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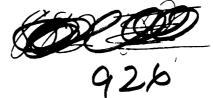
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Experience with Resection

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 1950) 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 cincluding 90 patients with metastases from colorectal cancer, and histologically benign hepatic lesions in 152 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 S6 years old, with a mean of 55. Fifty-six were male, and 50 were female.

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Table 1. Incidence of Hepatic Resection by 5-Year Period and Indication

YEARS	NUMBER OF PATIENTS	PRIMARY MALIGNANCY	SECONDARY MALIGNANCY	BENIGN LESION
1964-1970	6	2	0	4
1971-1975	25	10	5	10
1976-1980	77	17	28	32
1981-1985	151	43	51	57
1986-1987	122	34	39	49
Total	411	106	123	152

RESECTION TECHNIQUES AND CLASSIFICATION

Our operative techniques have been described in detail elsewhere with emphasis on right trisegmentectomy and left trisegmentectomy. ^{13, 14, 16} The extent of hepatic resection was classified into the following six categories (Fig. 1): right and left trisegmentectomy, right and left lobectomy, left lateral segmentectomy, and nonanatomic local resection. In brief, right trisegmentectomy is the complete removal of the right lobe plus the medial segment of the left lobe, where the caudate lobe is also completely removed or its left posterolateral portion is spared, depending on the location of the hepatic lesion. Extended right lobectomy, which removes only a portion of quadrate lobe and of the right side of the caudate lobe with the right lobe, was classified as right lobectomy in this report. Left trisegmentectomy is the complete removal of the left lobe plus the anterior segment of the right lobe, where the caudate lobe alongside the retrohepatic vena cava is removed or spared as dictated by the location of the hepatic lesion. Extended left hepatic lobectomy, which removes only a portion of the anterior segment of the right lobe with the left lobe, was classified as the left lobectomy.

Nonanatomic local excision in our classification is not equivalent to "wedge resection." This type of hepatic resection was applied mostly for benign hepatic lesions, but when it was utilized for malignant lesions, the anatomic resection could not be done because of associated cirrhosis or the presence of severe cardiopulmonary disease. The tissue mass excised by nonanatomic local resection is as large as or larger than the left lateral segment.

The kinds of hepatic resection used for primary hepatic malignancy are summarized in Table 3, including the operative deaths.

RESULTS

Operative Mortality

Any death within a month after hepatic resection was counted as an operative death. Nine of the patients with primary hepatic malignancy died within this time, for an operative mortality rate of 5.5 per cent. The rate was considerably higher after trisegmentectomy (seven deaths, 12 per cent operative mortality rate than after lobectomy (1 of 35, 3 per cent) or lateral segmentectomy or nonanatomic resection (1 of 13, 8 per cent).

The circumstances of the operative deaths are summarized in Table 4. Four of the deaths occurred in patients with grossly cirrhotic livers. Five patients died intraoperatively, three from hemorrhage and one each from myocardial infarction and perforation of the atrium by a central venous catheter. Four more patients died from liver failure, two within a week and two within a month after hepatic resection.

Table 2. Histologic Dv

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Survival Rates

Overall survival rat at 3 months, 79.1 per cyears, 45.1 per cent at years after hepatic resec

All of the 12 patier cellular carcinoma are years after resection. a years after resection. From the first resection of the first resecti

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Five-Year Survival

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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 \$4.9 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, 68.2 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).

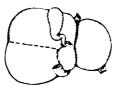
The six patients with bile duct cancer (Klatskin tumor) were treated with right trisegmentectomies (five cases) or left lateral trisegmentectomy (one case). One of the patients treated with trisegmentectomy died from hepatic failure within a month, and another patient died in the eighth month from recurrence. 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.

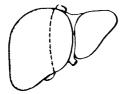
Five-Year Survival

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 trisegmentectomics (14 of 15). Three

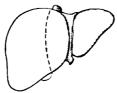




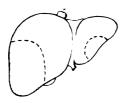
RIGHT LOBECTOMY



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	()
Left lateral segmentectomy	4	0
Nonanatomic resection	9	1
Total	106	9

RESECTION OF PRIMARY HEPATIC X

Table 4. Time a

AGE SEX	DIAGNOSIS*	
50/M	HCC in cirrhosis	Rt. lob
77/M	HCC in cirrhosis	Nonan
55 F	Cholangiocarcinoma	Lt. tris
52 F	Neuroendocrine tumor	Rt. tris-
36 F	HCC in cirrhosis	Rt. tris-
45/M	HCC	Rt. tris-
63/M	HCC in cirrhosis	Lt. tris-
64 F	Cholangiocarcinoma	Rt. trise
62 M	Bile duct cancer	Rt. triv
Abb	reviation: HCC = her	oatocellu

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

Hepatic resection can now be p

the world with an operative mortalirecent review of 411 hepatic resection 3.2 per cent. The mortality rate was trisegment ectomy and only 1.9 pc $^{\circ}$ rate in treating primary hepatic $m_{\rm c}$.

