# Results of Hepatic Resections at S. N. U. H. : A Ten-year Experience<sup>†</sup>

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= Abstract = The medical records of 399 patients who underwent hepatic resection between January 1981 and December 1990 were reviewed. Information regarding the results of hepatic resection in terms of operative indication, operative procedure, operative morbidity and mortality, was abstracted. Until the end of 1990, a total of 402 hepatic resections were completed including 319 primary malignancies, 4 secondary malignancies, 2 gallbladder carcinomas, 42 intrahepatic cholelithiasis, 35 benign masses. Major hepatic resections were performed on 117 patients(29%). Of the 117 patients, 60(51%) had histologically proven liver cirrhosis. Minor hepatic resections were performed on 285 patients (71%). Sepsis was the most frequent complication, manifested primarily as wound infection(71 cases) or intra-abdominal infection(25 cases). Nonfatal hepatic failure occurred in 9 patients with cirrhosis and 1 patient without cirrhosis. There were 38 operative deaths among 402 hepatic resections, for an overall operative mortality of 9.4 %. Twenty five of these patients died from hepatic failure after operation, accounting for 66 % of the total operative mortality. There has been an increasing frequency of hepatic resection during the last five years. Indications for resection increased from 87 to 195 resections for hepatocellular carcinoma. The cumulative data show a decrease in the complication rate and operative mortality. In the recent period, nonlethal postoperative complications have occured in 135 of 286 patients (47%). The overall survival rates in 172 patients with hepatocellular carcinoma excluding operative mortalities and palliative resections and reresections, were 71.0 %, 39.8%, 28.3% for 1, 3, and 5 years, respectively.

Key Words: Liver resection, Hepatocellular carcinoma, Complication, Mortality

#### INTRODUCTION

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In Korea, the major indication for hepatic resection is hepatocellular carcinoma and the incidence of concomitant cirrhosis is extremely high. Resecting the cirrhotic liver encounters several difficult problems. Its poor functional reserve and technical difficulty have restricted hepatic resection and increased the operative morbidity and mortality. We analyzed the results of hepatic resection performed during a ten

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year period from January 1981 to December 1990 in terms of operative indication, operative morbidity and mortality, and long-term survival.

### PATIENTS AND METHODS

The medical records of 399 patients who underwent hepatic resection at Seoul National University Hospital between January 1981 and December 1990 were reviewed. There were 402 hepatic resections in 399 patients because two patients had undergone repeated hepatic resections due to recurrence of hepatocellular carcinoma, including one who had undergone a third hepatic resection. Information regarding the patient population, diagnosis, pathology, operative procedure, and outcome summarized. Indications for hepatic resections were classified into groups of primary maligsecondary malignancy, gallbladder nancy, carcinoma, intrahepatic cholelithiasis, and bemass. Primary malignancy includes hepatocellular carcinoma(HC), cholangiocel-Iular carcinoma(CC), combined or mixed carciand other malignancies. Operative procedures were divided into the following two categories: major hepatic resections, which include massive hepatic resections such as lobectomy and trisegmentectomy; and minor hepatic resections, which include sublobectomies such as segmentectomy and wedge resection. In cases of major hepatic resection, bilateral subcostal incision was used with an upper midline extension to the xiphoid process. Thoracic extension was not necessary in most cases. In the case of malignant disease, dissection of the lymph nodes was performed with hepatic resection. Postoperative complications were carefully monitored. Any death within 30 days after hepatic resection as well as any death during the initial hospitalization for hepatic resection, regardless of time, was counted as an operative mortality. Survival rates after hepatic resection were obtained using the life table method.

#### **RESULTS**

The mean age of the patients was 52 years, and the age range was 16 to 75 years. Three hundred and twelve were men (78%) and 87 were women(22%). This male predominance was attributable to the high incidence of HC in this sex.

#### Indications

Until the end of 1990, a total of 402 hepatic resections were completed including 319 primary malignancies, 4 secondary malignancies, gallbladder carcinomas, 42 intrahepatic cholelithiasis, 35 benign masses. The annual number and indications of hepatic resections is shown in Table1. Three hundred and twenty two of the 399 patients had malignant diseases. Three hundred and sixteen of the 322 patients had primary liver cancer, which was the most frequent disease in this series. Two hundred seventy nine patients had HC with a male to female ratio of 5.8 to1; Twenty nine patients had CC with a male to female ratio of 3.1 to 1; Three patients had mixed carcinoma, and 5 patients had other primary malignancies. Other primary malignancies included hepatoblastoma, malignant lymphoma, biliary cystadenocarcinoma, undifferentiated embryonal sarcoma, and leiomyosarcoma. Two hundred and forty two of the 399 patients also had liver cirrhosis when the resected specimen was examined histologically. Cirrhosis here includes not only true cirrhosis but also chronic active hepatitis. This was common in the patients with HC. Details of each disease are given.

