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Gastric cancer surgery in cirrhotic patients: Result of gastrectomy with D2 lymph node dissection

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Abstract

AIM: To explore the feasibility of performing gastrectomy with D2 lymphadenectomy in gastric cancer patients with liver cirrhosis.

METHODS: A total of 7 178 patients were admitted with a diagnosis of liver cirrhosis from January 1993 to December 2003. We reviewed the records of 142 patients who were diagnosed with liver cirrhosis and gastric adenocarcinoma during the same period. Gastrectomy with D2 lymph node dissection for carcinoma of the stomach was performed in 94 patients with histologically proven hepatic cirrhosis.

RESULTS: All but 12 patients were classified as Child's class A. Only 35 patients (37.2%) were diagnosed with cirrhosis before operation. Seventy-three patients underwent a subtotal gastrectomy (77.7%) and 21 patients (22.3%) underwent a total gastrectomy, each with D2 or more lymph node dissection. Two patients (3.8%) who had prophylactic intra-operative drain placement, died of postoperative complications from hepatorenal failure with intractable ascites. Thirty-seven patients (39.4%) experienced postoperative complications. The extent of gastric resection did not influence the morbidity whereas serum aspartate aminotransferase level (P = 0.011) and transfusion did (P = 0.008). The most common postoperative complication was ascites (13.9%) followed by wound infection (10.6%).

CONCLUSION: We concluded that the presence of compensated cirrhosis, i.e. Child class A, is not a contraindication against gastrectomy with D2 or more lymph node dissection, when curative resection for gastric cancer is possible. Hepatic reserve and meticulous hemostasis are the likely determinants of operative prognosis.

Key words: Gastric cancer; Liver cirrhosis; D2 lymph node dissection; Morbidity; Mortality

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INTRODUCTION

Although the prognosis of gastric cancer has improved significantly as a result of early diagnosis, radical operation, and advances in adjuvant therapy, gastric cancer remains the most common cause of cancer-related death in Korea[1]. Extended lymph node dissection is regarded as an essential criterion for the treatment of gastric cancer[2-4]. It not only makes the surgical therapy more radical but also provides adequate lymph node staging.

Liver cirrhosis is another major health problem in Korea, where it is the fourth most common cause of death, and is probably linked to the high prevalence of HBV infection and a culture that encourages high alcohol consumption[5]. Because of the high prevalence, cirrhosis of the liver is not infrequently encountered among candidates for gastric cancer surgery in Korea. Most surgeons are reluctant to perform a D2 lymph node dissection in patients with liver cirrhosis due to the risk of liver dysfunction[6].

Recent advances in peri-operative patient care and surgical techniques, however, have reduced the morbidity and mortality rates associated with gastric cancer surgery even after a D2 lymph node dissection. This study was conducted to explore the feasibility of performing gastrectomy with D2 lymphadenectomy in gastric cancer patients with liver cirrhosis, in terms of the morbidities and mortalities.

MATERIALS AND METHODS

Patients

A total of 7 178 patients were admitted with a diagnosis of liver cirrhosis to Yonsei University Medical Center from January 1993 to December 2003. We reviewed the records of 142 patients who were diagnosed with liver cirrhosis and gastric adenocarcinoma at the Department of Surgery, Yonsei University College of Medicine during the same

period. All patients had no previous history of abdominal surgery or other malignancies. Thirty-four patients who had palliative surgery and 14 patients who did not have surgery due to impaired liver function were excluded from the study. The remaining 94 gastric cancer patients with liver cirrhosis who underwent curative gastric resection for gastric cancer were included in this study.

Cirrhosis was diagnosed primarily by liver biopsy. In patients in whom liver biopsy was not performed, the diagnosis was made by gross findings during the operation, a history of liver disease, with impaired liver function tests and CT scan or ultrasonography imaging.

Characteristics of the patients including age, sex, Child-Pugh classification, extent of gastric resection, stage of the tumor, and postoperative outcomes including operation time, the number of retrieved lymph nodes, complications, hospital stay, survival rates were analyzed. The χ^2 test was used for discrete variables and Student's *t* test for continuous variables. Survival rates were estimated using the Kaplan-Meier method and the difference between the curves was assessed using the log-rank test. *P* values less than 0.05 indicated statistical significance.

