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Liver resection for benign liver tumors: indications and outcome

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Abstract

Background: The indications for intervention in cases of benign liver tumors include symptoms, suspicion of malignancy, or risk of malignant change.
Methods: Eighty-four liver resections for benign tumors were performed in our hospital from June 1996 to December 2004. The patient records were reviewed retrospectively.
Results: The study group (41 females, 43 males; average age, 41.4 ± 10.5 y) included 46 cavernous hemangiomas, 27 focal nodular hyperplasias, 5 hepatic adenomas, and 6 liver cysts. The indications for resection were inability to rule out malignancy (50 [59.5%]), symptoms (33 [39.3%]), and others (1 [1.2%]). Postoperatively, 28 of the 33 patients had resolution of symptoms. Twenty-nine patients (34.5%) had chronic hepatitis B infection.
Conclusions: Liver resection for benign liver tumor is safe, but indications for intervention must be evaluated carefully. The presence of chronic parenchymal liver disease does not increase morbidity in these patients.

Keywords: Benign liver tumor; Liver resection; Chronic parenchymal liver disease

Benign liver tumors are now being diagnosed frequently with the advent of greater use of radiologic investigations [1]. The most common lesion is the cavernous hemangioma, with an incidence rate at autopsy ranging from 3% to 20% [2]. The second most common benign liver tumor is focal nodular hyperplasia, making up approximately 8% of all primary hepatic tumors [3]. Surgical intervention is indicated if these lesions are symptomatic or if there is an inability to exclude malignancy [1,4,5]. Among these so-called benign liver tumors, the hepatic adenoma has 2 added indications: they have a risk of bleeding that can be life-threatening and a risk of malignant change [1,2].

Hepatectomy is now associated with lower morbidity and mortality [6–8]. This has led to a more liberal use of this surgical procedure and its indications have extended to those with patients with benign liver lesions. However, liver resection is still a major surgical procedure.

Our center is in an endemic area for hepatitis B and hepatocellular carcinoma [9,10], which may affect liver resection for benign liver tumors in our practice. In this article, we delineate the indications and complication rates of liver resection for benign liver tumors and analyze whether the presence of hepatitis B infection and chronic parenchymal liver disease affects the outcome.

Patients and Methods

Eighty-four liver resections for benign liver tumors were performed by the Department of Surgery at Chang Gung Memorial Hospital-Kaohsiung Medical Center, from June 1996 to December 2004. Liver resections for liver abscess and hepatolithiasis were excluded. The records of these patients were reviewed retrospectively.

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Preoperative assessment

The evaluation of patients who present with a lesion in the liver and who may need a liver resection begins with a thorough physical examination and history-taking. A complete blood count and liver and renal function tests are obtained. The patients' hepatitis status also is determined. The patients undergo an electrocardiogram and chest radiograph. The first-line radiologic investigation used in our institution to investigate patients with possible hepatobiliary diseases is ultrasound. This is followed-up by computed tomography scans. These are our mainstay radiologic investigations for a diagnosis of a liver lesion. These radiologic investigations are the same for patients with or without a history of chronic liver disease or chronic hepatitis infection. If necessary, we may follow these up with magnetic resonance imaging or transarterial angiography with lipiodol. In our center, percutaneous biopsy of suspicious liver lesions is not practiced, routinely or selectively. This is to prevent the possibility of peritoneal seeding and it may be dangerous if dealing with a cavernous hemangioma.

Anesthetic management

Anesthesia management for liver resection is conducted using the protocol set in this institution [11]. A central venous catheter is inserted and arterial pressure is measured by radial catheter and non-invasive blood pressure measuring device. The patient is maintained on minimal intravenous fluids (1–1.5 mL/kg/h) during extrahepatic dissection and parenchymal transection with a target central venous pressure (CVP) between 5 and 10 cm H_2O. If the CVP remains greater than 10 cm H_2O despite diuresis induced with furosemide, then no further attempt is made to reduce the CVP either with intravenous nitroglycerine or morphine. No Swan-Ganz catheter is inserted. The cumulative fluid deficit is replaced immediately after the completion of parenchymal transection to expand the intravascular volume and to preserve the renal function.

