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Major Hepatic Resection

A 25-Year Experience

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Major hepatic resections were performed on 138 patients for a variety of conditions. There was one intraoperative death. Including this patient, there were 15 deaths within 30 days of the operation (operative mortality 10.9%). Important postoperative complications were intra-abdominal sepsis (17%), biliary leak (11%), hepatic failure (8%), and hemorrhage (6%). The results of 30 resections for the benign lesions, liver cell adenoma, focal nodular hyperplasia, hemangioma, and cystadenoma showed no operative mortality and low morbidity. Of 26 patients with hepatocellular carcinoma, seven died within a month of operation. The cumulative survival of the 26 at five years was 38%, and of the 19 who survived the procedure, 51%. Poor survival followed resections for cholangiocarcinoma and "mixed tumors." The five-year cumulative survival of 22 patients who had colorectal metastases excised was 31%. Apart from a patient with carcinoid, prolonged survival was rare after resection of other secondaries and after en bloc resections for tumors directly invading the liver. Hepatic resection was of value in the management of some patients with hepatic trauma, Caroli's disease, liver cysts, and intrahepatic stones.

SINCE THE FIRST elective hepatic resections were performed nearly a century ago,[1-3] the basic anatomic,[4-5] pathophysiologic,[6,7] and operative principles[8,9] of liver surgery have been elucidated. Advances in the diagnosis and assessment of liver diseases,[9] anesthesia, and postoperative care have made liver resection a reasonably safe surgical procedure. However, major hepatic resection remains a rarely performed operation. In the Liver Tumor Survey of 1974, Foster and Berman[10] needed to visit 98 centers throughout the United States in order to collect 621 cases of major hepatic resection for liver tumors. Cady and his colleagues found that only 48 hepatic resections had been performed at the Lahey Clinic, a center renowned for its interest in hepatobiliary surgery, over a 26-year period up to 1978.

Opinions differ regarding several aspects of hepatic resection. These include the nature of the preoperative assessment[5,12,13] and the operative technique.[8,9] More importantly, there is no consensus regarding the indications for hepatic resection and the prognosis following resection for neoplastic and nonneoplastic conditions.[9] This report details the experience of major hepatic resection gained at one center over a 25-year period. An attempt is made to define its role in surgical practice. Particular emphasis is given to complications and survival after operation.

Patients and Methods

Notes of patients who had undergone major hepatic resections at UCLA Hospital and Clinics between 1955 and 1980 were retrieved using the computerized diagnostic indices of the medical records and pathology departments. From these, relevant information concerning diagnosis, operative procedure, and outcome was gathered. Further follow-up information was obtained by contacting the patient and the referring doctor, or if this failed, by contacting known relatives.

The nomenclature of the liver tumors is based upon that of Foster and Berman's[10] modification of Edmondson's classification.[14] "Cholangiocarcinoma" is used to

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TABLE 1. *Number of Various Procedures Performed in Adults and Children*

	RL		ERL		LL		LLS		En Bloc		Wedge		Combination		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Child	6	32	2	10	6	32	1	5	0	0	4	21	0	0	19	100
Adult	36	30	11	9	15	13	21	18	7	6	25	21	4	3	119	100
Total	42	30	13	10	21	15	22	16	7	5	29	21	4	3	138	100

describe a solid intrahepatic tumor derived from small bile ducts, whereas "bile duct carcinoma" is used to describe a tumor arising from the major bile ducts. A "mixed tumor" is one that contains features of both the hepatocellular carcinoma and the cholangiocarcinoma. Mesenchymal and embryonal tumors were frequently difficult to classify.

Operative procedures were classified into right lobectomy (RL), extended right lobectomy (ERL), left lobectomy (LL), left lateral segmentectomy (LLS), wedge resection, and en bloc resection according to the definitions of previous authors.[9,10]

Survival following resection in those diagnostic groups with a sufficient number of patients is expressed as the percentage cumulative survival.[15]

TABLE 2. *Number of Resections Performed for Various Neoplastic Lesions in Adults and Children*

	Children		Adult		Total	
	No.	%	No.	%	No.	%
1) Malignant Primary						
Hepatocellular carcinoma	7	37.0	19	16.0	26	18.8
Cholangiocarcinoma	—	—	2	1.7	2	1.5
Mixed hep-chol	—	—	3	2.5	3	2.2
Hepatoblastoma	3	16.0	—	—	3	2.2
Cystadenocarcinoma	—	—	1	0.8	1	0.7
2) Benign						
LCA	—	—	5	4.2	5	3.6
FNH	2	10.5	5	4.2	7	5.1
Cystadenoma	—	—	1	0.8	1	0.7
Hemangioma	—	—	17	14.3	17	12.3
3) Secondary						
Colon	—	—	22	18.5	22	15.9
Others	—	—	8	6.7	8	5.8
4) Direct Invasion						
Bile Duct	—	—	4	3.4	4	2.9
Others	—	—	10	8.4	10	7.2
5) Cholangioma? Secondary?	—	—	2	1.7	2	1.5
6) Mesenchymal and Embryonal	4	21	4	3.4	8	5.8

The per cent value refers to the total number of resections in the groups.

Results

One hundred thirty-eight major liver resections were performed during the 25-year period. Sixty-four per cent of these were carried out during the last ten years of the study period. The mean age of the patients was 43 years, and the age range was three months to 79 years. There were 19 children (patients less than 16 years old). Fifty-nine per cent of the adult patients were female. This slight female predominance was attributable to the higher incidence of benign liver tumors (liver cell adenoma, focal nodular hyperplasia, and hemangioma) found in this sex.

The numbers of each procedure performed in adults and children are shown in Table 1. Fifty-six per cent of patients had a hepatic lobectomy.

Indications

The various diagnoses for which resection was performed are shown in Tables 2 and 3. Details of the patients with some of these are given below. The symptoms of patients with selected diagnoses are tabulated in Table 4.

Hepatocarcinoma. The mean age of the 26 patients with hepatocarcinoma was 41 years, and the age range was nine months to 79 years. Seven of the patients were children. The mean length of history at presentation was 11 months; one patient had a history of an abdominal mass for eight years. Eighteen patients had abdominal pain or discomfort, five had noticed an abdominal mass, and four had no symptoms referrable to the hepatic tumor; for example, in one patient a small tumor was found as an incidental finding during cholecystectomy and in another, the liver was found to be enlarged while the patient was being investigated for anemia. Two patients presented acutely with rupture of and hemorrhage from the tumor. Another patient presented seven years after a mastectomy and bilateral oophorectomy for carcinoma of the breast. She is alive and well 12 years after her liver resection. It is conceivable that her liver tumor could have been mistakenly diagnosed as a secondary breast carcinoma and not have been resected. Three patients had been on steroids (oral contraceptives one, steroids for asthma one, estrogens for urticaria one).

