients with cirrhosis have increased in-hospital morbidity and mortality after an open as opposed to a laparoscopic or conversion to an open cholecystectomy. LC should be the preferred initial approach in cirrhotic patients.

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Introduction

A laparoscopic cholecystectomy (LC) is the standard approach in treating benign gallbladder diseases. The advantages of LC over an open cholecystectomy (OC) are well established and documented. More than 700 000 operations are performed each year with satisfactory results.[1] While LC has become the standard treatment for symptomatic cholelithiasis, it is not always the first choice undertaken by surgeons in cirrhotic patients with calculus biliary tract disease. The incidence of gallbladder disease in cirrhotic patients is more than double that for non-cirrhotic adults.[2–10] As the number of cirrhosis cases in the US is on the rise, more biliary tract operations in cirrhosis patients will be performed.[3–6,9,10] Therefore, a verified and uniform approach to the selection of treatment modalities in this group of patients must be established. This will undoubtedly lead to a better understanding and reduction of complications seen in cirrhosis patients.

The definitive treatment of decompensated cirrhosis is liver transplantation. While the number of donors remains limited, the number of patients living with cirrhosis continues to increase. This trend will lead to an increase in co-morbid conditions including biliary tract disease.[11] Factors implicated in the higher incidence of gallstone formation include hypersplenism, increased levels of oestrogen, and increased intravascular haemolysis with a reduction in gallbladder emptying and motility.[10]

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Surgical literature throughout the 1980s has uniformly reported discouraging results when biliary surgery was attempted on cirrhotic patients.[3,4,8,9,12,13] In 1992, the National Institute of Health (NIH) consensus statement on LC defined those with end-stage cirrhosis with portal hypertension to be poor candidates for LC.[14] Surgeons were reluctant to attempt LC in patients with cirrhosis owing to its perceived complications and practical inexperience with LC. Since then, multiple authors have identified and reported advantages of LC over OC in this particular group of patients, leading the way for a more regular use of this minimally invasive procedure. Still, no uniform consensus has been established in studies and in the surgical community in reference to the procedure selection in cirrhotic patients.

The purpose of this study was to assess the impact of surgical approach selection in cirrhotic patients undergoing a cholecystectomy on the outcome using the Nationwide Inpatient Sample (NIS). This is the largest population-based and geographically representative all-payer database of hospital discharges in the US.

Methods

Data source

This retrospective cohort study examined the outcomes of a cholecystectomy in cirrhosis patients using discharge data from the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), and Agency for Healthcare Research and Quality. The NIS is the largest all-payer inpatient care database in the US, which contains about 20% of stratified samples of U.S. community hospitals. The stratification is based on five hospital characteristics: geographical region (Northeast, Midwest, West and South), control [government non-Federal (public), private not for profit (voluntary) and private investor-owned (proprietary)], location (urban or rural), teaching status (teaching or non-teaching) and bed size (small, medium and large). It contains data from about 8 million hospital stays each year.

Diseases and procedures of interest

The population of interest was all adult patients (age ≥18 years) with cirrhosis who underwent a cholecystectomy (OC or LC) between 2003 and 2006. The disease status and procedures were categorized according to the *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM).

Groups with ICD-9-CM codes

All patients with a primary diagnosis of calculus of the gallbladder (ICD-9-CM codes: 574.00, 574.01, 574.10, 574.11, 574.20, 574.21) and a primary procedure of an OC (ICD-9-CM codes: 51.22) or LC (ICD-9-CM codes: 51.23), with the secondary diagnosis of cirrhosis (ICD-9-CM codes: 571.2, 571.5, 571.6) were included in this study. Some patients with a LC had conversion to an OC (ICD-9-CM codes: v64.4, v64.41). A summary of the ICD-9-CM codes used is summarized in Table 1.