Operative technique

Gastric cancer surgery in our institution is done according to the following standardized operative protocol: (1) A total or distal subtotal gastrectomy is performed depending on the location and the macroscopic type of gastric cancer. (2) A D2 or more lymph node dissection is preferred regardless of the clinical stage[7]. Lymph nodes along the hepato-duodenal ligament and common hepatic artery were retrieved and tied with #3 silk. After gastric resection, the gastrointestinal continuity is restored by either a gastro-duodenostomy or a gastro-jejunostomy, depending on the location of the tumor after a distal subtotal gastrectomy. A Roux-en-Y esophago-jejunostomy is done after a total gastrectomy. Gastro-duodenostomy is done using interrupted 3-0 silk Lembert sutures for the outer layer and interrupted 3-0 polyglycolic sutures for the transmural inner layer. The gastro-jejunostomy is performed using interrupted 3-0 silk Lembert sutures for the outer layer and a running 3-0 polyglycolic suture for the transmural inner layer. Esophago-jejunostomy is done using an EEA stapler (Ethicon, Somerville, NJ, USA). Before the abdominal wall is closed, a two-armed suction drain (Hemovac, Sewoon Medical Co., Seoul, South Korea) is inserted through a new stab wound on the right flank toward the subhepatic area after a subtotal gastrectomy. An additional suction drain is inserted through the left flank toward the left sub-diaphragmatic space after a total gastrectomy. The abdominal fascia is closed with continuous polydioxanone sutures reinforced by interrupted 1-0 silk sutures. The subcutis and cutis are restored with interrupted 3-0 silk sutures and skin staplers.

RESULTS

Characteristics of the patients, tumors, and surgeries

There were 73 (77.7%) males and 21 (22.3%) females. The median age was 59 years (range, 36-76 years). All but 12 patients were classified as Child's class A. Thirty-five patients (37.2%) were diagnosed with cirrhosis before the operation and the other 59 (62.8%) patients were diagnosed with liver cirrhosis during the operation. Cirrhosis was related to HBV in 52 (55.3%) patients, HCV in 8 (8.5%) patients, and alcohol abuse in 30 (31.9%) patients. Cirrhosis was cryptogenic in 4 (4.3%) patients.

Seventy-three (77.7%) patients had a subtotal gastrectomy and 21 (22.3%) patients underwent a total gastrectomy. All patients underwent D2 or more lymph dissection. The mean number of the retrieved lymph nodes was 35 (range, 15-71). The mean operation time was 195 min (range, 110-345 min). Prophylactic drainage was done in 51 (73.9%) patients. The median hospital stays in this cohort of 94 patients was 13.5 d (range, 7-90 d). The characteristics of patients, tumors, and surgeries are summarized in Table 1.

Table 1 Characteristics of patients, tumors, and surgeries

Patients				
Variables	Number	%	Variables	
Sex			Age (yr)	
Male	73	77.7	Median	59
Female	21	22.3	Range	36-76
Diagnosis of cirrhosis			Retrieved nodes	
Preoperative	35	37.2	Median	35
Intraoperative	59	62.8	Range	15-71
Cause of cirrhosis			Positive nodes	
HBV-related	52	55.3	Mean	3.5
Alcohol	30	31.9	Range	0-27
HCV-related	8	8.5	Operation time (min)	
Cryptogenic	4	4.3	Mean	194.6
Extent of gastric resection			Range	110-345
Subtotal	73	77.7	Hospital stay (d)	
Total	21	22.3	Median	13.5
TNM stage			Range	7-90
I	51	54.3		
II	25	26.6		
III	10	10.6		
IV	8	8.5		

Mortality and morbidity

Two patients who had prophylactic intra-operative drains died after the operation (2.1%) as a result of hepato-renal failure related with intractable ascites. One patient was classified as Child's class B and the other patient as Child's class C. The most common post-operative complication was ascites (13 patients, 13.9%) followed by wound infection (10 patients, 10.6%). Ascites was well controlled with medications in nine patients (six patients had prophylactic intra-operative drain placement and three patients had not) and with paracentesis in four patients who had prophylactic intra-operative drain placement. All the patients who experienced post-operative bleeding (four patients) and anastomotic leakage (two patients) were managed conservatively (Table 2).

