

Experience with Resection of Primary Hepatic Malignancy

Shunzaburo Iwatsuki, MD,* and Thomas E. Starzl, MD, PhD†

Although hepatocellular carcinoma is one of the most common malignancies worldwide, primary hepatic malignancy (including hepatocellular carcinoma) is a relatively uncommon neoplasm in the United States and other Western countries. Nevertheless, the authors had treated 106 patients with primary hepatic malignancy by various kinds of hepatic resection by the end of 1987. The experience is summarized here with emphasis on operative mortality, some aspects of surgical technique, and long-term follow-up. Portions of our experience have been reported earlier.^{5,6,12-16}

CASE MATERIALS

During the 23-year period from October 1964 to December 1987, 411 patients underwent hepatic resection at the University of Colorado Health Sciences Center (1964 to 1980) and the University Health Center of Pittsburgh (1981 to 1987). The number of hepatic resections increased sharply through the years (Table 1), 78 patients being treated in 1987 alone. The indications for hepatic resection in the total series were primary hepatic malignancy in 106 patients, secondary hepatic malignancy in 123 patients (including 90 patients with metastases from colorectal cancer), and histologically benign hepatic lesions in 182 patients. Histologic diagnoses of the 106 patients with primary hepatic malignancy are listed in Table 2. The liver was grossly cirrhotic in 16 of these 106 patients. The ages of the 106 patients ranged from 5 to 86 years old, with a mean of 55. Fifty-six were male, and 50 were female.

From the Department of Surgery, University Health Center of Pittsburgh, University of Pittsburgh, and the Veterans Administration Medical Center, Pittsburgh, Pennsylvania.

*Associate Professor

†Professor

Supported by research grants from the Veterans Administration and Project Grant No. AM 29961 from the National Institutes of Health.

Table 2. *Histologic Diagnoses of 106 Patients with Primary Hepatic Malignancy*

	NO
Hepatocellular carcinoma	67
Fibrolamellar	12
Nonfibrolamellar	55
Cholangiocarcinoma	14
Bile duct cancer (Klatskin tumor)	6
Carcinoma of hepatic cyst wall	4
Leiomyosarcoma	2
Rhabdomyosarcoma	2
Hepatoblastoma	1
Angiosarcoma	1
Adenocarcinoma of gallbladder	1
Sarcoma, undetermined cell type	1
Neuroendocrine tumor	1
Adenocarcinoma	1
Unclassified malignancy	2

Survival Rates

Overall survival rates of the 106 patients with malignancy were 54.9 per cent at 3 months, 79.1 per cent at 6 months, 68.5 per cent at 1 year, 53.9 per cent at 2 years, 45.1 per cent at 3 years, 37.2 per cent at 4 years, and 31.9 per cent at 5 years after hepatic resection (Fig. 2).

All of the 12 patients who had had hepatic resection for fibrolamellar hepatocellular carcinoma are alive, nine of whom are free of tumor between 1 and 15 years after resection, and three of whom are living with recurrence 1, 2, and 6 years after resection (Fig. 3). One- to five-year survival rates of 55 patients with nonfibrolamellar hepatocellular carcinoma were 76.2 per cent, 65.2 per cent, 49.0 per cent, 36.7 per cent, and 25 per cent, respectively, and those of 14 patients with cholangiocarcinoma were 78.6 per cent, 45.6 per cent, 39.5 per cent, 39.5 per cent, and 39.5 per cent (Fig. 3).

The six patients with bile duct cancer (Klatskin tumor) were treated with right trisegmentectomies (five cases) or left lateral trisegmentectomy (one case). One of the patients treated with trisegmentectomy died from hepatic failure within a month, and another patient died in the eighth month from recurrence. One patient is alive with disease in the eighth month, and two are alive, free of disease, in the seventh and twelfth month after trisegmentectomy. One patient who had had left lateral segmentectomy died in the fourth year from recurrent tumor.

The four patients with single hepatic cysts that had malignant degeneration in the wall were treated by three trisegmentectomies and one local nonanatomic resection. Three patients treated with trisegmentectomy died from recurrence of squamous cell cancer 6, 10, and 16 months after trisegmentectomy. The fourth patient, whose solitary cyst contained a small adenocarcinoma, is alive and free of tumor 15 months after local excision.

