Original Article

Laparoscopic Colorectal Surgery for Cirrhotic Patients

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Key Words
Colorectal cancer;
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Purpose. In Taiwan, colorectal cancer is the third leading cause of cancer death and the prevalence of liver cirrhosis is high. Cirrhotic patients have higher surgical morbidity and mortality, especially in colon and rectal surgery. This study reports our experience of minimally invasive surgery for colorectal cancer patients with liver cirrhosis.
Methods. Patient demographics, pre-operative laboratory data, operative data, peri-operative data, and postoperative morbidity and mortality of patients with liver cirrhosis who underwent minimally invasive surgery for colorectal cancer between January 2004 and December 2016 were retrospectively reviewed and analyzed.
Results. Twenty-six patients were included. There were 21 male and five female patients. The mean age was 67.9 ± 10.8 years, and the mean body mass index was 24.4 ± 3.3 kg/m^2. The causes of hepatitis were hepatitis B virus in 14 patients, hepatitis C virus in five, alcoholic hepatitis in two, and nonalcoholic steatohepatitis in five. Twenty-two patients (84.6%) were Child-Pugh class A and four (15.4%) were Child-Pugh class B. The mean operative time was 260 ± 68 min, and the mean estimated blood loss was 419 ± 605 mL. Six patients (23.1%) received intraoperative transfusion and one patient (3.8%) was converted to open surgery. The mean intensive care unit stay was 1 ± 1.41 days, and the mean postoperative hospital stay was 17 ± 21 days. The 30-day major morbidity and mortality rates were 26.9% and 3.85%, respectively.
Conclusions. Laparoscopic colorectal surgery for patients with mild to moderate cirrhosis is feasible and safe with comparable postoperative morbidity and low 30-day mortality.
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In Taiwan, colorectal cancer is the third leading cause of cancer death, and the prevalence of liver cirrhosis is high. Although the use of vaccines has decreased the incidence of hepatitis virus-related cirrhosis, there has been an increasing incidence of alcoholic hepatitis and nonalcoholic-steatohepatitis (NASH). As a result, surgically treating cancer patients with concomitant liver cirrhosis is an issue of clinical concern in Taiwan.

Cirrhotic patients have higher surgical morbidity and mortality than non-cirrhotic patients.[1] Ziser et al. reported 30.1% morbidity and 11.6% mortality in cirrhotic patients undergoing anesthesia and surgery.[2] In patients undergoing colon and rectal surgery, liver disease is the most significant factor predicting in-hospital mortality (odds ratio = (OR) = 3.02),[3] and

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liver cirrhosis is associated with higher morbidity and mortality in non-hepatic abdominal surgeries. In a 2003 study, Gervaz et al. reported 46% morbidity and 13% mortality in 72 liver cirrhotic patients with colorectal cancer who underwent open colectomy.[4] Today, however, laparoscopic surgery is widely practiced in treating colorectal disease. Although varices, portal hypertension, and coagulopathy frequently coexist in cirrhotic patients, Cobb et al. concluded that laparoscopic procedures are safe for patients with mild to moderate liver cirrhosis.[5] However, studies evaluating the safety of laparoscopic surgery in cirrhotic colorectal cancer patients are lacking. Therefore, we present our experience and safety analysis of laparoscopic surgery in colorectal cancer patients with liver cirrhosis.

Materials and Methods

From January 2004 to December 2016, 1,936 patients received laparoscopic colorectal surgery in our hospital. Twenty-six (1.34%) had liver cirrhosis and were included in this study. We reviewed their medical records and collected demographic data such as sex, age, body mass index (BMI), comorbidities, cause of liver cirrhosis, Child Pugh classification, model for end-stage liver disease (MELD) score, American Society of Anesthesiologists (ASA) classification, previous operation and tumor location. We also collected pre-operative laboratory data including creatinine (Cr), total bilirubin (t-bil), albumin (Alb), prothrombin time (PT), international normalized ratio (INR), and carcinoembryonic antigen (CEA), and operative data, including surgical procedure, operation time, estimated blood loss (EBL), conversion to open surgery, intraoperative transfusion, and protective stoma construction. Perioperative data such as intensive care unit (ICU) stay, postoperative length of hospital stay, first time to flatus, postoperative major morbidity (Clavien-Dindo classification grades III and IV), and mortality were also recorded.

All patients were diagnosed with liver cirrhosis pre-operatively by liver biopsy or abdominal imaging with ultrasound or computed tomography (CT) or intraoperatively by direct vision of the liver by the surgeon during surgery. One team well-experienced in minimally invasive colorectal surgery performed all surgeries. Post-operatively, patients routinely received prophylactic antibiotics and initiated oral intake after the first flatus with a sequence of water, gruel, and soft diet. If soft diet was tolerated, we removed the drainage tube regardless of the amount of drainage as long as there was no sign of leakage. Patients were discharged on the day after drainage tube removal.