Surgical techniques

Patients undergoing liver resection are generally exposed through a reversed L-incision. A thorough laparotomy is performed. The liver is inspected and is mobilized by freeing its ligamentary attachments.

An intraoperative ultrasound is performed to delineate the lesion and to detect any other lesions. The relationship of the lesion with the liver vasculature also is mapped.

We do not routinely use total inflow control (Pringle's) or hemivascular inflow control for simple liver resection. We do, however, use hemivascular inflow control for major liver resection. For hemivascular inflow control, a careful hilar dissection is performed and the necessary portal vein and hepatic artery are isolated in a similar manner as in living donor hepatectomy dissection [11]. The vein and artery then are bulldog-clamped to delineate the line of demarcation. However, if the patient has chronic hepatitis B and liver cirrhosis, our preferred method of inflow control is total inflow control. This is because hilar dissection in a cirrhotic liver can lead to bleeding. It also is necessary to limit the adhesions around the hilar in patients who may in the future need liver transplantation for their chronic parenchymal liver disease. Total vascular inflow control is applied intermittently in cycles, applied for 30 minutes, and released for 10 minutes.

Parenchymal transection is performed using a combination of the clamp fracture technique and the Cavitron Ultrasonic Surgical Aspirator (CUSA System 200; Valleylab Inc, Boulder, CO). All vessels less than 2 mm in diameter are coagulated with bipolar electrocautery with an outlet for dripping water and then divided. Larger vessels are cut between ligatures. All bleeding points are stopped with suture ligatures before proceeding with the parenchymal transection.

At the end of the liver resection, hemostasis is secured. The raw surface of the liver is checked for bile leaks. An abdominal drain is placed near the raw surface of the liver and in the most dependent area. The wound is closed in layers with frequent washing at each stage of the closure.

Postoperatively, patients are monitored in the intensive care unit and discharged to the general wards once they are stable. Antibiotics are given only at induction and are not continued unless complications occur. Chest therapy and mobilization therapy are commenced early in the postoperative period.

Statistical analysis

All values are expressed as mean ± SD. The Mann-Whitney *U* test was used for nonparametric variables. For categoric data, the chi-square test or the Fisher exact test was used. A *P* value of less than .05 was considered significant. Analyses were performed using SPSS computer software (SPSS version 13 for Windows; SPSS Inc., Chicago, IL).

Results

The demographic, characteristic, and perioperative parameters for the different types of benign liver tumors resected are shown in Table 1. The main indications for liver resection were inability to rule out malignancy (50 patients, 59.5%), symptoms (33 patients, 39.3%), and others (1 patient, 1.2%). Postoperatively, 28 of the 33 patients with symptoms had resolution of their symptoms. Among the 84 patients, 29 patients (34.5%) had chronic hepatitis B infection. Thirteen patients had chronic parenchymal liver disease (CPLD) at surgery and 12 of them had chronic hepatitis B infection. One patient had CPLD but was not positive for hepatitis B or C.

Among the 36 patients whose indication for resection was the inability to exclude malignancy, 24 patients had chronic hepatitis B infection. There were 5 patients with chronic hepatitis B infection among the 14 patients who requested surgical intervention.

Cavernous hemangiomas

Forty-six patients underwent liver resection for cavernous hemangiomas as shown in Table 1. There were 19 right hepatectomies, 12 left lateral segmentectomies, 2 left hepatectomies, and 13 segmental resections.

The indications for surgical intervention were the presence of symptoms in 23 patients, inability to rule out malignancy in 22 patients, Kasabach-Meritt syndrome in 1

Table 1
Demographic, characteristic, and perioperative parameters for the different types of benign liver tumors resected (as proven by histology)