Table 1 ICD-9 codes used in this study

Calculus of gallbladder	574.00, 574.01, 574.10, 574.11, 574.20, 574.21
Cirrhosis	571.2, 571.5, 571.6
Laparoscopic cholecystectomy	51.23
<< conversion to open >>	V64.4, V64.41
Open cholecystectomy	51.22
Postoperative infection	998.1, 998.59, 682.2, 567.22
PRBCs blood transfusion	99.03, 99.04
Post-operative haemorrhage	998.1, 998.11, 998.12
Reoperation	54.12, 39.98
Liver failure	570, 572.2, 572.4
Ascites	789.5
Portal hypertension	456.0, 456.1, 456.20, 456.22, 572.3

Outcome variables

The primary outcome for this study was in-hospital mortality. The post-operative complications were also outcomes of interest, including: post-operative infection (ICD-9-CM codes: 998.1, 998.59, 682.2, 567.22), ascites (ICD-9-CM codes: 789.5), packed red blood cells transfusion (ICD-9-CM codes: 99.03, 99.04), post-operative haemorrhage (ICD-9-CM codes:998.1, 998.11, 998.12), reoperation (ICD-9-CM codes: 54.12, 39.98) and liver failure (ICD-9-CM codes: 570, 572.2, 572.4).

Statistical analysis

The weighted number of procedures and rates were calculated to take into consideration the stratified sampling design of NIS data. Patient characteristics were summarized using means, standard deviations (SDs), frequencies and percentages. Wilcoxon's rank sum test was used to compare the age distributions between the groups. The Rao–Scott chi-square test was used to compare discrete variables between or among groups. Multiple logistic regression models were used to assess the association between types of procedures and in-hospital mortality while controlling for potential confounding variables. The analyses were conducted using the R language with a 'survey' package.[15–17]

Results

Operative procedures

Three hundred and eighty-three of the 3240 cholecystectomies were planned OCs. Of the 2857 LCs, 412 (14.4%) were converted to open (LCC) and 2445 were laparoscopic (TLC). These data are summarized in Fig. 1.

Demographic data

Demographic information is shown in Table 2. There were no significant differences between the groups studied with respect to age, race and insurance status. Females were more likely to have TLCs than LCCs or OCs.

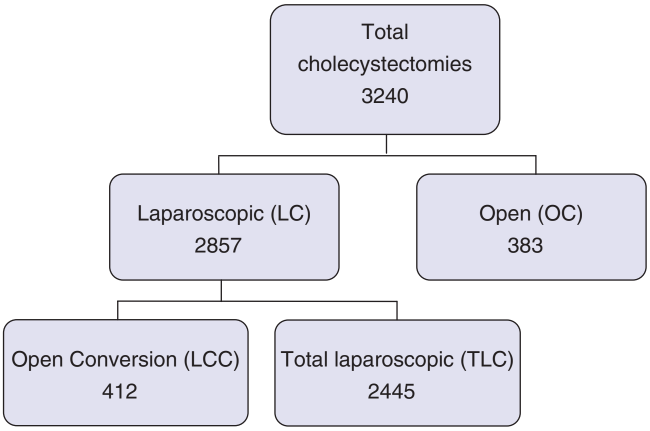

Figure 1 Operative procedures

Complications analysed based on the intent to treat

Post-operative infections were significantly higher in the OC group compared with the LC patients (3.5% versus 0.6%; $P <$ 0.0001, respectively) (Table 3). Post-operative haemorrhage was higher in the OC patients compared with the LC patients (6.6% versus 3.9%; $P = 0.01$, respectively) as was the number of packed red blood cell (PRBC) transfusions in the OC as compared with the LC patients (19.2% versus 7.4%; $P < 0.0001$, respectively). There was no difference in the re-operation rate of the OC as compared with the LC patients ($P = 0.431$). Liver failure was significantly higher in the OC group compared with the LC patients (7.0% versus 1.4%; $P < 0.0001$, respectively).

Complications based on actual operations

Post-operative infection was significantly higher in the OC group compared with TLC and LCC patients (3.5% versus 0.7% versus 0.2%; $P < 0.0001$, respectively) (Table 3). Post-operative hemorrhage was higher in the OC and LCC patients compared with the TLC group (6.6% versus 9.4% versus 3.0%; $P < 0.0001$, respectively). A PRBC transfusion was given more often in OC and LCC patients compared with the TLC group (19.2% versus 14.4% versus 6.2%; $P < 0.0001$, respectively). The reoperation rate was higher in the OC and LCC patients compared with the TLC group (1.5% versus 2.5% versus 0.8%; $P = 0.007$, respectively). The liver failure rate was significantly higher in the OC group compared with TLC and LCC patients (7.0% versus 1.4% versus 1.4%; $P <$ 0.0001, respectively).