Eighteen patients had a palpably enlarged liver, one had jaundice, and one had fever. In 23 patients in whom the result was available, the serum alkaline phosphatase (SAP) was elevated in 15. Similarly, the serum aspartate transaminase (AST) was raised in 12 out of 23 and the serum alanine transaminase (ALT) in 11 of 18. Rarely was the transaminase level greater than three times the upper limit of normal. Serum alpha fetoprotein estimations were performed in nine patients and found to be significantly raised in four.

Mixed hepatocellular-cholangiocellular carcinoma. One of the three patients in this group presented with hypercalcemia, presumably due to ectopic production of parathormone by the tumor. His serum calcium level fell after hepatic resection, only to rise again when the tumor recurred. This and another patient in this group had a history of alcohol abuse.

Hepatoblastoma. The three patients with this diagnosis were all under two years old. One had vomiting as the only symptom at presentation. All three had easily palpable livers. Serum alpha fetoprotein was considerably elevated in the two patients in whom it was estimated.

Liver cell adenoma (LCA). The mean age of the five LCA patients was 32 years, with a range of 22 to 44 years. All were women. Two presented acutely with bleeding into the tumor, one of which had ruptured with a resulting hemoperitoneum. The longest history was ten months. Two patients had been taking oral contraceptives and one Premarin. In three the liver tumor was palpable. The SAP was elevated in three out of four patients, the AST in three out of four, and the ALT in two out of three patients in whom results were available.

Focal nodular hyperplasia (FNH). The mean age of the seven patients with FNH was 34 years with a range of seven to 51 years. All were women. Four were asymptomatic. In four the liver tumor was palpable. Two had been taking oral contraceptives. The SAP was elevated in four out of the seven. The AST was elevated in one out of five and the ALT in one out of four patients in whom they were measured.

Cystadenoma. The single patient with this diagnosis had been having estrogen injections.

Hemangioma. The mean age of the 17 patients with hemangioma was 48 years with a range of 32 to 65 years. Fourteen had abdominal pain or discomfort and seven had noticed an abdominal mass. The longest history was 15 years. Two had been taking oral contraceptives and two had been on Premarin. Thirteen had a palpable liver mass. The SAP was elevated in two of 14 patients in whom it was measured. The AST was elevated in one of 12 and the ALT in one of eight patients in whom the results were available. One patient also had primary biliary cirrhosis. Another patient had had his hemangioma previously treated by deep radiograph therapy (DXT). He subsequently developed cholangitis secondary to necrotic tumor passing into the biliary tree. Two other patients had had DXT prior to their liver resections, both without regression of their tumors. No patient presented with bleeding from a hemangioma.

TABLE 3. *Non-neoplastic Conditions for which Liver Resection was Performed*

	Children		Adult		Total	
	No.	%	No.	%	No.	%
1) Inflammatory						
Caroli's disease	—	—	4	3.4	4	2.9
Intrahepatic stones	—	—	2	1.7	2	1.5
Granuloma	2	10.5	—	—	2	1.5
Hepatic abscess	—	—	1	0.8	1	0.7
2) Trauma	—	—	3	2.5	3	2.2
3) Miscellaneous						
Caroli's and hepatoma	—	—	1	0.8	1	0.7
Infarction liver	—	—	1	0.8	1	0.7
Cysts	1	5.0	4	3.4	5	3.6

In the patient with both Caroli's and a hepatocarcinoma, the indication for the resection was Caroli's disease. The per cent value refers to the total number of resections in the groups.

Secondary colon. The mean age of the 22 patients with secondary colonic tumors was 54 years with a range of 25 to 71 years. Four patients had synchronous excisions of the primary tumor and the liver metastases. In the remaining 18 patients, the liver resection was performed between one month and eight years after the colectomy. Ten patients were known to have lymph node involvement at the time of their colectomy. Ten patients presented with abdominal pain or discomfort, seven were asymptomatic as regard to the liver tumor. Four had a palpable liver. The SAP was elevated in 13

TABLE 4. *Symptoms of Patients with Various Diagnoses*

	Hepatocarcinoma	Hepatoblastoma	LCA	FNH	Hemangioma	Secondary Colon
Total number of patients	26	3	5	7	17	22
Abdominal pain	15	1	4	2	9	7
Abdominal discomfort	3	—	—	—	5	3
Abdominal mass	5	1	1	2	7	—
Jaundice	1	—	—	—	—	—
Malaise	6	1	1	—	—	2
Anorexia	5	1	—	—	—	1
Weight loss	9	—	—	—	2	5
Fever	4	1	2	—	1	—
Nil	4	1	1	4	2	7

TABLE 5. *Mesenchymal and Embryonal Tumors*

	Procedure	Status	
Children			
Embryoma	LLS	Alive	67 months
Embryonal carcinoma	Wedge	Alive	18 months
Mesenchymal hamartoma	Wedge	Alive	209 months
Capillary hemangioma	RL	Alive	67 months
Adult			
Malignant hemangiopericytoma	ERL	Died	5 months
Malignant mesenchymoma	ERL	Died	4 months
Leiomyosarcoma	Wedge	Died	18 months
Hemangioendothelioma	LL	Alive	135 months

of 20 patients in whom it was measured, and similarly, the AST was raised in three out of 20 and the ALT in four out of 14.

Other secondaries. These were from the following primaries: adenocarcinoma stomach, reticulum cell sarcoma of the stomach, periampullary, pancreas, leiomyosarcoma of the duodenum, carcinoid of the ileum, kidney, and breast.

Direct invasion. These consisted of carcinoma of the bile ducts (4), carcinoma of the gallbladder (3), carcinoma of the stomach (4), and lymphoma of the stomach (2).

Cholangiocarcinoma? Secondary carcinoma? In two patients it was not possible for the pathologist to say whether the liver tumor was a cholangiocarcinoma or a secondary adenocarcinoma.

Mesenchymal and embryonal tumors. These are listed in Table 5.