	Cavernous hemangioma (n = 46)	Focal nodular hyperplasia (n = 27)	Hepatic adenoma (n = 5)	Liver cysts (n = 6)
Age, y	43.6 ± 7.5	36.0 ± 11.0	37.2 ± 6.7	52.7 ± 17.1
Sex, M/F	22/24	13/14	4/1	4/2
Size of lesion, cm	8.2 ± 6.7	4.3 ± 2.6	8.1 ± 5.9	14.2 ± 6.8
Mean number of lesions (range)	1.24 (1–5)	1.19 (1–3)	1	1
Preoperative radiologic investigations	35 CT scan only; 9 CT scan + MRI; 2 CT scan + angiography	14 CT scan only; 5 CT scan + MRI; 6 CT scan + angiography; 2 MRI + angiography	2 CT scan only; 2 CT scan + angiography; 1 CT scan + MRI	6 CT scan only
Preoperative bilirubin level, mg%	.6 ± .2	.7 ± .2	.7 ± .1	.8 ± .32
Preoperative AST level, U/L	20.9 ± 7.9	24.4 ± 11.6	24.6 ± 6.03	31.8 ± 22.2
Preoperative ALT level, U/L	22.5 ± 16.5	24.5 ± 14.3	29.0 ± 25.1	38.3 ± 37.7
Preoperative PTT, s	11.1 ± 1.2	10.9 ± .9	10.9 ± .8	10.5 ± .5
Preoperative aPTT, s	31.1 ± 4.4	30.5 ± 3.05	30.3 ± 3.8	32.5 ± 5.9
α-fetoprotein level, U/L	22 ± 118	5.4 ± 9.9	8.3 ± 11.01	3.37 ± .54
Chronic hepatitis B carriers, *n*	15	11	3	0
Presence of CPLD	7	4	1	1

patient, and the request for removal of these lesions by 11 patients.

Among the 11 patients whose surgical indication was inability to rule out malignancy, 15 were chronic hepatitis B carriers, of whom 7 were found at surgery to have CPLD.

Twenty-three patients had upper-abdominal pain, in 6 of these patients there was associated early satiety. Among those patients who had symptoms, 20 had resolution of their symptoms after resection.

The average size of the cavernous hemangioma resected was 8.2 ± 6.7 cm. The average size of the cavernous hemangioma in patients with symptoms (n = 23) was 12.0 ± 7.0 cm, whereas of those patients who did not have symptoms (n = 23) it was 4.1 ± 3.1 cm. Those patients with symptoms had statistically larger lesions ($P < .0001$).

The preoperative radiologic investigations are listed in Table 1.

Focal nodular hyperplasia

Twenty-seven patients underwent liver resection for focal nodular hyperplasia (Table 1). There were 12 right hepatectomies, 7 left lateral segmentectomies, 3 left hepatectomies, and 5 segmental resections. The indications for surgery were inability to exclude malignancy in 23 patients, and symptoms in 4. Among the 4 patients who had symptoms, 3 had resolution of symptoms. In 21 patients whose indication for liver resection was inability to exclude malignancy, 11 had chronic hepatitis B infection, of whom 4 were found to have CPLD at surgery.

The preoperative radiologic investigations are listed in Table 1.

Hepatic adenoma

Five patients had hepatic adenoma (Table 1). The indications for surgery were inability to exclude malignancy in 4 patients and symptoms in 1 patient. There were 3 chronic hepatitis B carriers among the 4 patients whose indication was inability to exclude malignancy. Of these 3 patients, 1 had CPLD. The patient who had symptoms had resolution of her symptoms after resection.

There were 3 right hepatectomies, 1 left lateral segmentectomy, and 2 patients had segmental resections only.

The preoperative radiologic investigations are listed in Table 1.

Liver cysts

Six patients with liver cysts underwent liver resection (Table 1). The indications for resection were symptoms in 5 patients and 1 recurrence after cyst fenestration. All patients with symptoms said they felt better after surgery. There were no hepatitis B carriers in this group of patients but 1 patient had CPLD from an unknown cause.

The preoperative radiologic investigations and the results for the different benign liver tumors are summarized in Table 1.

Comparison of patients with and without CPLD

Among the 84 patients who underwent liver resection for benign liver tumors, 13 patients were found to have CPLD at surgery, proven by histology (Table 2).

The difference in the average age of the patients with CPLD and those without CPLD was significant ($P < .02$). The types of surgery in the 2 groups are shown in Table 2. Major liver resection is defined as resection of more than 3 segments. There were no significant differences in terms of type of resection between the 2 groups of patients. The diagnosis in each group also is shown in Table 2.