Hepatocellular carcinoma. The mean age of 279 patients with HC was 53 years, and the age range was 16 to 75 years. HC was predominant in the 5th and 6th decades. One hundred and eighty eight patients belonged to these 2 decades. Two hundred and thirty eight patients were men(85 %) and 41 were women(15 %). There were 282 hepatic resections in 279 patients because two patients underwent a second resection at a later date, including one

who underwent a third resection. One who three hepatic underwent resections has survived over 6 years from the time of the first Не underwent right operation. inferior segmentectomy for a 10cm sized mass, 2 years later, right lobectomy for two 6cm and 4cm sized recurrent masses, and 2 years later, left lateral segmentectomy for two 8cm and 4cm sized recurrent masses. Preoperative serum levels of AFP were measured by radioimmunoassay. This was higher than 20, 200 ng/ml in 187 (67 %), and 106 patients (38 %), respectively. HBs-antigen was positive in 72%, HBsantibody in 19%, and HBc-antibody in 75% of the patients. Two hundred and twenty one patients (79 %) had liver cirrhosis.

Cholangiocellular carcinoma Hepatic resection was performed on 29 cases of histologically proven intrahepatic peripheral cholangiocarcinoma. Among them, 5 cases were associated with Clonorchis sinensis infection. The mean age was 56 years, and the age range was 37 to 68 years. Twenty two patients were men (76 %) and 7 were women (24 %). AFP level was elevated in 4 cases. Serum carcinoembrionic antigen (CEA) level was elevated above 5 ng/ml in 18 cases. HBs-antigen was positive in 14 %, HBs-antibody in 28 %, and HBc-antibody in 31 % of the patients. Seven patients (24 %) had liver cirrhosis.

Gallbladder carcinoma. The age was 38, 84 years, respectively. Both patients were men and

neither of these patients had associated gallstones.

Metastatic carcinoma Hepatic resection was performed for metastatic liver cancer when the primary focus was irradicated and metastases were not demonstrated except for in the liver. The primary disease of the 4 patients with metastatic liver cancer was colorectal cancer. Hepatic resections performed on patients with direct invasion of gastric malignancies were excluded in this study. There was one patient with metachronous colorectal liver metastasis. In 3 patients, hepatic resection was performed synchronously. The mean age was 48 years, and the age range was 39 to 56 years. Three patients were men and one was a woman. CEA was elevated in all of the 4 patients.

Intrahepatic cholelithiasis. Because most of the benign lesions were intrahepatic duct stones (42 cases), these were seperated from benign masses. Intrahepatic cholelithiasis is defined as a stone involving the right and left hepatic duct, and their branches, peripheral to their junction at the hepatic hilum. The mean age was 43 years, and the age range was 22 to 69 years. Nineteen patients were men (45%) and 23 were women (55%).

Benign mass. Hepatic resection was carried out on 35 patients with a variety of benign masses. The mean age was 51 years, and the age range was 34 to 69 years. Twenty patients were

Table 1. Annual trends in the number of hepatic resection

	Year										
Diagnosis	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	Total
Hepatocellular carcinoma	9	12	13	26	27	25	29	50	46	45	282
Cholangiocarcinoma					5	3	6	7	5	3	29
Mixed carcinoma						1	1	1			3
Hepatoblastoma and others						1	3		1		5
Metastatic carcinoma		1				1		1	1		4
Gall bladder cancer							1		1		2
Hepatolithiasis		2	2	1	7	8	2	11	3	6	42
Benign mass	2	1	3		5	4	8	3	4	5	35
Total	11	16	18	27	44	43	50	73	61	59	402

men (60 %) and 14 were women (40 %). These disorders included hemangioma(12 cases), abcess(8 cases), cyst(7 cases), adenomatous hyperplasia(3 cases), harmatoma(2 cases), adenoma(1 case), cystadenoma(1 case), and pseudolymphoma(1 case). Classification of seven cysts are congenital non-parasitic cyst(4 cases), ecchinococcal cyst(2 cases), and adult polycystic disease (1 case).