Inflammatory conditions. Four patients had Caroli's disease that predominantly affected one part of the liver. Two patients, both children, had large granulomata excised by wedge resection. The pathology of the lesions was not apparent until after the resection. In neither case was a cause for the granulomata found. There was one hepatic abscess. This was secondary to cholangitis complicating from an iatrogenic stricture of the bile duct.

Miscellaneous conditions. One patient was operated upon for Caroli's disease in an attempt to control his septicemia. It was only after the resected specimen had been examined histologically that it was realized that he also had a hepatoma. A patient with liver infarction had rheumatoid arthritis and was on steroids. She presented acutely with bleeding from the liver. The operative diagnosis was rupture of a liver abscess. Examination of the resected specimen and the rest of the liver at autopsy showed the whole of the liver to be infarcted.

Liver cysts. Five patients had liver cysts. Two had polycystic disease of the liver, one had a solitary liver cyst, and two echinococcal cysts.

Preoperative Investigations

The success of radioisotope liver scanning, ultrasonography, computerized axial tomography, and selective arteriography in demonstrating the more commonly seen tumors is shown in Table 6. All appear to be adequate in detecting tumors of the dimensions found in this series. Usually the tumors were large. The first three methods were useful initial investigations, arteriography being reserved for those with a positive result from either of these tests. As well as indicating the pathology of a tumor, arteriography demonstrated the anatomy of the blood supply of the liver and the tumor. Such information was valuable during the subsequent resection. Inferior venography and splenoportography were rarely used in this series.

Percutaneous liver biopsy was considered hazardous for lesions suspected of being primary liver tumors. Hepatomas, LCAs, and hemangiomata may bleed profusely following this procedure. This investigation was rarely performed.

Fifty of the 138 patients had a laparotomy for their liver pathology prior to the laparotomy for the liver resection. This procedure was usually performed at another center and then the patient was referred to UCLA Hospital. Often the liver lesion was biopsied at this initial operation.

Operative Procedure

The incidence of multiple liver lesions for the various tumors and the cysts is given in Table 7. Half the patients

TABLE 6. *Results of Imaging Techniques Used to Demonstrate Liver Tumors*

	Hepatoma		Hepato-blastoma		LCA		FNH		Hemangioma		Secondary Colon	
	No.	Pos	No.	Pos	No.	Pos	No.	Pos	No.	Pos	No.	Pos
Isotope scan	15	14	3	3	2	2	3	1	9	9	18	16
Ultrasonography	6	5	3	3	1	1	3	2	3	3	6	5
CAT	3	2	—	—	—	—	1	1	—	—	5	4
Arteriography	12	11	2	2	4	3	3	3	14	14	15	14

No. = Number performed. Pos = Number positive.

with hepatocarcinoma had multiple liver lesions. Multiple lesions were also seen in patients with LCA, FNH, hemangiomata, and secondary tumors.

In 62 cases, the weight of the resected specimen exceeded 500 gm. The largest specimen was a colonic secondary that weighed 6.8 kg.

The various procedures performed for selected diagnoses are shown in Table 8.

The most frequently used incision (71% of operations) was a right subcostal, usually extended across the midline to form an inverted chevron. Upper midline or paramedian incisions were occasionally used. The indications for these were firstly, the patient had had a previous laparotomy using such an incision, secondly, the patient had a narrow subcostal angle, or thirdly, such an incision was considered the most appropriate for the resection of the primary tumor when an en bloc resection was contemplated or when synchronous excision of a primary tumor and a liver secondary was to be undertaken. In 51% of operations, a thoracic extension to the incision was made. This was usually made through the eighth intercostal space. The costal margin was divided so that the extension and the subcostal incision produced a T-shaped incision. Ninety per cent of RLs required a thoracic extension as did 92% of ERLs. It was less often required for LL (33%), wedge resection (24%), and LLS (4%). Children were less likely to require a thoracic extension than adults for a similar procedure.

Dissection of the porta hepatis with identification of the hilar structures was performed in nearly all lobectomies and also in 46% of LLSs and 10% of wedge resections. In two recent resections use has been made of the Cavitron, an ultrasonic instrument,[16] to divide the liver parenchyma. In eight of the earlier resections, total body hypothermia prior to clamping the vessels in the gastrohepatic ligament was employed. Subsequent work has shown this to be unnecessary. The Pringle maneuver[17] was usefully employed in several cases to control intraoperative hemorrhage. Mattress sutures to secure the blood vessels and bile ducts at the cut edge were used more often in the smaller resections (95% of LLSs and 83% of wedge resections) than in the lobectomies (76% LLs, 67% RLs, 54% ERLs).

TABLE 7. *Number of Patients with Various Diagnoses Having Solitary and Multiple Lesions*

	Single	Multiple
Hepatocarcinoma	13	13
Cholangiocarcinoma	1	1
Mixed hep-chol	2	1
Hepatoblastoma	3	0
LCA	2	3
Cystadenoma	1	0
Cystadenocarcinoma	1	0
Other cysts	1	4
Hemangioma	12	5
FNH	5	2
Secondary colon	13	9
Other secondaries	3	5

Since 1971 a specially designed liver clamp[18] has been used to control hemorrhage during the resection. It was found to be most useful for RL and LLS, being used in 71% and 62% of these resections, respectively, performed since this date. It was less often employed in LL, ERL, and wedge resections, being used in 42%, 33%, and 25% of these procedures, respectively. It was particularly useful in controlling hemorrhage during emergency procedures for either trauma or a ruptured tumor.

Frozen section diagnosis at the time of surgery was attempted on 54 occasions and was correct in 50. It was incorrect in three out of 14 hepatocarcinomas and in one out of two LCAs. One LCA was falsely reported to be a hepatocarcinoma.

Biliary tubes, usually a T tube in the common bile duct, were inserted in 42 (30%) cases. Through these tubes saline was injected so as to reveal any patent bile ducts at the cut surface of the liver.

Complications

The important complications are listed in Table 9. The one intraoperative death occurred in a patient with a hepatocarcinoma. Death was from uncontrollable hemorrhage.

Intra-abdominal infection was common, probably secondary to sloughing of devitalized liver tissue at the site of resection. The resection site was drained by large sump drains to obviate the effects of this complication.