All patients had normal preoperative liver function tests. However, there was statistically higher aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels in patients with CPLD (Table 2). The preoperative partial thromboplastin time (PTT) and activated partial thromboplastin time (aPTT) were normal in all patients, although there was a statistically longer aPTT in patients with CPLD (Table 2).

There was no difference between the 2 groups of patients in terms of preoperative α-fetoprotein level, blood loss, and surgical time. All patients had normal platelet levels and there was no difference between the 2 groups. There was

Table 2
Comparison of patients with and without CPLD

	Patients with CPLD (n = 13)	Patients without CPLD (n = 71)	*P* value
Age	48.00 ± 11.43	40.21 ± 9.9	.02
Sex, M/F	8/5	35/36	.455
Major resection, %	46.2	49.3	.202
Type of resection	5 LLS; 1 left hepatectomy; 5 right hepatectomy; 2 segmental resection	17 LLS; 6 left hepatectomy; 29 right hepatectomy; 19 segmental resection	
Blood loss, mL	145 ± 202	97 ± 99	.265
Mean parenchymal time, min	84 ± 30	85 ± 35	.965
Preoperative AST, U/L	**36.5 ± 16.9**	**20.67 ± 7.17**	**.001**
Preoperative ALT, U/L	**42.6 ± 28**	**21.42 ± 14.24**	**.003**
Preoperative bilirubin level, mg%	.75 ± .28	.64 ± .22	.253
Preoperative PTT, s	11.38 ± 1.49	10.9 ± .93	.370
Preoperative aPTT, s	29.51 ± 6.00	31.19 ± 3.57	.04
Preoperative α-fetoprotein level, U/L	72.26 ± 229.3	4.68 ± 7.3	.860
Histologic diagnosis	7 cavernous hemangiomas; 4 focal nodular hyperplasia; 1 hepatic adenoma; 1 liver cysts	39 hemangiomas; 23 focal nodular hyperplasia; 4 hepatic adenoma; 5 liver cysts	
Complication rate (%)	7.7	8.5	.345

Significant values are shown in bold type.
LLS = left lateral segment.

also no difference between the 2 groups in terms of complication rates.

Morbidity

There was no 30-day mortality in this series. None of the patients required any blood transfusions. Seven of the patients (8.3%) had postoperative complications. Three patients had bile leaking through the drain, which resolved spontaneously after a few days. One patient had superficial wound infection. One patient had a urinary tract infection and 2 patients had basal atelectasis requiring antibiotic treatment.

Comments

Hepatectomy is now associated with much lower morbidity and mortality and its use has been expanded to include many nonmalignant liver lesions [12]. In a review of hepatectomy surgeries performed in the United States, resection for benign liver lesion ranged from 1% to 3% [13]. Poon et al [14], in an analysis of 1222 hepatectomies, reported that liver resection was for benign liver lesions in 15.4% of the patients. Similarly, Jarnagin et al [15], in an analysis of 1803 hepatectomies, stated that 9% of these were benign liver lesions.

Although it appears safe to perform liver resection for benign liver tumors, the indications to resect these lesions must be evaluated clinically and thoroughly before proceeding. Most experts agree that surgical intervention is indicated if the patients are symptomatic and if there is suspicion of malignancy or fear of malignant transformation [1]. For hepatic adenoma, there is an added risk of bleeding and rupture, and therefore most advocate resection for these lesions [16].

In this series, we decided not to include patients with hepatolithiasis and liver abscess because the surgical plan for these patients already is well defined. The most common benign liver lesion resected was cavernous hemangiomas and this is not surprising because it is the most common benign liver lesion [1]. Buell et al [12] found that the most common benign liver lesion resected was the hemangioma, followed by focal nodular hyperplasia, which was similar to our own series.

The common indications were symptoms and inability to exclude malignancy. Subsequent to the resection, 85% of patients had their symptoms resolved. In patients whose indication for resection was inability to exclude malignancy, two thirds were chronic hepatitis B carriers. Patients with chronic hepatitis B infection who present with a mass in the liver are treated aggressively in our center. These patients are at risk of developing hepatocellular carcinoma and if any doubt exists we do not hesitate to resect these lesions.