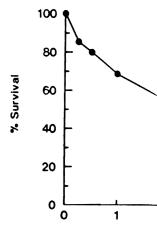


Figure 2. Actuarial survival rates of hepatic resection.

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 + ⁷ 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 8.5 per cent (9 of 106), but there

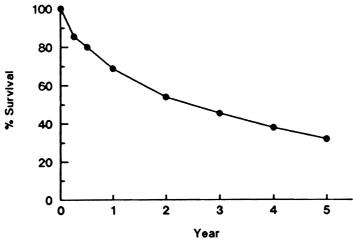


Figure 2. Actuarial survival rates of 106 patients with primary hepatic mahgnancy after hepatic resection.

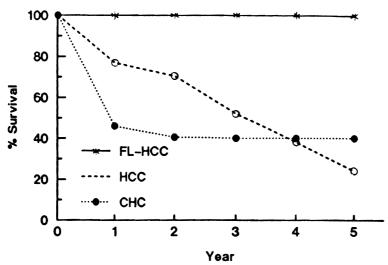


Figure 3. Survival of patients with fibrolamellar hepatocellular carcinoma (n = 12) was better (P < 0.01) than that of patients with nonfibrolamellar hepatocellular carcinoma (n = 55) and with cholangiocarcinoma (n = 14) after hepatic resection.

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 § 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. 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 18 Patients with Primary Hepatic Malignancy Who Lived 5 Years after Hepatic Resection

	FIBROLAMELLAR	HCC	CHC	OTHERS*	TOTAL
Number	5	6	4	.}	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+,8	16.16.16	

^{*}Hepatoblastoma, leiomyosarcoma, and rhabdomyosarcoma.

RESECTION OF PRIMARY HEFAT

than 5 years after hepatic resection. sextended lobectomy, must be free margins.

Identification of the fibrolant. This tumor is usually fir other types of hepatocellular prognosis after partial hepatic better than that of other types is warranted for fibrolamellar!

The results after liver trabeen quite as good. § 5.9 H Alwery high, late tumor recurrent has resulted in the long-term been reported previously. § 5.9 as with resection, are the fibre dothelioma. § 5.10 H Apparent malignancies after liver transgadyanced cirrhosis have been.

We have commented in the without having the competent trisegmentectomies. ¹² Today . ¹, atory armamentarium at the management of the m

Our experience with her has been summarized as a part various indications. The operation treating primary hepath of treating hepatic metastases 411 hepatic resection was 3.2 with gross cirrhosis, trauma and 5-year survival rates of pathocent, 45.1 per cent, and 31.4 glibrolamellar hepatocellular patients with nonfibrolamellar more than 5 years after her trisegmentectomy. The most trisegmentectomy rather than massive tumors with adequations.

[†]Living with recurrence.

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

¹ Adson MA, Weiland LH, Bes 21, 1951

² Berman MM, Libbey NP, F s fibrous stoma—an atypica 1980

Craig JB, Peters RL, Edmors of adolescents and young 46.372–379, 1980

than 5 years after hepatic resection, and 14 did so after trisegment ectomy. Therefore, extensive hepatic resection, such as right or left trisegment ectomy 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. So So No. 18 Aggressive surgical treatment is warranted for fibrolamellar hepatocellular carcinoma.

The results after liver transplantation for primary hepatic malignancy have not been quite as good.^{6,5,10,11} 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.^{6,5,10,11} The most favorable lesions for transplantation, just as with resection, are the fibrolamellar hepatoma and the epithelioid hemangioendothelioma.^{7,5,10,11} Apparent cures have been achieved in about half of these malignancies after liver transplantation.^{7,5,10,11} Small hepatocellular carcinomas in advanced cirrhosis have been cured in nearly all cases after transplantation.^{7,5,10,11}

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.

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