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Surgical Treatment of Giant Liver Hemangioma Larger Than 10 cm: A Single Center's Experience With 86 Patients

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Abstract: The ideal surgical treatment of giant liver hemangioma is still controversial. This study aims to compare the outcomes of enucleation with those of resection for liver hemangioma larger than 10 cm in different locations of the liver and establish the preoperative predictors of increased intraoperative blood loss.

Eighty-six patients underwent enucleation or liver resection for liver hemangioma larger than 10 cm was retrospectively reviewed. Patient demographic, tumor characteristics, surgical indications, the outcomes of both surgical treatment, and the clinicopathological parameters influencing intraoperative blood loss were analyzed.

Forty-six patients received enucleation and 40 patients received liver resection. Mean tumor size was 14.1 cm with a range of 10–35 cm. Blood loss, blood product usage, operative time, hepatic vascular occlusion time and frequency, complications and postsurgical hospital stay were similar between liver resections and enucleation for right-liver and left-liver hemangiomas. There was no surgery-related mortality in either group. Bleeding was more related to adjacency of major vascular structures than the size of hemangioma. Adjacency to major vascular structures and right or bilateral liver hemangiomas were independently associated with blood loss >550 mL ($P = 0.000$ and 0.042, respectively).

Both enucleation and liver resection are safe and effective surgical treatments for liver hemangiomas larger than 10 cm. The risk of intraoperative blood loss is related to adjacency to major vascular structures and the location of hemangioma.

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Abbreviations: ALT = alanine aminotransferase, AST = aspartate aminotransferase, CT = computed tomography, CVP = central venous pressure, HCC = hepatocellular carcinoma, IVC = inferior vena cava, MRI = magnetic resonance imaging, PTC = portal triad clamping, ROC = receiver operating characteristics, SD = standard deviation, TB = total bilirubin.

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INTRODUCTION

Hemangioma is the most common benign liver tumor, and affects 3% to 20% of the general population.[1] These benign tumors can occur in people of all ages, but are more commonly found in young adult females.[2] The hemangioma is usually asymptomatic and diagnosed incidentally. For most patients, the natural history of cavernous hemangiomas in the liver remains uneventful and surgical intervention can be avoided. Observation of asymptomatic lesions by means of routine follow-up and imaging is usually adequate.[3–5]

Indications for surgery include the presence of progressive abdominal symptoms, spontaneous or traumatic rupture, rapidly enlarging lesions, Kasabach–Merritt syndrome and unclear diagnosis.[6] Four types of surgical procedures including liver resection, enucleation, hepatic artery ligation, and liver transplantation have been reported as treatments for liver hemangiomas.[7–10] Resection and enucleation remain the most commonly used surgical methods. Most surgeons have advocated enucleation of liver hemangioma because of its associated lower intraoperative blood loss, fewer overall complications, and shorter hospital stay.[11–14] Others, however, have advocated formal liver resection.[15–18] Until now, only limited data have been published comparing the results of surgical hemangioma excision by means of enucleation with liver resection.[11–14,19,20] Among these studies, the mean size of lesions reported was generally <10 cm in diameter, and the choice of enucleation or resection for liver hemangioma in different locations of the liver has not been precisely defined.

Recent advances in surgical techniques and established perioperative management have now made it possible to perform liver resection or enucleation safely in most specialized units. However, massive intraoperative hemorrhage remains a risk, especially giant hemangiomas >10 cm in size, because of the likelihood of major vascular injury when resecting or enucleating the hemangioma.[15,21] Identifying the discriminatory factors that predict intraoperative bleeding requiring blood transfusion are important in establishing effective hemostatic strategies. These include low central venous pressure (CVP) anesthesia, hepatic vascular occlusion, and a variety of hemostatic devices. However, data regarding the predictors of intraoperative blood loss in patients with liver hemangioma undergoing surgical treatment are lacking.

The purpose of this retrospective single-center study was to compare the outcomes of enucleation with those of resection for liver hemangiomas >10 cm in size in different locations of the liver, and to establish preoperative factors predictive of increased intraoperative blood loss requiring blood transfusion.

PATIENTS AND METHODS

Patients

Between March 1, 2007 and December 1, 2014 a total of 86 patients underwent surgical removal of a giant hepatic cavernous hemangioma of size >10 cm in the Hepatic Surgery Center at Tongji Hospital. Patients were included in the study if they met the following criteria: 1 lesion >10 cm; or multiple lesions with at least 1 >10 cm in size. Patient medical records were reviewed retrospectively. The collected data included the following: patient characteristics; hemangioma characteristics; indication for surgery; laboratory variables; tumor removal technique; surgical variables; length of hospital stay; postoperative complications; and mortality.