Mortality

Mortality was significantly higher in the OC group compared with the LC (TLC and LCC) group (8.3% versus 1.3%; $P < 0.0001$) (Table 3). After controlling for potential confounding factors which were significantly different between the OC and LC groups at the 0.1 level of significance, the LC group had a significantly lower chance of mortality as compared with the OC group [adjusted odds ratio (OR): 0.202, 95% confidence interval (CI): (0.121, 0.339), $P < 0.0001$]. While controlling the same factors, both LC groups (TLC and LCC) had significantly lower mortality as compared with the OC group [TLC: adjusted OR: 0.202, 95% CI: (0.118, 0.345), $P < 0.0001$; LCC: adjusted OR: 0.203, 95% CI: (0.079, 0.527), $P = 0.001$]. There was no difference in the mortality rate when comparing the LCC group with the TLC group [adjusted OR: 1.006, 95% CI: (0.393, 2.577)].

Discussion

This retrospective analysis of a large dataset supports the laparoscopic approach for cholecystectomy in cirrhotic patients. While this hypothesis would optimally be tested with a prospective randomized trial no such study has been undertaken. One meta-analysis found only three prospective trials with a total of 220 patients.[5,18,19] Although the power of the study was low, the conclusion supports the concept that a laparoscopy should be the initial approach. Similarly, a previous meta-analysis study also used a limited group of cirrhotic patients undergoing LC to deduct parallel results.[20] Multiple retrospective studies also compare well to our findings.[20–23] This study provides an update to previous articles, while broadening the evidence pool using a large dataset.

Our study identified several major advantages of LC over OC, some of which have been documented in previous articles. Even patients who had to be converted (LCC) to an open cholecystectomy, had lower infection, transfusion and liver failure rates and comparable reoperation rates to the OC group. Moreover, including the LCC in the LC group (intent-to-treat) did not increase the risk of operation that was seen in the OC group. One possible explanation is that the dissection done during LC may decrease the amount of time spent during the open part of the procedure below the operative time of OC. We suspect that the total open operative has a direct impact on the complication rate of the operative procedure.

It should be noted that mortality rates in cirrhotic patients who had abdominal surgery have declined in the 2000s, presumably as a result of improved medical management and critical care.[6] Overall, the complication rate inferred in this study is much lower than when OC is the initial approach. A large retrospective study analysing admissions for acute cholecystitis (AC) using the NIS data for all patients, identified an overall mortality rate of 0.5% for LC and 4% for OC. This study demonstrated an increased mortality for patients undergoing OC over LC (8.3% and 1.3%, respectively). This can be attributed to the medically complex patient population that has been evaluated in this study. Importantly, this study demonstrates a six-fold increase in mortality rate when OC is compared with LC. While there may be some pre-selection bias, it is difficult to explain such a morbid outcome on this basis alone. Even more remarkable is a similarly low mortality rate noted in LCC when compared with LC.

Indications for conversion include massive adhesions, inability to define the anatomy and bleeding not readily controlled laparoscopically.[24,25] Common bile duct exploration and suspected bile