Table 2 Morbidities and mortalities

	Patients		Total (%)
	No drainage (*n* = 37, %)	Drainage (*n* = 57, %)	
Morbidities			
Absent	27 (73.0)	30 (52.6)	57 (60.6)
Present	10 (27.0)	27 (47.4)	37 (39.4)
Wound infection	2 (5.4)	8 (14.0)	10 (10.6)
Ascending infection	0 (0.0)	3 (5.3)	3 (3.2)
Pneumonia	2 (5.4)	3 (5.3)	5 (5.3)
Bleeding	1 (2.7)	3 (5.3)	4 (4.3)
Anastomosis leakage	1 (2.7)	1 (1.8)	2 (2.1)
Ascites	3 (8.1)	10 (17.5)	13 (13.9)
Mortalities	0 (0.0)	2 (3.8)[1]	2 (2.1)

[1]Mortalities were caused by hepatorenal syndrome.

The association between clinico-pathological parameters and the risk of post-operative complications are summarized in Table 3. Transfusion and serum aspartate aminotransferase levels were the independent predictive factors of morbidity ($P<0.05$) (Table 4). The extent of gastric resection or tumor stage did not influence the morbidity, while intra-operative drain placement showed marginal significance ($P = 0.055$). Ten out of the thirty-seven patients, who had no prophylactic drains (27.0%) experienced postoperative complications, whereas 27 out of the 57 patients who had prophylactic drains (47.4%) experienced complications.

Survival of the patients

The overall 5-year survival rate of the patients was 65.9%. The overall 5-year survival rate of the Child's class A patients was 69.1% and 44.4% for the Child's class B and C patients. There was a significant difference between the survival rates at Child's class ($P = 0.0195$).

DISCUSSION

Postoperative complications in cirrhotic patients after gastrectomy with D2 lymph node dissection were associated with serum aspartate aminotransferase levels and transfusion. We observed that the post-operative morbidity was more common among patients with prophylactic drains after gastrectomy with D2 lymph node dissection, than among patients without prophylactic drains. Two patients who had prophylactic intra-operative drain placement died of postoperative complications from hepato-renal failure with intractable ascites.

The prevalence of gastric cancer among cirrhotic patients in this study was higher than other reports (2.0%, 142 patients out of 7 178 cirrhotic patients). Gastric cancer among cirrhotic patients have been rarely reported in the literature[8]. A recent nationwide cohort study from Denmark revealed that the risk of gastric carcinoma in cirrhotic patients is not low compared to other cancers, except for hepatocellular carcinoma[9]. The study identified 40 gastric carcinoma patients (0.34%) among 11 605 cirrhotic patients during a 12-year follow-up. A group of Italian endoscopists has made similar observations[10]. Zullo *et al*., reported that the prevalence of latent gastric cancer in liver cirrhosis patients could be significantly higher than that expected in the general population (a 2.6-fold increase). The reasons for the high prevalence of gastric cancer in our study remain unclear but probably are associated with the generally high prevalence of gastric cancer and a culture that encourages high alcohol consumption in Korea[5,11].

The data presented here demonstrates that gastrectomy with D2 lymph node dissection in cirrhotic patients is feasible. Abdominal operations in cirrhotic patients have been a technical challenge with mortality rates around 30%[12-14]. Therefore, gastric cancer surgery for cirrhotic patients remains controversial. Our peri-operative morbidity and mortality rates compared favorably with most series on abdominal procedures in the literature. The Child–Pugh classification has proven to be a reliable tool in identifying patients at risk of post-operative complications. In our series, the morbidity rate was related to serum aspartate aminotransferase levels and peri-operative transfusion status. Peri-operative transfusion has been reported to be associated with morbidities in gastric cancer patients due to immunosuppressive effects[15]. Lowering the serum aspartate aminotransferase levels and meticulous hemostasis during operation are probably the best way to decrease post-operative complication rate in patients with liver cirrhosis.

Our data showed that D2 lymph node dissection in cirrhotic patients is feasible without drains, if the hepatic reserve is not severely compromised and no usage of prophylactic drain. All the patients underwent D2 lymph node dissection and the mean number of retrieved lymph nodes was 35 in this study. This result is comparable to the results of other studies concerning D2 lymph node dissection[3,6]. Prophylactic drain placement showed no beneficial effect in terms of post-operative morbidity in this study. Although three patients, who did not have intraoperative drain placement, developed ascites after surgery, they were easily controlled with medications. Three out of ten patients who needed paracentesis were all patients who had intra-operative drain placement. Similar results were reported by Urbach *et al*., who performed a metaanalysis on colorectal cancer patients and concluded that they could not find any benefit of routine intra-operative drain placement after colon and rectal anastomoses in reducing the rate of anastomotic leakage or other complications[16].