Data are presented as percentages or mean values with standard deviation. Statistical analyzes were performed using SPSS software, version 22.0 (SPSS Inc., Chicago, IL, USA).

Results

Patient demographics and laboratory data are shown in Table 1. Twenty-one patients were men, and five were women. The mean age was 67.9 ± 10.8 years (range, 60-83), and the mean BMI was 24.4 ± 3.3 (range, 17.6-30.1). Eleven patients (42.3%) had hypertension, eight (30.8%) had diabetes mellitus, five (19.2%) had chronic kidney disease, four (15.4%) had coronary artery disease, and two (7.7%) had a history of stroke. Hepatitis pathology was as follows: hepatitis B virus in 14 patients (53.8%), hepatitis C virus in five (19.2%), alcoholic hepatitis in two (7.7%), and nonalcoholic steatohepatitis in five (19.2%).

Pre-operative ascites was observed in eight patients (30.8%). Nine (34.6%) had undergone previous surgery, including laparoscopic cholecystectomy, subtotal gastrectomy, hysterectomy, laparoscopic hemicolectomy and radiofrequency ablation for hepatocellular carcinoma. Twenty-two patients (84.6%) were classified as Child-Pugh class A, and four (15.4%) were classified as Child-Pugh class B. There were no Child-Pugh class C patients. The mean MELD score was 8. Five patients (19.2%) were ASA class II, 19 (73.1%) were ASA class III, and two (7.7%) were ASA class IV. The mean pre-operative lab values were as follows: Cr, 1.01 mg/dL; t-bil, 0.97 mg/dL; Alb, 3.9 g/dL; PT, 11.24 sec; and CEA, 5.78 ng/mL.

Tumor location was right colon in nine patients (34.6%), transverse colon in one (3.8%), left colon in eight (30.8%), and rectum in eight (30.8%). Colon re-

section was performed based on tumor location, and all surgeries were conducted using a standard procedure with complete mesocolon resection.

All patients underwent minimally invasive procedures (25 laparoscopic and one robotic-assisted). We performed 10 right hemicolectomies, four left hemicolectomies, four anterior resections, and eight low anterior resections (Table 2). The mean operative time was 260 ± 68 min (range, 163-510). In our hospital, blood loss less than 50 mL is recorded as "minimum." In order to calculate the mean EBL, we converted "minimum" to 49 mL. The mean EBL was 419 ± 605 mL (range, 49-2500). Six patients (23.1%) received an intraoperative blood transfusion because of massive blood loss. Protective ileostomy was performed in four patients (15.4%). One patient (3.8%) was converted to open surgery because of massive intraoperative venous hemorrhage. The mean ICU stay was 1 ± 1.41 days (range, 0-6), and the mean postoperative hospital stay was 17 ± 21 days (range, 8-123).

The 30-day morbidity rate was 26.9% (7/26 patients). This included that one patient converted to open surgery and six patients who experienced 12 events, including anastomosis leak, sepsis due to intra-abdominal infection, pneumonia, enterocutaneous fistula, intra-abdominal abscess, temporary renal or liver failure, and upper gastrointestinal bleeding (Table 3). One patient with an anastomosis leak had a protective ileostomy performed. Another patient developed leakage that caused intra-abdominal abscess that was diagnosed using CT imaging and required re-operation. In addition, one patient who developed

Table 1. Patient demographic data and laboratory data

Age (years)	67.9 ± 10.8 (60-83)
Sex (M/F)	21/5
BMI (kg/m^2)	24.4 ± 3.3(17.6-30.1)
Comorbidities	
Diabetes mellitus (DM)	8 (30.8%)
Hypertension (HTN)	11 (42.3%)
Chronic kidney disease (CKD)	5 (19.2%)
Coronary artery disease (CAD)	4 (15.4%)
Stroke	2 (7.7%)
Cirrhosis etiology	
HBV	14 (53.8%)
HCV	5 (19.2%)
Alcohol	2 (7.7%)
Nonalcoholic steatohepatitis (NASH)	5 (19.2%)
Previous operation	9 (34.6%)
Pre-operative ascites	8 (30.8%)
Child-Pugh classification (A/B/C)	22 (84.6%)/4 (15.4%)/0
MELD score	8 ± 1.9
ASA classification (I/II/III/IV)	0/5/19/2
Tumor location	
Right side colon	9 (34.6%)
Transverse colon	1 (3.8%)
Left side colon	8 (30.8%)
Rectum	8 (30.8%)
Laboratory data	
Creatinine (Cr)	1.01 ± 0.27 (0.8-1.5)
Total bilirubin (t-bil)	0.97 ± 0.41 (0.4-2.0)
Albumin (Alb)	3.90 ± 0.65 (2.3-5.2)
Prothrombin time (PT)	11.24 ± 0.95 (9.6-13.8)
International normalized ratio (INR)	1.04 ± 0.08 (0.97-1.28)
Carcinoembryonic antigen (CEA)	5.78 ± 8.95 (0.49-35.60)

MBI, body mass index; HBV, hepatitis B virus; HCV, hepatitis C virus; MELD, model for end-stage liver disease; ASA, American Society of Anesthesiologists.