## Operative procedures

Table 2. shows details of 402 operative procedures performed on 399 patients. Major hepatic resections were performed on 117 patients (29%). Of the 117 patients, 60 (51%) had histollogically proven liver cirrhosis. Minor hepatic resections were performed on 285 patients (71%). Of the 285 patients, 182 (64 %) had liver cirrhosis. In the case of HC, the ratio of major hepatic resection and minor hepatic resection was 1:2.5. In the cirrhotic patients with considerable liver function, extensive resection was performed, while in the patients with a small HC and poor liver reserve function, subsegmental or partial resection was performed with the aid of intraoperative ultrasonography. In the case of HC, 85 patients were considered to have undergone palliative resections. Nineteen were due to adjacent organ invasion, 26 were due to gross angioinvasion, 16 were due to residual tumor. Postoperative pathologic examinations revealed a positive resection margin in 24 patients. The remaining 194 patients uderwent a curative resection. In the case of CC, 3 patients were considered to have undergone palliative resections due to a positive resection margin on permanent histology. The remaining 26 patients underwent a curative resection. In the case of metastatic carcinoma, pathologic examinations revealed tumor in the margins of none of the 4 resections. In the case hepatolithiasis, left lateral segmental resections were carried out in most cases (39/42). But 2 cases of left lobectomies and 1 case of right lobectomy were required when the medial segment was also affected or the right lobe was the affected portion.

#### Postoperative complications

Two hundred and fourteen patients surviving operation experienced 241 nonlethal complications. Complications were frequently seen in patients with liver cirrhosis (58.6%) (Table 3). One hundred and fifty seven of 241

**Table 2.** Details of 402 hepatic resections classified by diagnosis, operative procedure and operative death

	Operative procedure*								
Diagnosis	RTS	LTS	RL	LL	CBS	RS	LS	SP	Total
Hepatocellular carcinoma	4[1]**	1[1]	53[7]	20[0]	2[0]	49[9]	15[1]	138[13]	282[32]
Cholangiocarcinoma			6[2]	8[0]	1[1]		11[0]	3[ 1]	29[4]
Mixed carcinoma			1[0]	2[0]					3[0]
Hepatoblastoma and others			3[0]					2[ 0]	5[0]
Metastatic carcinoma			2[0]				2[0]		4[0]
Gall bladder cancer							1[0]	1[0]	2[0]
Hepatolithiasis			1[0]	2[0]			39[1]		42[ 1]
Benign mass			7[0]	4[0]			4[0]	20[ 1]	35[1]
Total	4[1]	1[1]	73[9]	36[0]	3[0]	49[9]	72[2]	164[15]	402[38]

<sup>\*</sup> RTS, right trisegmentectomy;

LTS, left trisegmentectomy;

RL, right lobectomy;

LL, left lobectomy;

CBS,central bisegmentectomy;

RS, right segmentectomy;

LS, left segmentectomy;

SP, subsegmentectomy or partial resection

<sup>\*\* [ ],</sup> number of cases of operative deaths

Table 3. Nonfatal complications of hepatic resection

	No. of cases					
Complication	Cirrhosis	No cirrhosis	Total			
Wound infection	44	27	71			
Intra-abdominal infection	17	8	25			
Other sepsis	1	1	2			
Hepatic failure	9	1	10			
Pneumonia	11	6	17			
Atelectasis	9	7	16			
Pleural effusion	37	24	61			
Bile fistula	3	5	8			
Coagulopathy	9	1	10			
Postoperative bleeding	4	2	6			
Renal failure	9	2	11			
Esophageal varix bleeding	4	0	4			
Total	157	84	241			

complications were found in 142 patients with cirrhosis. Sepsis was the most frequent complication, manifested primarily as wound infection(71 cases) or intra-abdominal infection(25 cases). Nonfatal hepatic failure occured in 9 patients with cirrhosis and 1 patient without cirrhosis. Other complications included pleural effusion(61 cases), pneumonia(17 cases), atelectasis(16 cases), bile fistula(8 cases), coagulopathy (10 cases), postoperative bleeding (6 cases), renal failure(11 cases), esophageal varix bleeding(4 cases) and other sepsis(2 cases).