TABLE 8. *Procedures Performed for Various Diagnoses*

	RL	ERL	LL	LLS	En Bloc	Wedge	Combination	Total
Hepatocarcinoma	11	2	7	3	—	3	—	26
Hepatoblastoma	1	2	—	—	—	—	—	3
LCA	2	—	—	1	—	1	1	5
FNH	3	—	1	1	—	2	—	7
Hemangioma	4	—	4	4	—	4	1	17
Secondary colon	7	4	3	5	—	2	1	22
Other secondaries	2	—	—	2	—	3	1	8
Non-neoplastic cysts	1	1	1	1	—	1	—	5

TABLE 9. *Complications of Major Liver Resection*

	RL (42)	ERL (13)	LL (21)	LLS (22)	En Bloc (7)	Wedge (29)	Combination (4)	Total (138) No.	Total (138) %
Intraoperative death	—	—	—	—	—	1	—	1	0.7
Chest infection	22	8	4	7	3	7	1	52	38.0
Intra-abdominal infection	14	4	2	—	2	1	—	23	17.0
Wound infection	3	2	1	1	2	1	—	10	7.0
Bile leak	5	3	3	1	1	1	1	15	11.0
Hemorrhage	5	2	1	1	—	—	—	9	6.0
Hepatic failure	6	3	—	—	—	2	—	11	8.0
Temp 38 C for 7 days	19	10	8	4	1	5	1	48	35.0
Costal cartilage infection	1	1	1	—	—	—	—	3	2.0
Prolonged subcostal drainage	4	2	2	—	—	1	—	9	6.0
Renal failure	4	2	—	1	—	2	—	9	6.0

However, in 14 cases an intra-abdominal abscess required surgical drainage. An additional four patients with a persistent postoperative pyrexia had a laparotomy, but no focus of infection was found. It was not unusual for patients who had major resections to have a postoperative pyrexia lasting more than one week (35% of operations). An infective cause was not found in all of these. It may be that this pyrexia is a reaction to the necrotic liver tissue at the margin of resection. Nine patients had a prolonged subcostal drainage; in two of these, Ivalon had been used to bolster the mattress sutures at the cut edge. It was not until this material was removed that the drainage ceased. Three patients developed costal cartilage infections. These were particularly indolent and difficult to treat.

A bile leak occurred in 15 patients. This was usually confined and stopped spontaneously, but one patient required a laparotomy for biliary peritonitis. Two additional patients, who had both been operated upon through thoracoabdominal incisions, developed biliary-pleural-bronchial fistulae.

Postoperative hemorrhage from the operation site occurred in nine patients, five of whom required a re-exploration. Eleven patients developed hepatic failure. Other complications included upper gastrointestinal hemorrhage (5), pancreatitis (1), cerebral ischemia secondary to an intraoperative cardiac arrest due to hemorrhage (1), pulmonary embolus (1) myocardial infarction (1), gram negative septicemia (1), and post-transfusion hepatitis (1).

Deaths

There were 15 deaths within a month of the operation (10.9%). Twelve of these deaths could be attributed to the procedure. Five followed RL, three ERL, one LL, one LLS, one wedge resection, and one en bloc resection when a wedge of liver was removed during a gastrectomy for a lymphoma of the stomach. In four of the 12, hemorrhage from the liver was the primary cause of death, and in another four it was a major contributing factor. Liver failure was a major contributory cause of death in five patients and intra-abdominal sepsis a major contributory cause in three patients. Other factors contributing to the deaths of these 12 patients were hemorrhage from antral ulcers (2), renal failure (2), perforated duodenal ulcer (1), acute pancreatitis (1), and severe chest infections (8).

Three deaths that occurred within the first postoperative month were considered not to be the direct result of the procedure. One patient had both Caroli's disease and a hepatoma. He presented very ill with septicemia secondary to the Caroli's disease. He had a wedge resection but died from a combination of liver failure, renal failure, and a chest infection. It appeared that his death was attributable to his disease rather than the result of the operation. The second patient had an emergency wedge resection for a ruptured hepatoma. He also had cirrhosis. He died after operation from bleeding esophageal varices. The third patient had rheumatoid arthritis. She died soon after a RL. At the time of operation, it was thought that she had ruptured a liver abscess, but later it was shown that she had infarcted her entire liver, possibly due to an arteritis associated with her rheumatoid disease.

Three deaths that occurred later than one month after operation were attributed to the procedure rather than the pathology. One patient had a RL for a mixed tumor. He also had cirrhosis. He died six months after operation, having never left the hospital. Death was a result of a chest infection, liver failure, and an intra-abdominal abscess. The second patient had a 6 kg malignant hemangiopericytoma excised by a ERL. During this procedure the left hepatic duct was divided and anastomosed. After operation the anastomosis broke down and he eventually died from liver failure and a chest infection. The third patient had a LL for a secondary colonic lesion. The main cause of death was liver failure, but renal failure, a chest infection, an intra-abdominal abscess,

TABLE 10. *Patients with Cirrhosis*

Diagnosis	Procedure	Liver Failure	Time of Death or Survival Time	Cause of Death
Hepatocarcinoma	RL	No	12 Hours po	Hemorrhage
Hepatocarcinoma	Wedge	Yes	17 Days po	Liver failure, bleeding esophageal varices
Hepatocarcinoma	LL	No	18 Months	Recurrence
Hepatocarcinoma	LLS	No	52 Months alive	—
Hepatocarcinoma	LLS	No	3 Months	Recurrence
Mixed	RL	Yes	6 Months	Liver failure
Mixed	RL	No	4 Months	Recurrence
Hepatic abscess	RL	Yes	1 Month	Liver failure
Carcinoma stomach	En Bloc LLS included	No	14 Months	Recurrence
Polycystic liver	REL	No	87 Months alive	—

po = postoperative.

and an upper gastrointestinal bleed were contributory factors.

Postoperative Blood Tests

Eighty-six out of 119 patients, in whom the test result was available, had elevated serum bilirubin levels in the postoperative period. Sixteen patients had serum bilirubin levels of greater than 165 micromol/l within the first 14 days after operation. Thirteen of these had lobectomies, two had wedge resections, and one a LLS. Twelve of these patients died; in 11 liver failure was either the cause of death or a major contributory factor. Two of ten patients with cirrhosis had postoperative bilirubin levels greater than 165 micromol/l; both died. Five patients with this degree of hyperbilirubinemia did not develop liver failure. One of these, who had a LLS for intrahepatic stones, died after operation from a perforated duodenal ulcer and pancreatitis. The remaining four patients all had lobectomies. Their diagnoses were Caroli's disease, hemangioma, hepatoma, and secondary periampullary carcinoma. In all the bilirubin fell to normal levels and all are alive and well. The blood transfusion requirements of four of these five patients who did not develop liver failure exceeded those of most other patients. This may provide an explanation for the raised bilirubin in these patients.