Table 2. Operative data and postoperative outcomes

Surgical procedure	
Right hemicolectomy	10 (38.7%)
Left hemicolectomy	4 (15.4%)
Anterior resection	4 (15.4%)
Lowe anterior resection	8 (30.8%)
Laparoscopic/robotic surgery	25/1
Operative time (min)	260 ± 68 (163-510)
Estimated blood loss (mL)	419 ± 605 (49-2500)
Intraoperative transfusion	6 (23.1%)
Conversions	1 (3.8%)
Protective ileostomy	4 (15.4%)
Start of peristalsis (days)	4.19 ± 1.29
ICU stay (days)	1 ± 1.41 (0-6)
Postoperative hospital stay (days)	17 ± 21 (8-123)
Morbidity	7 (26.9%)
Mortality	1 (3.8%)

ICU, intensive care unit.

Table 3. 30-day morbidities

Anastomosis leak	2
Sepsis	1
Pneumonia	1
Enterocutaneous fistula	2
Intra-abdominal abscess	1
Renal failure	2
Liver failure	2
Massive UGI bleeding	1

UGI, upper gastrointestinal.

an enterocutaneous fistula after being discharged presented to the emergency department on postoperative day 25 and was treated conservatively. The mortality rate in this cohort was 3.85% (1/26 patients). This patient developed postoperative hepatic failure with refractory upper gastrointestinal bleeding as well as sepsis with multiple organ failure in the ICU and expired on postoperative day 33.

Discussion

Despite improvements in peri- and postoperative patient care, patients with liver cirrhosis remain challenging to care for surgically. Lin et al. reported morbidity and mortality in a large study of patients who underwent non-hepatic surgery in Taiwan, 25.1% of whom received gastrointestinal operations.[6] Patients with cirrhosis (n = 24,282) had higher morbidity rate (13.8% vs. 11.2%; OR, 1.22) and mortality (1.2% vs. 0.7%; OR, 1.88) compared to patients without cirrhosis (n = 97,128).

Liver cirrhosis causes even higher morbidity and mortality in patients with colorectal cancer. Meunier et al. reported postoperative morbidity of 77% and mortality of 26% in a study of 44 patients with cirrhosis who underwent colorectal surgery.[7] Using the American College of Surgeons National Surgical Quality Improvement Program, Ghaferi et al. reported that cirrhotic patients experienced 41.9% morbidity and 21.5% mortality, whereas for non-cirrhotic patients, the rates were 15.4% (relative risk (RR), 2.71) and 3.2% (RR, 6.53), respectively.[8] Two nationwide population studies in the United States[9] reported 35% morbidity in non-cirrhotic patients, and 43% in cirrhotic patients (adjusted OR, 3.91). Morbidity was even higher in patients with cirrhosis and portal hypertension (55%; adjusted OR, 11.3) after colorectal surgery. Another nationwide study from Danmark reported higher mortality in cirrhotic patients than in non-cirrhotic patients (24.1% vs. 8.7%; adjusted RR, 2.59).[10]

More recently, Sabbagh et al. compared 40 cirrhotic patients receiving colorectal surgery with 80 matched non-cirrhotic patients.[11] Major morbidity (Clavien-Dindo classification III and IV) was 57.5% in those with cirrhosis, compared to 26.5% in the non-cirrhotic patients. In subgroup analysis, Child-Pugh class B patients had significantly more complications overall than their matched non-cirrhotic patients (67% vs. 30%, $p = 0.005$). However, no significant difference was found between the Child-Pugh class A patients and their matched controls (52% vs. 24%, $p = 0.06$).[11] More recently in 2017, Lee et al. reported morbidity and mortality rates of 37.3% and 3.1%, respectively, following colorectal cancer surgery in patients with liver cirrhosis.[12]