#### Operative mortality

There were 38 operative deaths among 402 hepatic resections, for an overall operative mortality of 9.4%. Table 4 shows the causes of death of the 38 patients. Twenty five of these patients died from hepatic failure after operation, accounting for 66% of the total operative mortality. Hemorrage from the liver was the primary cause of death in 3 patients and intra-abdominal sepsis a major contributory cause in 5 patients. Other factors contributing to the death of patients were esophageal varix bleeding(3), renal failure(1), and severe chest infection(1). Twenty eight of the 38 deaths were of patients who had pre-existing cirrhosis. Mortality rates varied with the magnitude of the operative procedure. Details of mortality after various kinds of resection are given in Table 2. These are RTS, 1/4; LTS, 1/1; RL, 9/73; LL, 0/36; CBS, 0/3; RS, 9/49; LS, 2/72; SP, 15/164. The mortality rates after resection for HC, CC, intrahepatic cholelithiasis, and benign mass, respectively, were 11.3%, 13.8%, 2.4%, and 2.9% (Table 2). There were 36 operative deaths in the primary malignancy group of 319 patients. These deaths were due predominantly to hepatic failure after resection. Twenty four patients(67%) died of this disorder, with 12 having undergone SP, 6 having undergone RL, 5 having under gone RS, and one having undergone RTS. Two patients died of postoperative bleeding. One

Table 4. Causes of death after hepatic resection for various diagnoses

			Diagnosis		
Cause of death	Hepatocellular carcinoma	Cholangio- carcinoma	Hepato- lithiasis	Benign Mass	Total
Hepatic failure	22(19)*	2(1)		1(1)	25(21)
Hemorrage from liver	2(2)	1(0)			3(2)
Intra-abdominal sepsis	4(3)	1(1)			5(4)
Renal failure			1(0)		1(0)
Chest infection	1(0)				1(0)
Varix bleeding	3(1)				3(1)
Total	32(25)	4(2)	1(0)	1(1)	38(28)

<sup>\* ( ),</sup> number of cases of liver cirrhosis

other patient died of varix bleeding and one of sepsis. There were 32 operative deaths(11.3%) in 282 patients with HC. Mortality rates of HC with and without cirrhosis were 11.3% and 11.5%, respectively. The rate was 11.2% in major hepatic resections for HC and 11.4% in minor hepatic resections (Table 5). There were no operative deaths among the patients who had resection for mixed carcinoma, other primary malignancy, metastatic carcinoma, or gallbladder carcinoma.

# Comparison in indication, operative procedure, complication, and operative mortality by year of operation

Table 6 summarizes differences in indication, operative procedure, complication, and operative mortality between the patients operated on from January 1981 to December1985 (n = 116) and those operated on from January 1986 to December 1990 (n = 286). There has been an increasing frequency of hepatic resection during the last five years. The increased number of hepatic resections was mainly due to resections for HC. Indications for resection increased from 87 to 195 resections for HC. The number of major resections increased from 41 cases in the earlier period to 76 cases in the recent period. The number of minor resections increased from 75 cases in the earlier period to 210 cases in the recent period. The cumulative data show a decrease in the complication rate and operative mortality. In the recent period,

**Table 5.** Mortality rates in patients with hepatocellular carcinoma

	Number of patients	Operative deaths
Operative procedure		
Major resection	80	9
Minor resection	202	23
Presence of cirrhosis		
With cirrhosis	221	25
Without cirrhosis	61	7
Total	282	32
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Table 6. Comparison in diagnosis and operative procedure by year of operation

	Period of study		
		1986-1990 (n = 286)	
Diagnosis			
Hepatocellular carcinoma	87	195	
Cholangiocarcinoma	5	24	
Mixed carcinoma		3	
Hepatoblastoma and others		5	
Metastatic carcinoma	1	3	
Gallbladder cancer		2	
Hepatolithiasis	12	30	
Benign mass	11	24	
Operative procedure			
Major resection	41	76	
Minor resection	75	210	

nonlethal postoperative complications have occured in 135 of 286 patients (47%).

#### Long-term survival

The overall survival rates in 172 patients with HC excluding operative mortalities and palliative resections and reresections, were 71. 0%, 39.8%, 28.3% for 1, 3, and 5 years, respectively. The survival rates of palliatively resected patients with HC were 54.7%, 17.3%, 7.8% for 1, 3, and 5 year, respectively. The overall survival rates of the 26 patients who had undergone curative resection with CC were 67.2%, 59.5%, 45.0% for 1, 3, and 5 years, respectively.

#### DISCUSSION

Our data strongly suggested that most patients with HC in Korea were related with hepatitis B virus and usually accompanied by complications of cirrhosis. Hepatic resection plays an important role in the treatment of primary liver cell carcinoma on the basis of better methods for early diagnosis and many new techniques. The spectrum of diagnostic moda-

lities comprises scintigraphy, ultrasonography, angiography, CT scan, and NMR. Hepatic resection for HC represents the main reason for the increased frequency of hepatic resection in our hospital in the last five years. The results of such resections were often palliation with extended survival rather than complete cure.