The SAP was elevated during the first 14 days after operation in 75% of patients. In 41%, it was elevated to levels greater than twice the upper limit of normal. In 95% of 113 patients in whom the result was available, the AST was elevated at some time during the first 14 days after operation. In 76% it was elevated to levels greater than twice the upper limit of normal. The ALT was elevated in 93% of 95 patients. In 80% values greater than twice the upper limit of normal were reached. It was not unusual for serum transaminase levels to reach levels of ten times normal within the first few days after operation, but they rapidly fell to normal.

Before operation, the parameters to assess blood coagulation were within the normal range in those patients in which they were measured. The postoperative values depended more on the number of units of blood transfused during the procedure than the amount of liver resected.

After operation, the serum albumin fell to below 24 gm/l in 12 patients (seven RL, two ERL, three wedge resection).

The white blood cell count rose to above 14,000 within 14 days of the operation in 55% of patients.

Patients with Cirrhosis

Ten patients had cirrhosis diagnosed when the resected specimen was examined histologically. This diagnosis was not always apparent at the time of the operation. Details of these patients are shown in Table 10. Three died with liver failure, one died from postoperative hemorrhage, and four from recurrent tumor. Two patients are alive with no symptoms or signs of liver disease.

Survival

Benign tumors. Thirty patients had the diagnoses LCA, FNH, hemangioma, and cystadenoma. The postoperative follow-up period of these patients ranged between one month and 20 years. The only death in this group of patients occurred in a medical practitioner who had DXT to a liver hemangioma 16 years prior to the resection of his tumor. Three years after the operation, he died from a malignant hemangiopericytic sarcoma of the left chest. Several histopathologists were consulted, and all agreed that this and the liver tumor were separate primaries.

Malignant primary tumors. **Hepatocarcinoma.** The percentage cumulative survival of the 26 hepatocarcinoma patients at intervals up to five years is shown in Figure 1. The cumulative survival at five years is 38%.

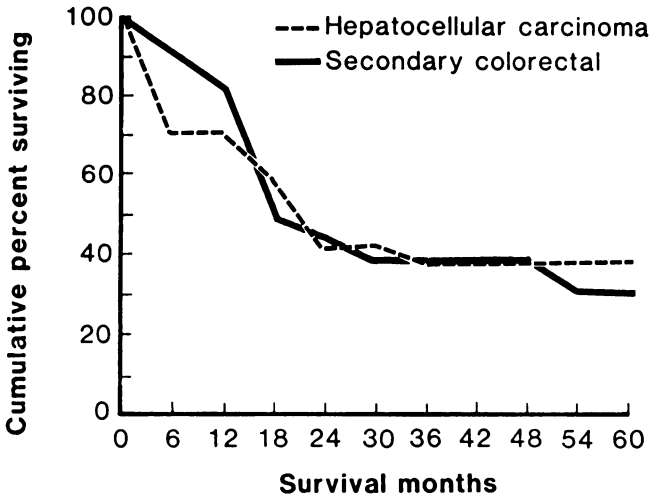

FIG. 1. Survival of patients with hepatocellular carcinomas and metastases of colorectal carcinomas who underwent hepatic resection.

There were seven deaths within a month of operation or later, but attributable to the operation. If these are excluded, then the 5-year cumulative survival of the remaining 19 is 51%. Six patients are known to have survived five years; the longest survival is 19 years.

Nineteen of the hepatocarcinoma patients were adults. The deaths of five of these were attributable to the operation. Another patient died after operation from bleeding esophageal varices. Six died with recurrent tumor between one year and three years after operation. Seven of these adult patients are alive between two and 13 years after the resection.

Seven of the hepatocarcinomas were in children. One death was attributable to the operation. Three died from recurrent tumor between two months and two years after the operation. Three are alive and disease-free four, seven and 19 years after operation.

One patient was seen to have tumor in a vein when the specimen was examined histologically. He is alive and well 11 years after operation.

Hepatoblastoma. Three children had hepatoblastomas resected. One died with disease 12 months after operation, having suffered irreversible brain damage following a cardiac arrest during the operation. The other two cases have survivals of six and 36 months. Both had intensive postoperative chemotherapy.

Other primary malignant tumors. The two patients with cholangiocarcinomas died with recurrent tumor 15 and 23 months after the resection. Of the three patients with mixed hepatocellular-cholangiocellular carcinomas, one with cirrhosis died from liver failure six months after his operation, having never left the hospital. The remaining two died from recurrent tumor four and nine months after their resections. The patient with a cystadenocarcinoma is alive over 12 years after her operation.

Secondary tumors. **Colonic secondaries.** There were no deaths within a month of the operation in the 22 patients who had colonic secondaries resected. The percentage cumulative survival of these patients at various intervals after the resection is shown in Figure 1. The cumulative survival at five years is 31%. The follow-up period for the 22 patients ranged between two and 104 months. One death was attributable to the operation. This patient died two months after a LL from a combination of liver failure, renal failure, an intra-abdominal abscess, a gastrointestinal bleed, and a chest infection. Fourteen patients are known to have died with tumor between two and 104 months after resection. Six patients are known to have lived three years or more and three patients for five years or more. Eleven patients had postoperative chemotherapy; eight of these died with recurrent disease.

Thirteen patients had solitary secondaries resected. Six of these are alive, three with recurrent disease. Seven had died from recurrent disease between two and 104 months (mean 26 months) after the operation. Nine patients had multiple liver secondaries resected. One of these patients died as a result of the procedure. Two patients are alive, one of whom is known to have recurrence. Six have died from recurrent disease between 13 and 52 months (mean 22 months) after the operation.

In this small series, there appeared to be no correlation between the interval of time separating the colonic and the liver resection and the length of survival following the liver operation. Also, the nodal status of the colectomy specimen did not appear to affect survival.

Other secondaries. Of the eight patients in this group, five died between 5 and 30 months after resection, and three are alive seven, eight and 47 months after resection. The only long-term survivor had a synchronous excision of an ileal carcinoid and a RL for a metastatic deposit.

Direct invasion. One patient with a bile duct carcinoma died after operation from liver failure. The remaining three with this tumor died from recurrent disease at 14, 18, and 53 months. The longest survivor was also treated with DXT and chemotherapy. The three patients with carcinoma of the gallbladder died at eight, 26, and 48 months after operation. Of the eight patients with gastric neoplasms, one died as a result of the procedure, and seven died between three and 20 months with recurrent tumor. One patient with a colonic tumor directly invading the liver died at eight months. There were no patients still alive who had a liver resection for a nonhepatic primary tumor directly invading the liver.