Today, laparoscopic colectomy is widely accepted and has known advantages. However, most previous studies mainly included patients who underwent open surgery. Only two studies to date have reported on patient outcome after laparoscopic colectomy. In 2003, Martinez et al. reported 17 cirrhotic patients who underwent laparoscopic-assisted colectomy; five developed postoperative complications, for a morbidity of 29%.[13] Zhou et al. studied 62 patients with liver cirrhosis; 30 patients received laparoscopic colectomy, and 32 received open surgery. There was no significant difference between the two groups in overall complication rate (50.0% vs. 68.8%, $p = 0.133$). However, the laparoscopic group had a significantly lower grade II complication rate (20.0% vs. 50.0%, $p = 0.014$).[14]

Telem et al. reported that ASA score > 3, presence of ascites, t-bil level > 1.5 mg/dL, Alb level < 3 mg/dL, emergent procedures, intraoperative blood transfusion, and intraoperative blood loss > 150 mL were risk factors predicting postoperative adverse outcomes and mortality in patients with advanced cirrhosis receiving abdominal surgery.[15] Similarly, Lee et al. found that hyperbilirubinemia ($p = 0.002$), PT prolongation ($p = 0.020$), and intraoperative transfusion ($p = 0.003$) were significant factors predicting postoperative morbidity and mortality of patients with liver cirrhosis following colorectal cancer surgery.[12] Thus, a comprehensive pre-operative examination, correction of Alb level, and limiting intraoperative packed red blood cell transfusion may reduce the probability of postoperative adverse outcomes.

In the current study, there were 12 events of grade III or IV postoperative complication in six patients, and one patient was converted to open surgery. The 26.9%

morbidity that we found is comparable to previous studies that reported complication rates ranging 24.1%-77%.[13,14] That one patient converted to open surgery in this study had Child-Pugh class B cirrhosis. The six other patients with morbidities had Child-Pugh class A disease. Among these six patients, one had an anastomosis leak caused an enterocutaneous fistula and intra-abdominal abscess accumulation that required surgical drainage. Another patient with leakage received an ileostomy. In addition, one patient was successfully discharged but presented to emergency department because of an enterocutaneous fistula on postoperative day 25; this was treated conservatively.

In our cohort, protective ileostomy was performed in four patients without postoperative complication. All patients who experienced morbidity did not have a protective ileostomy. Although there were four events of anastomosis leak and enterocutaneous fistula, which might have been prevented by protective ileostomy, routine protective ileostomy construction is not suggested by this study because the overall morbidity was relatively low and the complications could be managed with ileostomy and/or conservative treatment.

The 3.85% mortality rate found in our study was lower than previous reports, which included patients undergoing open surgery or laparoscopic colectomy (range, 14%-26%). Though the mean EBL was higher in this study (419 ± 605 mL) compared to previous ones, after excluding four patients with an extremely large amount of blood loss (more than 1000 mL), the mean blood loss was a comparable 195 ± 142 mL.[13,14]

This study has some limitations, including its retrospective nature, small number of patients, and possible selection bias in surgical decision-making. Further large-scale randomized studies are needed.

In conclusion, laparoscopic colorectal surgery in patients with mild to moderate cirrhosis is feasible and safe with comparable postoperative morbidity and low 30-day mortality.

Conflicts of Interests and Source of Funding

The authors declare no conflicts of interests. The study received no research grant.

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原　著

肝硬化病人接受腹腔鏡大腸直腸切除手術

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目的　大腸直腸癌在台灣為致死率第三高的癌症，且肝硬化的盛行率於台灣仍居高不下。肝硬化病人接受手術時有較高的併發症及死亡率，尤其是接受大腸直腸相關手術。本研究報告本院肝硬化病人接受腹腔鏡大腸直腸切除手術之經驗。

方法　回溯性收集 2004 年 1 月至 2016 年 12 月間於本院接受腹腔鏡大腸直腸切除手術的病人，統計人口學資料、術前實驗室檢查數據、手術數據、術中及術後數據以及術後併發症及死亡數據。

結果　共納入 26 位病患，其中 21 位為男性，5 位為女性。平均年齡為 67.9 ± 10.8 歲，BMI 為 24.4 ± 3.3。造成肝硬化的原因：14 位病人為 B 型肝炎、5 位為 C 型肝炎、2 位為酒精性肝炎、5 位為非酒精性脂性肝炎。22 位病人為 Child–Pugh class A 肝硬化，4 位為 Child–Pugh class B 肝硬化。平均手術時間為 260 ± 68 分鐘而平均失血量為 419 ± 605 毫升。6 位病人術中接受輸血且有 1 位病人轉為開腹手術。術後平均於加護病房住院 1 ± 1.41 天，平均術後住院天數為 17 ± 21 天。三十天產生重度併發症率為 26.9%，死亡率為 3.85%。

結論　輕度至中度肝硬化病人接受腹腔鏡大腸直腸切除手術是可行且安全的，因有較低的併發症率及死亡率。

關鍵詞　大腸直腸癌、肝硬化、微創手術、安全性。