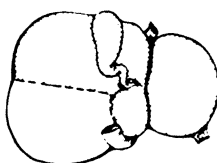
Five-Year Survival

There were 18 patients who survived more than 5 years after hepatic resection for primary hepatic malignancy (Table 5). The histologic diagnoses were varied, but 5-year survivors were more frequent among the patients with fibrolamellar hepatocellular carcinoma (5 of 12) and among patients with cholangiocarcinoma (4 of 14) than among the patients with hepatocellular carcinoma (6 of 55). It is also worth noting that there was an overrepresentation of trisegmentectomies (14 of 18). Three

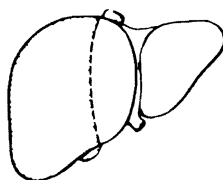
RT. TRISEGMENTECTOMY



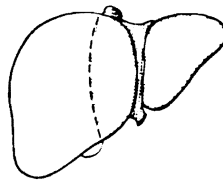
LT. TRISEGMENTECTOMY



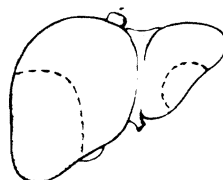
RIGHT LOBECTOMY



LEFT LOBECTOMY



NON-ANATOMICAL RESECTION



LT. LATERAL SEGMENTECTOMY

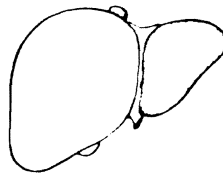


Figure 1. Six categories of hepatic resection.

Table 3. Extent of Hepatic Resection Used for Primary Hepatic Malignancy and Operative Mortality Rate

EXTENT OF RESECTION	NUMBER OF PATIENTS	NUMBER OF OPERATIVE DEATHS
Right trisegmentectomy	50	5
Left trisegmentectomy	8	2
Right lobectomy	17	1
Left lobectomy	18	0
Left lateral segmentectomy	4	0
Nonanatomic resection	9	1
Total	106	9

RESECTION OF PRIMARY HEPATIC A

Table 4. Time to

AGE SEX	DIAGNOSIS*	
50 M	HCC in cirrhosis	Rt. lob.
77 M	HCC in cirrhosis	Nonan.
55 F	Cholangiocarcinoma	resec
52 F	Neuroendocrine tumor	Lt. tris
36 F	HCC in cirrhosis	Rt. tris
45 M	HCC	Rt. tris
63 M	HCC in cirrhosis	Lt. tris
64 F	Cholangiocarcinoma	Rt. tris
62 M	Bile duct cancer	Rt. tris

Abbreviation: HCC = hepatocellular

of the 5-year survivors died from the disease between 5 and 7 years after

Hepatic resection can now be performed in the world with an operative mortality rate of 3.2 per cent. The mortality rate of trisegmentectomy and only 1.9 per cent in treating primary hepatic malig-

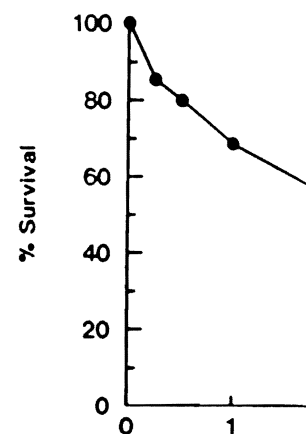


Figure 2. Actuarial survival rates of hepatic resection.

Table 4. Time and Cause of Operative Death

AGE SEX	DIAGNOSIS*	PROCEDURE	TIME OF DEATH (DAY)	CAUSE OF DEATH
50 M	HCC in cirrhosis	Rt. lobectomy	0	Perforation of CVP catheter into pericardium
77 M	HCC in cirrhosis	Nonanatomical resection	0	Myocardial infarction
55 F	Cholangiocarcinoma	Lt. trisegmentectomy	0	Hemorrhage
52 F	Neuroendocrine tumor	Rt. trisegmentectomy	0	Hemorrhage
36 F	HCC in cirrhosis	Rt. trisegmentectomy	0	Hemorrhage
45 M	HCC	Rt. trisegmentectomy	6	Hepatic failure in transplant
63 M	HCC in cirrhosis	Lt. trisegmentectomy	7	Hepatic failure
64 F	Cholangiocarcinoma	Rt. trisegmentectomy	20	Hepatic failure; celiac axis thrombosis
62 M	Bile duct cancer	Rt. trisegmentectomy	29	Hepatic failure

Abbreviation: HCC = hepatocellular carcinoma.

of the 5-year survivors died from tumor recurrence, and three more are living with disease between 5 and 7 years after hepatic resection.