Secondary cholangiocarcinoma? These two patients

died from recurrent disease at nine and 40 months after their resection.

Mesenchymal and embryonal tumors. The outcome of these eight patients is shown in Table 5. Those patients with benign lesions did well while three of four patients with malignant lesions have died.

Inflammatory lesions. One patient with Caroli's disease died of liver failure in the postoperative period. The other three are alive 97, 112, and 121 months after operation and all have benefited from the procedure. One patient with intrahepatic stones died after operation from gram-negative septicemia secondary to a perforated duodenal ulcer and pancreatitis. The other patient is alive and symptom-free 95 months after her resection. Two children had wedge resections for granulomata. Both made good recoveries. The patient who had a RL for a hepatic abscess died after operation with liver failure.

Trauma. One patient died three days after operation from hemorrhage at the operative site. One patient died at ten months from a cause unrelated to the resection, and one patient is alive and well at five months.

Miscellaneous. The five patients who had cysts removed are all alive between four and 87 months after operation.

The patient with Caroli's disease and a hepatoma and the patient with infarction of the liver died in the early postoperative period and have been referred to above.

Discussion

Detailed accounts of the history of major hepatic resection can be found in several publications.[9,10] The important landmarks were the appreciation of the segmental anatomy of the blood vessels and the bile ducts within the liver,[4] the capacity of the liver to regenerate even after major resections,[6] and the blunt methods for dissecting through the hepatic parenchyma.[19,20] More recently, the introduction of liver clamps has enabled resections to be carried out with less blood loss.[18,21,22] In spite of reports of low operative mortality,[8,23,24–26] major hepatic resection is still a formidable undertaking. In addition to the surgeon needing the expertise and facilities to perform the operation, he must have knowledge concerning its indications, the assessment of the patient before operation, the likely complications and the prognosis following a successful procedure. Lack of information regarding these points may have deterred many surgeons from performing this operation.

Major hepatic resection is usually contraindicated if there is unresectable metastatic tumor outside the liver or if tumor is present throughout the liver including the left lateral segment.[27] Some authors[13] consider that these are only relative contraindications and suggest that in some cases the excision of large malignant liver tumors may provide worthwhile palliation even though it is known that tumor has been left. Involvement of the inferior vena cava or the main trunk of the portal vein are contraindications to resection.[28] Undoubtedly, the main obstacle to resection is cirrhosis.[22,29,30] Wedge resections may be possible in mild cirrhosis, but even these operations are contraindicated if the cirrhosis is severe.[8] This point is particularly relevant because of the association between hepatocellular carcinoma and cirrhosis.[10]

Except in emergencies, a thorough preoperative workup should be undertaken. In the case of tumors, this should be directed toward assessing the extent of the tumor and the function of the remaining liver rather than achieving a tissue diagnosis. Hepatocellular carcinomas, LCAs, and hemangiomas are highly vascular and can bleed profusely following percutaneous needle biopsy. This procedure should generally be avoided.[13] Usually the diagnosis can be made at operation with the aid of frozen section histopathology, yet in some cases it may be appropriate to resect the tumor even though its exact pathology is uncertain. If it is thought that the lesion is inoperable but a tissue diagnosis is required, then laparoscopic biopsy may be the best method of achieving this.[9]

The serum alkaline phosphatase and serum transaminases are often elevated in patients with benign and malignant tumors of the liver,[5,31] less often in the patients with hemangiomata. These tests are of little value in assessing liver function and, thus, the likelihood of cirrhosis. Jaundice is usually considered a contraindication to major liver resection, particularly in patients with no evidence of major bile duct obstruction or cholangitis.[30] Conversely, many patients with cirrhosis are not jaundiced. Mizumoto et al.[32] have used the clearance of indocyanine green as a more accurate means of assessing liver function prior to major hepatic resection. The authors have not routinely used such tests and occasionally mild cases of cirrhosis were only diagnosed after the specimen had been examined histopathologically.

Radionuclide scanning, using technetium^{99m}, and more recently, ultrasonography and computerized tomography, are useful methods for detecting filling defects in the liver[9,23,24,33] and will provide information regarding their number and site. Each has its advantages and disadvantages and they should be used to complement each other. However, none is capable of detecting small lesions (less than 2 cm) with any degree of reliability.[33] Estimation of the tumor markers, alpha-1-foetoprotein,[34] and carcinoembryonic antigen[9] may be more useful in detecting such lesions. Hepatic arteri-

ography[23,24,35] should not be used as a screening test but to investigate further a lesion demonstrated by the imaging techniques mentioned. It may provide information regarding the pathology of the tumor, its resectability, and the anatomy of the blood vessels of the liver. The latter information enables the planning of the operative approach and indicates any anatomical anomalies. Several authors[5,28] use splenoportography to visualize the portal vein so as to detect any thrombus or tumor within it. The authors have rarely used this investigation, relying on the venous phase of the arteriogram to visualize this vein. Inferior venocavography has been advocated by some workers.[5,28] However, it may be unable to distinguish between extrinsic compression of the vein from actual invasion by tumor. Cady et al.[11] have suggested preoperative cholangiography as a useful aid in planning the operative approach. Probably this is only important when the pathology primarily involves the biliary system. Laparotomy is often required to assess the resectability of a tumor; this has been stressed by Fortner and Papachristou.[13]

Much has been witten about the merits of various techniques of liver resection. Several authors[13,29] propose that a thoracic extension to the abdominal incision is rarely necessary. It is believed that adequate exposure is essential for the performance of a safe procedure and that a thoracoabdominal incision is a requisite for most RLs and ERLs and may be necessary for some of the other procedures. This gives access to the inferior vena cava and hepatic veins. The hepatic veins can be occluded in a controlled manner prior to dividing the liver parenchyma, and if bleeding occurs from the inferior vena cava, its source can be readily identified and controlled. The thoracic extension is made through the eighth intercostal space; other workers have preferred to split the lower 5 inches of the sternum.[36] In cases of hepatic trauma when rapid control of hemorrhage is required and in cases when a large tumor makes dissection of the porta hepatis difficult, a hepatic lobectomy may be performed without first dividing the appropriate vessels and bile duct at the porta hepatis. In this approach, described by Lin,[8] these structures are divided within the hepatic parenchyma. Preliminary occlusion of the blood supply to the liver by the Pringle maneuver[17] can be utilized without hypothermia now that it is known that the liver can withstand a period of normothermic ischemia.[37] In most lobectomies, the authors prefer to ligate the appropriate vessels at the hilum and also occlude the relevant hepatic veins, the so-called controlled method, prior to dividing the hepatic parenchyma.[9] Most workers[5,19,28,30] now divide the liver by a blunt technique. The authors use the handle of a scalpel to accomplish this.[23] Recently, a number of liver clamps[18,21,22] have been designed to reduce blood loss during the resection. The noncrushing Storm clamp[18] was found to be very useful. Lin[22,38] has devised a technique using two clamps, a noncrushing one to occlude the blood supply of that part of the liver to be resected, and a crushing clamp to divide the liver parenchyma but leaving the intrahepatic vessels and bile ducts for subsequent ligation and division. The authors have not used this method.