In patients who had focal nodular hyperplasia and hepatic adenoma, the main indication was suspicion of malignancy. This is not surprising because it is sometimes difficult to differentiate hepatocellular carcinoma from focal nodular hyperplasia by radiologic investigations [1,17]. In patients with hepatic adenoma, there was a significantly higher proportion of patients infected with chronic hepatitis B (3 of 5 patients); this could explain the indication for resection because lesions in such patients are viewed as being suspicious of hepatocellular carcinoma.

Liver cysts are the largest compared with other benign liver lesions. Smaller liver cysts usually do not cause symptoms and are treated only with percutaneous drainage or, if treated surgically, usually are marsupialized. Only large size cysts were included in this series. Focal nodular hyperplasia lesions are the smallest compared with other benign liver lesions and this is in concordance with the fact that the main indication for resection in this group of patients was suspicion of malignancy. Moreover, focal nodular hyperplasia often is asymptomatic and often is discovered only incidentally at routine investigations [1].

In comparing the size of hemangiomas between patients who had symptoms and those without symptoms, we found that those patients with symptoms had larger lesions. Hemangiomas can lead to symptoms when there is necrosis,

infarction, or thrombosis of the tumor. It also can cause Kasabach-Merritt syndrome, a rare clinical entity, as seen in 1 of our patients. All of the earlier-described findings most likely would occur if the hemangiomas are large, as seen from our study. This finding was similar to other series [18].

The gender distribution in this series was particularly interesting. Although all the earlier-described benign liver lesions are more common in females [1], the distribution of the sexes in this series of patients who underwent liver resection was about equal. Luciani et al [19], in reviewing his series of focal nodular hyperplasias in men, found that they are more likely to undergo liver resection for this lesion. They surmised that this is because the risk of developing hepatocellular carcinoma is greater in men [9,10,19]. This is probably why there is an equal distribution of the sexes in this series because males with liver lesions are more likely to be viewed as having a possible hepatocellular carcinoma.

We did not analyze the use of radiologic investigations in the diagnosis of these benign liver lesions for 2 reasons. First, because our center is a tertiary referral center, many of our patients were investigated by other institutions and they brought their radiologic investigations with them. As such, there is no consistency in these radiologic investigations. Second, because this study lasted more than 8 years, our institutional radiologic investigations and protocols also have changed over the years. However, it must be emphasized that we do not offer surgical resection as a first choice for these patients but rather would evaluate them further now with high-definition magnetic resonance imaging, which has specific characteristics that allows greater accuracy of diagnosis.

In the second half of our analysis, we analyzed the presence of CPLD in patients with benign liver tumors undergoing liver resection. Hepatic resection in the cirrhotic liver is technically more challenging than resection in normal liver, with increased risk of bleeding, septic complications, and postoperative liver failure [14]. Poon et al [14] found that cirrhosis was a risk factor for hospital morbidity and mortality in a univariate analysis but not in a multivariate analysis. In our series, all of our patients had normal liver enzyme levels before surgery, although the patients with CPLD had higher liver enzyme levels compared with those without CPLD. Similarly, patients with CPLD had a higher aPTT compared with those without CPLD. This reflects the presence of underlying liver parenchymal disease. However, all the patients with CPLD were Child's A, and on histology had mild cirrhosis only.

The parenchymal transection time was not different between the 2 groups of patients. Although there was no statistical difference between the 2 groups in terms of blood loss, patients with CPLD had a greater amount of blood loss compared with those without CPLD. The cirrhotic liver tends to be more fragile and when there is bleeding the vessels in the cirrhotic liver tend to remain open and thus cause more bleeding. As such, meticulous hemostasis during a parenchymal transection must be strictly adhered to when dealing with cirrhotic liver.

The complication rates were similar for both groups of patients. This reflects the fact that the presence of CPLD does not in any way affect the surgical outcome when performing liver resection for benign liver disease. This excellent result comes from our experience in dealing with hepatocellular carcinoma in cirrhotic liver.

In conclusion, liver resection for a benign liver lesion is a safe option for patients. But, to achieve good results, the indications for resection must be evaluated thoroughly. Patients with chronic parenchymal liver disease and benign liver tumors undergoing liver resection do not have a different outcome compared with those with normal livers.

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