DISCUSSION

Hepatic resection can now be performed safely at many medical centers around the world with an operative mortality rate of less than 5 per cent.¹⁻⁴ In our most recent review of 411 hepatic resections,⁵ the overall operative mortality rate was 3.2 per cent. The mortality rate was the highest, 6.3 per cent (9 of 142), after trisegmentectomy and only 1.9 per cent (3 of 158) after lobectomy. The mortality rate in treating primary hepatic malignancy was 5.5 per cent (9 of 106), but there

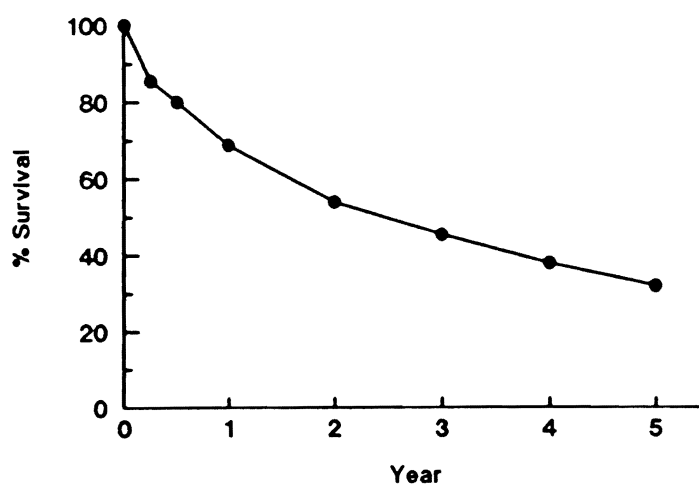


Figure 2. Actuarial survival rates of 106 patients with primary hepatic malignancy after hepatic resection.

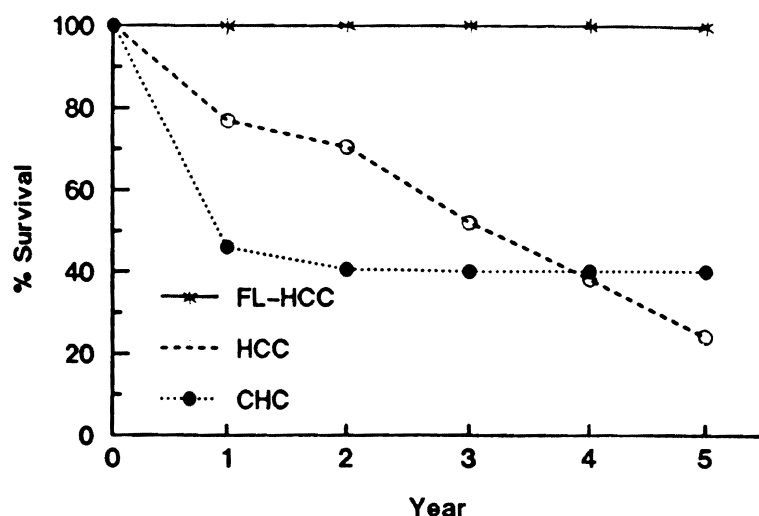


Figure 3. Survival of patients with fibrolamellar hepatocellular carcinoma ($n = 12$) was better ($P < 0.01$) than that of patients with nonfibrolamellar hepatocellular carcinoma ($n = 55$) and with cholangiocarcinoma ($n = 14$) after hepatic resection.

were no deaths in 123 resections for metastatic tumor. Of the 411 patients, 17 had gross cirrhosis, and five of these (29.4 per cent) died within a month after resection. Four of the nine deaths after resections for primary hepatic malignancy were of patients with obvious cirrhosis. In contrast, overall operative mortality rate in those without gross cirrhosis was 2 per cent (8 of 394). Excluding the 16 patients with gross cirrhosis, the mortality rate of patients with primary hepatic malignancy was 5.6 per cent (5 of 90) after resection. Further reduction of the operative mortality rate will be achieved by selecting some patients with massive tumor or with gross cirrhosis for orthotopic liver transplantation.^{7, 9, 10, 11}

Acknowledging the limitation in comparing the survival rates without proper staging of the malignant tumor, our 1-, 3-, and 5-year actuarial survival rates of 65.5 per cent, 45.1 per cent, and 31.9 per cent, respectively, are similar to or even better than those reported in the literature.^{1-4, 9} The fact that more than half of our patients required trisegmentectomy to remove their massive tumors illustrates the advanced stages of malignancy in our series. Despite this, 15 patients lived more

Table 5. Fate of 15 Patients with Primary Hepatic Malignancy Who Lived 5 Years after Hepatic Resection

	FIBROLAMELLAR	HCC	CHC	OTHERS*	TOTAL
Number	5	6	4	3	15
Operation					
Trisegmentectomy	5	4	2	3	14
Lobectomy	0	2	2	0	4
Died >5 years	0	2	1	0	3
Year of death	-	5,5	6	0	-
Living >5 years	5	4	3	3	15
Survival (years)	6,7,8,9,15	6,7,7,12	6,6,6,8	16,16,16	-

*Hepatoblastoma, leiomyosarcoma, and rhabdomyosarcoma.