Mattress sutures at the cut edge[25] should be used with care since they may lead to necrosis of tissue and subsequent infection.[23] Foreign material, either to bolster such stitches[39] or to cover the raw surface of the liver,[40] should be used with caution since it may lead to chronic sepsis. If such material is to be used, it should be absorbable.[41] If the liver edges cannot be apposed, they should be covered with omentum or the falciform ligament. These should not be stitched to the liver since this may produce a pocket in which blood and necrotic tissue can accumulate and become infected.[9] Much argument surrounds the use of biliary drains, usually a T tube, in hepatic resections.[8,25] The authors have used them as a means of identifying patent bile ducts at the cut surface of the liver by injecting saline down the tube.[23,36] Contrary to the suggestion by some workers[36,42] that draining the site of resection causes more harm, by predisposing to infection, than benefit, the authors prefer to use drains to obviate the effects of sepsis.

Serum alkaline phosphatase and the serum transaminases are often elevated following a major hepatic resection.[23,43–45] The transaminases may reach levels greater than ten times the upper limit of normal, but fall rapidly during the first week following the operation. This does not appear to indicate necrosis of the liver remnant. The serum bilirubin is commonly elevated in the postoperative period[8,28,43]: 72% of patients in this series had values above normal. Twelve of 16 patients who had a bilirubin level greater than ten times normal in the immediate postoperative period died, 11 with liver failure. It appears that a markedly elevated bilirubin after operation is a poor prognostic sign.[29] After operation, the prothrombin time was usually in the normal range except in patients who had had massive blood transfusions. It has been suggested[22,42] that the coagulopathy following hepatic resection is due to increased fibrinolysis rather than a primary deficiency in clotting factors. Similar to the experience of other workers,[7,43] no patient in this series suffered from postoperative hypoglycemia, a complication reported by some authors.[42] Serum albumin may fall in the postoperative period; in 12 of these patients it fell below 24 gm/l. This fall may be related more to loss of plasma proteins at the site of resection, especially if infection supervenes, than to underproduction by the liver.[23] The white blood cell count is often elevated after operation.[43] In some instances, this may be

more a response to trauma and necrotic tissue at the resection site than to infection.

Earlier workers reported death rates in the first 30 days after operation of 35.8[46] and 29%.[47] More recent reports[10,23–25,48] suggest figures between 5 and 20%; however, occasionally figures as high as 25[40] and 30%[45] are quoted. It is often difficult to compare results since authors use different definitions of operative mortality and series differ in the diagnoses for which the operations were performed and also in the nature of the operations. In this series, 15 deaths, including the one intraoperative death, occurred within a month of the operation (operative mortality 10.9%). Twelve of these could be attributed to the procedure; hemorrhage, intra-abdominal sepsis, and liver failure were the main causative factors. Three late deaths could be attributed to the procedure; in all three, liver failure developed after operation.

Ten patients had cirrhosis. Three of these died from liver failure and one from postoperative hemorrhage. Several authors[10,30] have stressed the high mortality following hepatic resection in cirrhotic patients.

The postoperative complications in this series are similar to those reported by other workers.[10,13,30] Intra-abdominal sepsis, hemorrhage from the operative site, liver failure, and biliary leaks are among the more important. Costal cartilage infections, though fortunately uncommon, are usually persistent and difficult to treat.

Thirty benign tumors (hemangioma, LCA, FNH, and cystadenoma) were excised. In agreement with previous reports,[12,23] hemangioma was the most common benign liver tumor. It is now accepted that LCA and FNH can be distinguished pathologically.[49] The former is a tumor often associated with the taking of oral contraceptives.[40] The neoplastic nature of FNH is disputed.[51] It may represent a response of the liver to injury.[10] Two of the cases of LCA presented acutely with hemorrhage into the tumor, one of which had ruptured. Isolated reports suggest that the mortality from ruptured LCA is high.[52] Foster and Berman[10] reviewed the literature, and of 21 patients who presented with intraperitoneal hemorrhage, six died during or soon after operation. Small liver hemangiomata are usually asymptomatic and rarely require excision.

Larger lesions (greater than 4 cm in diameter) may be associated with a variety of complaints that justify such treatment.[12,53] None of these patients with hemangiomata presented with intra-abdominal bleeding, but this complication has been reported.[12,30] It has been suggested that hemangiomata may respond to radiotherapy or steroids.[54] Three cases in this series received radiotherapy without benefit. The results of elective resections for benign hepatic tumors appear to be excellent. There were no deaths in this series attributable to the operation and morbidity was low. Most patients achieved symptomatic benefit, particularly if they presented with abdominal pain or discomfort.[12]

The survival of patients with unresectable hepatocellular carcinomas is short. Geddes and Falkson[55] reported the mean survival from diagnosis of 56 untreated patients as two months. However, the occasional unresected patient may live considerably longer. Eight cases reported by Davidson et al.[56] lived in excess of two years without resection. Only about 10%[11,29] of hepatocellular carcinomas are suitable for resection. Many patients either have cirrhosis[10] or widespread involvment of the liver.[29] Some workers[8,30] consider cirrhosis to be only a relative contraindication and are willing to undertake small resections of mildly cirrhotic livers. The operative mortality and long-term survival are, however, very dependent on the presence or absence of cirrhosis.[20] Operative mortality for resecting hepatocellular carcinomas has been reported between 3%[26] and 21%.[10] Five of the 26 patients (19%) died within a month of operation. This includes one patient who had an emergency resection for a ruptured tumor.[57]