Lymph node dissection around the hepato-duodenal ligament (station number 12 according to the classification

Table 3 Factors associated with complications

Variables	Complication		*P*
	Absent (*n*, %)	Present (*n*, %)	
Sex			0.351
Male	42 (57.5)	31 (42.5)	
Female	15 (71.4)	6 (28.6)	
Age (yr)			0.138
<55	34 (66.7)	17 (33.3)	
≥55	23 (53.4)	20 (46.6)	
Causes of cirrhosis			0.188
HBV-related	36 (69.2)	16 (30.8)	
Alcohol	14 (46.7)	16 (53.3)	
HCV-related	4 (50.0)	4 (50.0)	
Cryptogenic	3 (75.0)	1 (25.0)	
Anemia (<100 g / L)			0.370
Absent	46 (62.2)	28 (37.8)	
Present	11 (55.0)	9 (45.0)	
Thrombocytopenia ($<10^5$ / U)			0.619
Absent	45 (62.5)	27 (37.5)	
Present	12 (54.5)	10 (45.5)	
Albumin (g / L)			0.386
≥36	38 (64.4)	21 (35.6)	
<36	19 (54.3)	16 (45.7)	
Aspartate aminotransferase (IU / L)			0.030
≤40	40 (70.2)	17 (29.8)	
>40	17 (63.0)	20 (37.0)	
Bilirubin (mg / dL)			0.819
≤1.4	40 (59.7)	27 (40.3)	
>1.4	17 (63.0)	10 (37.0)	
Prothrombin (%)			0.656
≥80	39 (62.9)	23 (37.1)	
<80	18 (56.3)	14 (43.7)	
Child–Pugh class			0.207
A	52 (63.4)	30 (36.6)	
B or C	5 (41.7)	7 (58.3)	
Transfusion			<0.001
No	46 (75.4)	15 (24.6)	
Yes	11 (33.3)	22 (66.7)	
Extent of gastric resection			0.450
Subtotal	46 (63.0)	27 (37.0)	
Total	11 (52.4)	10 (47.6)	
Stage			0.835
EGC	26 (61.9)	16 (38.1)	
AGC	31 (59.6)	21 (40.4)	
Prophylactic drainage			0.055
No	27 (73.0)	10 (27.0)	
Yes	30 (52.6)	27 (47.4)	

Table 4 Logistic regression analysis of risk factors for postoperative complication

Covariate (observed value)	Coefficient	SE	RR (95%CI)	*P*
Causes of cirrhosis (Postnecrotic *vs* others)	0.9744	0.5543	2.6496 (0.8941-7.8517)	0.079
GPT (IU / L) (≤40 *vs* >40)	1.3899	0.5446	4.0143 (1.3807-11.672)	0.011
Transfusion (no *vs* yes)	1.6837	0.5000	5.3856 (2.0214-14.3485)	0.008

SE: standard deviation; RR: relative risk; CI: confidence interval.

by the Japanese Research Society on Gastric Cancer) and common hepatic artery (station number 8) in cirrhotic gastric cancer patients has been reported to be limited[6,17]. The lymphatic systems in these two lymph node stations are extensive and well developed, making these two lymph node stations as the frequent sites of lymphorrhea especially after lymph node dissection that is not easy to control[6]. Cirrhotic patients often suffer from ascites after gastric cancer surgery,

which can be aggravated by insertion of a drainage catheter [12,18]. Two patients who had prophylactic intra-operative drain placement died of post-operative complications from hepato-renal failure with intractable ascites. Downstaging Child's class B and C patients to Child's class A patients and meticulous tying of the lymphatic systems should be attempted first, instead of limiting the extent of lymph node dissection.

Since more than half of the patients in our study were diagnosed with liver cirrhosis during the operation and this study was a retrospective study with inherent sampling bias, the association of Child's class with morbidities and mortalities was not always clear. Therefore, it is difficult to compare our results against other reports in the literature. The reason why more than half of the patients in this study had been diagnosed as liver cirrhosis during the operations is unclear.

In conclusion, patients with compensated cirrhosis, i.e., Child's class A, may safely undergo gastrectomy with D2 lymph node dissection. Downstaging the Child's class and performing a D2 lymph node dissection with meticulous hemostasis and without a prophylactic drain placement appear to be the most reasonable treatment plan for gastric cancer patients with liver cirrhosis.

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