†Living with recurrence.

Abbreviations: Fibrolamellar = fibrolamellar variant of hepatocellular carcinoma, HCC = nonfibrolamellar hepatocellular carcinoma, CHC = cholangiocarcinoma.

than 5 years after hepatic resection. Extensive hepatic resection, such as extended lobectomy, must be performed with free margins.

Identification of the fibrolamellar variant of hepatocellular carcinoma is important. This tumor is usually found in other types of hepatocellular carcinoma. Its prognosis after partial hepatic resection is better than that of other types of hepatocellular carcinoma, and its resection is warranted for fibrolamellar hepatocellular carcinoma.

The results after liver transplantation for hepatocellular carcinoma have been quite as good.^{6, 9, 10, 11} Although the prognosis is very high, late tumor recurrence after transplantation has resulted in the long-term survival rates not being reported previously.^{6, 9, 10} As with resection, are the fibrolamellar variant of hepatocellular carcinoma, the fibroepithelioma.^{7, 9, 10, 11} Apparent benign malignancies after liver transplantation have been reported.

We have commented in the past on the importance of having the competent surgical armamentarium at the time of resection.

Our experience with hepatic resection has been summarized as a part of our review of various indications. The operative approach in treating primary hepatic malignancy after resection of 411 hepatic resection was 3.2 per cent, 45.1 per cent, and 31.9 per cent, respectively, for fibrolamellar hepatocellular carcinoma, patients with nonfibrolamellar hepatocellular carcinoma, and patients with cholangiocarcinoma, respectively. The most important indication for trisegmentectomy rather than massive tumors with adequate

1. Adson MA, Weiland LH, Bessner M. *Ann Surg*. 1981;193:21.

2. Berman MM, Libbey NP, Fink A. *Am J Surg*. 1980;140:100.

3. Craig JB, Peters RL, Edmonson AH. *Am J Surg*. 1980;140:372-379.

than 5 years after hepatic resection, and 14 did so after trisegmentectomy. Therefore, extensive hepatic resection, such as right or left trisegmentectomy rather than extended lobectomy, must be utilized to remove large tumors with adequate tumor-free margins.

Identification of the fibrolamellar variant of hepatocellular carcinoma is important. This tumor is usually firm and bulky and is found in younger patients than other types of hepatocellular carcinoma. Despite the large size of the tumor, its prognosis after partial hepatic resection or after liver transplantation is significantly better than that of other types of hepatoma.^{5, 6, 8, 10, 15} Aggressive surgical treatment is warranted for fibrolamellar hepatocellular carcinoma.

The results after liver transplantation for primary hepatic malignancy have not been quite as good.^{6, 8, 10, 11} Although the survival rate for the first year has been very high, late tumor recurrence has plagued these efforts. Yet, liver transplantation has resulted in the long-term success on more than the isolated occasion, as has been reported previously.^{6, 8, 10, 11} The most favorable lesions for transplantation, just as with resection, are the fibrolamellar hepatoma and the epithelioid hemangioendothelioma.^{7, 8, 10, 11} Apparent cures have been achieved in about half of these malignancies after liver transplantation.^{7, 8, 10, 11} Small hepatocellular carcinomas in advanced cirrhosis have been cured in nearly all cases after transplantation.^{7, 8, 10, 11}

We have commented in the past that no surgeon should explore a hepatic mass without having the competence to perform all the major resections, including the trisegmentectomies.¹² Today, liver transplantation should also be part of the obligatory armamentarium at the medical centers where hepatic tumors are often treated.