Table 2 Demographic data

Characteristics	OC	LC			Comparisons *P*-value	
		TLC & LCC	TLC	LCC	OC versus TLC & LCC	OC versus TLC versus LCC
No. of procedures	383	2857	2445	412		
Weighted no. of procedures	1852	13809	11794	2015		
Age (mean ± SD)	62.6 ± 14.5	61.3 ± 13.6	61.4 ± 13.6	60.8 ± 13.0	0.134	0.155
Female[a]	897 (48.4%)	6984 (50.6%)	6105 (51.8%)	879 (43.6%)	0.422	0.006
Race[b]					0.949	0.842
White	889 (68.1%)	7203 (67.8%)	6114 (67.5%)	1089 (69.5%)		
Black	120 (9.2%)	1020 (9.6%)	869 (9.6%)	151 (9.6%)		
Hispanic	226 (17.3%)	1853 (17.4%)	1589 (17.5%)	264 (16.8%)		
Asian or Pacific Islander	32 (2.4%)	221 (2.1%)	182 (2.0%)	39 (2.5%)		
Native American	5 (0.4%)	105 (1.0%)	105 (1.2%)	0 (0%)		
Other	33 (2.5%)	225 (2.1%)	200 (2.2%)	25 (1.6%)		
Insurance status[c]					0.325	0.536
Medicare	983 (53.1%)	7076 (51.3%)	6080 (51.6%)	996 (49.5%)		
Medicaid	295 (15.9%)	1755 (12.7%)	1509 (12.8%)	246 (12.2%)		
Private including HMO	439 (23.7%)	3743 (27.1%)	3154 (26.8%)	589 (29.3%)		
Self-pay	69 (3.7%)	702 (5.1%)	613 (5.2%)	89 (4.4%)		
No charge	9 (0.5%)	102 (0.7%)	89 (0.8%)	13 (0.6%)		
Other	56 (3.0%)	414 (3.0%)	336 (2.9%)	77 (3.9%)		
Teaching status[d]	741 (40.4%)	4481 (32.5%)	3654 (31.1%)	827 (41.2%)	0.006	<0.0001
Diabetes mellitus[e]	489 (27.0%)	4097 (30.0%)	3499 (30.0%)	598 (30.2%)	0.244	0.501
Hypertension[e]	701 (38.7%)	6293 (46.0%)	5445 (46.6%)	848 (42.7%)	0.009	0.010
Alcohol abuse[e]	320 (17.6%)	1998 (14.6%)	1650 (14.1%)	348 (17.5%)	0.123	0.063
Congestive heart failure[e]	284 (15.7%)	1426 (10.4%)	1262 (10.8%)	164 (8.3%)	0.002	0.002
Chronic pulmonary disease[e]	378 (20.9%)	2302 (16.8%)	1957 (16.7%)	345 (17.4%)	0.057	0.148
Coagulopathy[e]	391 (21.6%)	1788 (13.1%)	1554 (13.3%)	234 (11.8%)	<0.0001	<0.0001
Fluid and electrolyte disorders[e]	507 (28.0%)	2259 (16.5%)	1924 (16.5%)	335 (16.9%)	<0.0001	<0.0001
Obesity[e]	113 (6.2%)	1360 (9.9%)	1130 (9.7%)	230 (11.6%)	0.028	0.039
Renal failure[e]	141 (7.8%)	798 (5.8%)	718 (6.1%)	80 (4.0%)	0.147	0.091
Deficiency anaemias[e]	255 (14.1%)	1237 (9.0%)	1022 (8.7%)	215 (10.8%)	0.003	0.004
Hypothyroidism[e]	129 (7.1%)	1174 (8.6%)	1005 (8.6%)	168 (8.5%)	0.320	0.628

[a]One patient in TLC did not have gender information.
[b]RACE: In the data, 756 out of 3240 patients (23.3%) did not have record. The comparisons among the groups were based on the available records.
[c]Insurance status: four patients did not have the records.
[d]Hospital teaching status: seven patients did not have records of hospital teaching status.
[e]Thirty-seven patients did not have the records of comorbidities.
OC, open cholecystectomy; LC, laparoscopic cholecystectomy; LCC, open conversion; TLC, total laparoscopic; HMO, Health Maintenance Organization.

duct injury are other factors commonly leading to OC conversion.[24,25] The conversion rate of 14%, documented from the NIS data, is much higher when compared with the majority of the studies addressing this subject.[5,10,18,19,26–36] Surgical publications are often permeated with findings that reflect well on the author/surgeon who has performed the procedures in question. Rarely are mediocre results published, possibly contributing to an exaggerated and often misleading results. The NIS data sample gathers above and below par performances, closely reflecting the true national level.

An analysis of 1.4 million patients who underwent a cholecystectomy for AC,[23] revealed a decreased conversion rate from 14% in 2000 to 11% in 2005. This conversion rate in the cirrhotic patients was similar to the AC population. While the conversion rate for LC in cirrhotic patients may invariably remain higher than non-cirrhotic patients, it would be hoped that through a more widespread use of LC in this patient population, a steady decline in the conversion rate would be seen.