The true mortality for hepatic resectional therapy for HC is difficult to assay. One of the main determinants of mortality is the incidence cirrhosis in patients having resection. Another factor that makes it difficult to assay the mortality after hepatic resection for HC is the difference in the methods of reporting mortality. Some reports do not separate the results of primary HC and other liver tumors, and still others do not differentiate between palliative and curative resections (Edwards WH et al. 1990). As regards the operative mortality after resection of HC, the results of most reported series range from 10% to 20% (Iwatsuki et al. 1983; Thompson et al. 1983; Nagao et al. 1985). The difference is related to the number of patients with cirrhosis included in the different series. A mortality rate of 10% to 15% has been reported by authors who use a more conservative segmentary resection in cirrhotic patients (Kanematsu et al. 1984; Lim and Bongard et al. 1984; Okamoto et al. 1985). Operative mortality in our series of HC compares favorably with that reported in other studies. Although direct comparison is difficult since difstudies ferent use different methods presenting results (Iwatsuki et*al.* 1983; Thompson et al. 1983), the survival rate of our study is encouraging because our series included patients who had advanced cirrhosis.

CC is a type of carcinoma arising from any portion of the intrahepatic bile duct epithelium, and accounts for about 6.4% to 25% of the primary carcinomas of the liver (Edmondson and Steiner 1954; The Liver Cancer Study Group of Japan 1987). Of 29 cases of resected cholangiocarcinomas at our institution, 5 cases were associated with clonorchiasis. The general gross pathologic findings of C. sinensis associated CC in Korea, Hong Kong and

China, where C. sinensis infection is endemic, are not basically different from the usual peripheral cholangiocarcinomas; regardless of C. sinensis infection, the usual peripheral CCs grow similarly in a nodular infiltrative pattern and disclose no intraductal tumor growth dam YI et al. 1989). Reports of significant surveal resection for CC and following carcinomas are few. Often these tumors are included with HC in reports of survival following resection for primary carcinomas of the liver. If curative resection is done, the prognosis of peripheral CC will be better than that of HC because of less frequent association with cirrhosis. Hepatoblastoma is a rare malignancy in children and early surgical resection combined with chemotherapy and radiation, or both, has improved the prognosis. Our experience with hepatic resection for hepatoblstoma is too small for meaningful comparison with other series.

Gall bladder carcinomas are, when found, very often, untreatable for cure. The overall 5 year survival rate of patients whose tumors are resectable yet extend microscopically outside the wall is 10% to 15% (Meyers and Jones 1990).

As the morbidity and mortality for hepatic resection have decreased, there has been a more liberal use of resection of benign masses of the liver (Edwards et al. 1990). In this study, the most common benign primary lesion that required resection for pain or a mass was a hemangioma. Resection of segments or a lobe of the liver was occasionally indicated for nonparasitic for diffuse cysts, multiple abscesses confined to a resectable area, and for adenomatous hyperplasias. Mortality rates are low and long-term follow-up is excellent after resection of benign masses.

The overall incidence of complications in this series was 53.6%. In our patients, complications after hepatic resection compare favorably with those noted in other large series (Ekberg *et al.* 1986; Nagasue *et al.* 1985 ). The most frequent complication after hepatic resection was sepsis, manifested as wound infection

or intraabdominal infection. This finding is in accordance with others (Stone and Benotti 1989). To decrease the mortality and morbidity rates from hepatic resection, some clinicians have applied objective methods to asses the predictability of morbidity and death (Christou et al. 1986; Knaus et al. 1985). Overall mortality rate in our patients was similar to other major series (Nagao et al. 1985; Iwatsuki et al. 1983; Bengmark et al. 1982). The majority of postoprative deaths occured in patients who underwent resection of two or more segments of cirrhotic liver. Selection of patients by assessment of hepatic function and reserve is necessary before attempting extensive resection. We have seen a major change in the number of hepatic resections with a sharp increase in the number of resections for HC recently. There has also been a shift to a greater number of resections done for benign and other malignant conditions. Our results demonstrate that operative results improved steadily. However, the operative risk in hepatic resection is still higher than that in other surgical procedures and advanced cirrhosis generally precludes a major hepatic resection. The role of resection as treatment must be considered in relation to the selection of cirrhotic patients for resective surgery.

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