SUMMARY

Our experience with hepatic resection for 106 primary hepatic malignancies has been summarized as a part of a total experience with 411 hepatic resections for various indications. The operative mortality rate (death within a month) was 5.5 per cent in treating primary hepatic malignancy, which is significantly higher than that of treating hepatic metastases (0 of 123 resections). Overall operative mortality of 411 hepatic resection was 3.2 per cent. A high operative risk was noted in patients with gross cirrhosis, trauma, abscess, and large malignant tumors. The 1-, 3-, and 5-year survival rates of patients with primary hepatic malignancy were 65.5 per cent, 45.1 per cent, and 31.9 per cent, respectively. Survival rates of patients with fibrolamellar hepatocellular carcinoma were significantly higher than those of patients with nonfibrolamellar hepatocellular carcinoma. Eighteen patients survived more than 5 years after hepatic resection, 14 of whom had been treated by trisegmentectomy. The most extensive partial hepatectomy, such as right and left trisegmentectomy rather than extended lobectomies, should be used to remove massive tumors with adequate tumor-free margins.

REFERENCES

1. Adson MA, Weiland LH. Resection of primary solid hepatic tumors. *Am J Surg* 141:15-21, 1951
2. Berman MM, Libbey NP, Foster JH. Hepatocellular carcinoma. Polygonal cell type with fibrous stroma—an atypical variant with a favorable prognosis. *Cancer* 46:1445-1455, 1950
3. Craig JB, Peters RL, Edmonson HA, et al. Fibrolamellar carcinoma of the liver. A tumor of adolescents and young adults with distinctive clinicopathologic features. *Cancer* 46:372-379, 1950

= 12) was
oma (n =

ts, 17 had
resection.
v were of
e in those
ents with
nancy was
mortality
with gross

at proper
d rates of
o or even
alf of our
rates the
sed more

TOTAL
18
14
4
3
15
—

ma. HCC

4. Fortner JG, MacLean BJ, Kim DK, et al: The seventies evolution in liver surgery for cancer. *Cancer* 47:2162-2166, 1981
5. Iwatsuki S, Starzl TE: Personal experience with 411 hepatic resections. *Ann Surg* 208:421-434, 1988
6. Iwatsuki S, Shaw BW Jr, Starzl TE: Experience with 150 liver resections. *Ann Surg* 197:247-253, 1983
7. Iwatsuki S, Gordon RD, Shaw BW Jr, et al: Role of liver transplantation in cancer therapy. *Ann Surg* 202:401-407, 1985
8. Iwatsuki S, Starzl TE, Todo S, et al: Experience in 1,000 liver transplants under cyclosporine-steroid therapy: A survival report. *Transplant Proc* 20:498-504, 1988
9. Lin TY, Chen KM, Chen CC: Role of surgery in the treatment of primary carcinoma of the liver: A 21-year experience. *Br J Surg* 74:539-542, 1987
10. O'Grady JA, Polson RJ, Rolles K, et al: Liver transplantation for malignant disease: Results in 93 consecutive patients. *Ann Surg* 207:373-379, 1988
11. Pichlmayr R: Is there a place for liver grafting for malignancy? *Transplant Proc* 20:Suppl 1:475-482, 1988
12. Starzl TE, Iwatsuki S: Liver resection for primary hepatic neoplasms. *Acta Chirg Austria* 4:374-379, 1985
13. Starzl TE, Bell RH, Beart RW, et al: Hepatic trisegmentectomy and other liver resections. *Surg Gynecol Obstet* 141:429-437, 1975
14. Starzl TE, Iwatsuki S, Shaw BW Jr, et al: Left hepatic trisegmentectomy. *Surg Gynecol Obstet* 155:21-27, 1982
15. Starzl TE, Iwatsuki S, Shaw BW Jr, et al: Treatment of fibrolamellar hepatoma with partial or total hepatectomy and transplantation of the liver. *Surg Gynecol Obstet* 162:145-148, 1986
16. Starzl TE, Koep JL, Weil R III, et al: Right trisegmentectomy for hepatic neoplasms. *Surg Gynecol Obstet* 150:205-214, 1980

Shunzaburo Iwatsuki, MD
 Department of Surgery, Falk Clinic 4 West
 3601 Fifth Avenue
 Pittsburgh, PA 15213

Recent years have seen a change in the management of liver disease. In the late 1970's and only very recently, there has been a change of attitude towards the biliary tract, and a better understanding of the extent of the disease, closely related to liver atrophy, which is now appreciated and available as a result of CT scanning. A large number of patients who were once considered inoperable are now frequently diagnosed, and 50 per cent of cases are resectable.

Radical resection of the biliary apparatus, localized in the Roux-en-Y, is being less than in whom there is no liver or into the hilum, the hilar blood vessels, sectoral hepatic involvement of the removal of the liver. This article concerns whom hepatic resection operative approach.

*Professor of Surgery
 Transplantation

*Senior Lecturer
 graduate Medicine

Surgical Clinics of N