This study identified only 89 (0.6%) post-operative infections in patients who initially underwent a LC or were eventually

Table 3 Complications

Outcomes	OC	LC			Comparisons *P-value*	
		TLC & LCC	TLC	LCC	OC versus TLC & LCC	OC versus TLC versus LCC
Weighted no. of procedures	1852	13809	11794	2015		
Post-operative infection	66 (3.5%)	89 (0.6%)	84 (0.7%)	5 (0.2%)	<0.0001	<0.0001
Post-operative haemorrhage	122 (6.6%)	537 (3.9%)	348 (3.0%)	189 (9.4%)	0.01	<0.0001
PRBCs transfusion	355 (19.2%)	1023 (7.4%)	733 (6.2%)	290 (14.4%)	<0.0001	<0.0001
Reoperation	27 (1.5%)	141 (1.0%)	91 (0.8%)	50 (2.5%)	0.431	0.007
Liver failure	129 (7.0%)	197 (1.4%)	168 (1.4%)	29 (1.4%)	<0.0001	<0.0001
Ascites	333 (18.0%)	1339 (9.7%)	1108 (9.4%)	231 (11.5%)	<0.0001	<0.0001
Mortality[a]	153 (8.3%)	185 (1.3%)	160 (1.4%)	25 (1.3%)	<0.0001	<0.0001

[a]Four patients did not have the data for mortality.
OC, open cholecystectomy; LC, laparoscopic cholecystectomy; LCC, open conversion; TLC, total laparoscopic; PRBC, packed red blood cell.

converted to OC, whereas a rate of 3.7% is noted in the group that had OC as the initial approach. These data are consistent with post-operative infection rates identified in other studies. Puggioni *et al*. analysed 17 publications from 1993 to 2001, and found 0% and 0.13% infection rates in LC versus OC, respectively.[20] The overall increase in infection rates when compared with Puggioni's results could be attributed to the steady increase in infection rates over time in all surgical subspecialties. Also, it cannot be excluded that the meta-analysis was performed on published 'favourable' results. A more recent prospective study would have to be performed in order to extract sensible comparisons.

Studies from the pre-laparoscopic era have emphasized the association between transfusion requirements and mortality[8,9] and advised against a cholecystectomy in cirrhotic patients. In a small but carefully controlled randomized study, laparoscopic surgery was been shown to reduce blood loss and eliminate transfusion requirements in cirrhotic patients undergoing a cholecystectomy.[37] In a subsequent and larger retrospective study,[33] a LC was safely done in 23 of 26 patients for a conversion rate of 12%. Two of the three converted patients had to have open surgery because of uncontrolled bleeding in the bed of the liver. In spite of these two patients, the 26 patients who were in the LC group had a shorter length of hospital stay, less operative blood loss (no transfusion requirements) and less wound problems as compared with the OC group.

There are a number of limitations in this study as a consequence of using an administrative database. It could not determined whether the portal hypertension was present pre- or post-operatively. If present pre-operatively, it may have influenced the surgical approach. One of the main outcomes was in-hospital mortality. The database does not allow patients to be followed after discharge, and a longer follow-up post-discharge may have led to higher mortality rates. This database does not record the length of operative time. In addition it does not stratify if elective or emergent cases were initially performed laparoscopically and their conversion rates. The patient selection was likely affected by presentation of biliary tract disease (acute versus chronic) and degree of compensated versus uncompensated cirrhosis or Child–Turcotte–Pugh and model for end-stage liver disease (MELD) score. Furthermore, the database does not allow the correlation of complication rates with Child–Pugh classification or the MELD score.[9,26,27,34]

In summary, this study analysed the outcomes of operative therapy for biliary tract disease in cirrhosis patients in the United States. This study suggests that LC is well tolerated in cirrhotic patients. The advantages of LC are: decreased post-operative infection, haemorrhage, transfusion rate, liver failure and mortality rates. Smaller studies have shown similar results in support of our conclusions.[5,18,19,25,31,38] Based on the results of this study, the use of OC as the first-line therapy for cirrhosis patients should be questioned. Given the comparable outcomes between the LC and LCC as opposed to OC, the laparoscopic approach should be the preferred initial approach in cirrhotic patients requiring a cholecystectomy. With continuous improvement in the field of minimally invasive surgery, more patients with cirrhosis will benefit from the laparoscopic approach for the treatment of symptomatic biliary tract disease.

Conflicts of interest

None declared.

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