Reports of survival of patients with resected hepatocellular carcinomas are difficult to compare since different authors use different methods for presenting their results. Some[10] exclude deaths occurring within 30 days of the operation from their calculations or include patients with cholangiocarcinomas and mixed tumors in their calculations.[8,29] Longmire and Tompkins[9] analyzed 684 resections from nine reported series. They estimated that the three-year survival ranged between 20 and 50% and the five-year survival was about 10%. In their Liver Tumor Survey, Foster and Berman[10] found a five-year survival of 30%; they did not include deaths that occurred in the first 30 days after operation in their calculations. They also remark, after reviewing the literature, that the five-year survival in Asian patients is much less (7%) than in non-Asian patients (35%). The cumulative survival of the 26 patients with hepatocarcinoma at five years was 38%. If the seven deaths attributable to the operation are excluded, then the five-year cumulative survival was 51%. Six patients are known to have survived five years; the longest survival is 19 years. Two of the patients presented with acute rupture of their hepatocarcinomas; long-term survival after emergency resection for this has been reported.[57] Death from hepatocellular carcinoma after five years postresection has been reported.[10] None of the patients who survived three years subsequently died from their hepatocellular carcinoma. It may be that in some of the reported cases of late recurrence, a second primary has developed, particularly if the liver is cirrhotic.

Reports of significant survival following resection for cholangiocarcinomas and mixed carcinomas are few.[22] Often these tumors are included with hepatocellular car-

cinomas in reports of survival following resection for primary carcinomas of the liver. It appears that the mixed tumors behave more like the cholangiocarcinomas than the hepatocellular carcinomas.[10] In the Liver Tumor Survey,[10] of 18 patients who had mixed and cholangiocarcinomas resected, only six were alive and the longest survival was 25 months. Sanguily and Caldern,[58] however, did report a patient with cholangiocarcinoma treated by wedge resection who was alive and free of disease two and a half years after operation. One of the cases of mixed tumor presented with hypercalcemia. This and other systemic manifestations of primary liver carcinomas have been reported by other workers.[59]

Cystadenocarcinoma is rare. The authors resected only one case. She is alive and well 12 years after her operation. Long-term survival after resection of this tumor has been reported previously.[10]

Three resections were performed for hepatoblastoma. One patient died as a result of the operative procedure. The other two patients are alive and well; both have had postoperative chemotherapy. In children, hepatoblastomas are more likely to be resectable than hepatocellular carcinomas.[10] It has been estimated that the five-year survival for children following resection of these tumors is 65%. Unresected, most die within a year of diagnosis. Postoperative adjuvant chemotherapy may be valuable.[10]

Although a variety of metastatic tumors to the liver have been subjected to resection, metastases of colorectal cancer have been the most common.[9] Most patients with untreated colorectal secondaries in the liver are dead within a year of their detection.[60] Only a small number of patients with colorectal liver metastases will be suitable for resection.[26] After resection, three-year survival figures of 41[26] and 72%[25] and five-year survival of 18%[10] have been reported. Death from colorectal carcinoma can occur more than five years after the resection of a liver secondary so that five-year survival is not synonymous with cure.[10] The cumulative survival of the 22 patients who had colorectal secondaries resected was 31%. Three patients are known to have lived for five years or more after the operation. It is disputed whether factors such as the interval between the resection of the colonic primary and the liver resection,[10,61,62] the involvement of local colonic lymph nodes by tumor,[10,62] the size of the liver metastasis,[10,63] or whether the liver metastases are solitary or multiple[10,63] affect survival following liver resections. This series is too small and follow-up too short to comment on these issues.

Only one of eight patients who had secondaries resected other than those originating from colorectal primaries had an appreciable survival period. He had a liver secondary from an ileal carcinoid. Carcinoid is a slow-growing tumor and even if a cure is not achieved by liver resection, the patient may get worthwhile palliation from relief of the systemic effects of the tumor.[11,64] Resection of liver secondaries apart from those of carcinoid and colorectal origin have been rarely performed and the results reported have been disappointing. Foster and Berman[10] estimated a two-year survival of 22% and a five-year survival of 6% after resection for a miscellaneous group of liver secondaries.

En bloc resections for tumors directly invading the liver, including gallbladder and bile duct carcinomas, rarely are followed by long-term survival.[10,11,29,30] All the patients in this series who had this procedure are dead. If such a procedure is to be undertaken, it should be realized that at best it will provide palliation.[24] There are probably few indications to perform procedures other than wedge resections or left lateral segmentectomies in these patients.

Only rarely is a major hepatic resection required for trauma[36,65]; if the patient survives, the outlook is good. Nonparasitic cysts of the liver are usually treated by one of four methods: enucleation, unroofing, anastomosis to an Roux-en-Y jejunal limb, or, if infected, by external drainage. However, occasionally a large cyst may be best removed by hepatic resection.[9,66]

Echinococcal cysts are usually treated by enucleation[9] and hepatic abscesses drained,[67] but also if these lesions are large and anatomically situated to make hepatic resection feasible, this may be the treatment of choice.

Caroli's disease usually affects the entire liver, and resection has no place in management. However, localized Caroli's disease does occur and resection may then be beneficial.[68,69] In this series three patients had good results following resection. One patient with Caroli's disease also had a hepatocellular carcinoma. Cholangiocarcinoma in association with Caroli's disease has been reported by Gallagher.[70] Some patients with intrahepatic stones may be best treated by a resection, especially if the stones are confined to the left lateral segment and the duct to this segment is strictured. Salembier[71] performed only one resection in 44 patients with intrahepatic stones, but higher resection figures of 23 out of 85 cases[72] and 26 out of 115 cases[73] have been reported from the Far East.

Liver resection can be used to treat a variety of neoplastic and non-neoplastic hepatic lesions. Benign tumors can be resected with minimal morbidity and mortality with good symptomatic results. Unfortunately, only a few patients with malignant lesions are suitable for resection. Other treatments, including chemotherapy,[74] hepatic artery ligation,[75] and hyperthermia,[76] are being tried, but the results at present are inconclusive. Until an alternative method is found, hepatic resection provides the only chance of long-term survival in patients with certain primary liver malignancies and sec-

ondary colorectal tumors who satisfy the criteria for resection. Resection for trauma is rarely required, but can be life-saving. A variety of patients with other non-neoplastic conditions, including Caroli's disease, liver cysts, liver abscesses, and intrahepatic stones may benefit from a liver resection.

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