Preoperative Management

Ultrasonography and contrast-enhanced computed tomography (CT) are the preferred methods of diagnosing hemangioma. If the diagnosis was unclear, magnetic resonance imaging (MRI) was performed to confirm the presence of hepatic hemangioma. For giant hemangiomas adjacent to the main vascular structures, such as the inferior vena cava (IVC), portal vein or hepatic vein, preoperative CT angiography was often undertaken. Upper gastrointestinal endoscopy and colonoscopy were performed in patients with abdominal pain and dyspepsia to rule out any potential gastrointestinal diseases. Informed consent was obtained from all patients regarding the diagnostic and therapeutic procedures. All resected specimens were verified by histopathologic examination.

Surgical Techniques

The terminology used regarding anatomic liver resection was in accordance with the Brisbane 2000 system.[22] Anatomical resection involved resection of the hemangioma along with the related portal vein and its corresponding hepatic territory, and could include hemihepatectomy (right or left), sectionectomy, and segmentectomy (resection of Couinaud's segments).[23] Nonanatomic liver resection refers to the resection of a hemangioma without regard for segmental, sectional, or hemiliver anatomy. Enucleation refers to the removal of the hemangioma without the loss of any normal hepatic parenchyma. The decision as to the type of surgical procedure was made based on the size and location of the hepatic hemangioma, its relationship to major vascular and biliary structures, and the remnant volume of the liver parenchyma.

Surgery was performed through a right or bilateral subcostal incision. The main feeding artery was identified early and controlled with a bull-dog clamp. Intraoperative ultrasonography (Aloka, Inc., Tokyo, Japan) was routinely used to assist with the identification of the lesion, and its relationship to the major vascular and biliary structures. To reduce bleeding during liver resection or enucleation, the Pringle maneuver was performed before parenchymal transection. If massive bleeding from the main hepatic veins occurred, the infrahepatic IVC was occluded during liver transection. This technique has been described previously.[24]

Liver resection or enucleation was performed using a combination of Kelly forceps and ERBE VIO (Tuebingen, Germany) bipolar forceps. Small diameter vessels were electrocoagulated and the larger vessels ligated. Enucleation was carried out according to a technique described previously.[25] After transecting the peripheral liver parenchyma, a sheath of compressed liver tissue, that clearly defined the border between the cavernous tissue and the normal liver parenchyma, was encountered. The hemangioma was gradually separated from the parenchyma with a blunt instrument. Liver resection was performed using a standard technique in which inflow vessels were controlled and parenchymal transection followed.

After the hepatic hemangioma was removed, the residual bleeding sites were controlled with suture ligatures, electrocautery, or argon-beam coagulation. The raw surface of the liver was checked for bile leaks. After the completion of surgical resection, the omentum could be mobilized and placed over the free surface; a closed silicone drain was placed to allow postoperative bile leakage and hemorrhaging to be monitored.

Follow-Up

Patient follow-up included clinical examinations, liver function tests, and liver ultrasonography at 6-month intervals during the first year and yearly thereafter. Symptom relief was also assessed. Symptom control was categorized into the following types: (a) complete resolution; (b) amelioration; (c) aggravation; and (d) persistence.

Statistical Analysis

Continuous variables were expressed as the mean ± standard deviation. Categorical variables were compared using the Chi-square or Fisher exact tests. Student *t* test was applied to continuous variables. The Mann–Whitney *U* test was used for nonparametric variables. The cut-off level of blood loss was set at the predictive value for red cell transfusion using receiver operating characteristics (ROC) analysis. The median values regarding age, platelet count, prothrombin time, operation time, and postsurgical hospital stay were set as the cut-off values, to determine high or low levels in the univariate analysis of associations between intraoperative blood loss and various parameters. A logistic regression analysis was performed to identify the independent variables for increased blood loss. $P < 0.05$ was considered significant. Statistical analyses were performed using SPSS 19.0 software for Windows.

RESULTS

Patient and Hemangioma Characteristics

During the study period, 86 patients with giant cavernous liver hemangiomas that were >10 cm in size underwent surgery. Patient demographics and hemangioma characteristics are summarized in Table 1. Median patient age was 47 (range, 26–65) years. There were 59 (68.6%) women and 27 (31.4%) men. Eighteen of the 86 patients were asymptomatic and their hemangiomas were incidentally discovered during radiologic or physical examination. The most common symptoms were upper abdominal discomfort and indigestion (n = 30), right or left quadrant pain (n = 24), and abdominal mass (n = 3). Other indications for surgery included rapid growth (n = 10) and spontaneous rupture of the hemangioma (n = 1). Two patients had a reduced platelet count ($<100 \times 10^9$/L) with hemangiomas of size 22 and 25 cm.

Sixty-six percent of diagnostic studies were performed at the referring institutions. In 77 (89.5%) patients, the initial examination consisted of liver ultrasonography. Abdominal CT scans were performed in the vast majority of patients (90.1%) and MRI scans in 12 (14%) patients. In 73 (84.5%) patients, the

TABLE 1. Patient Demographics and Hemangioma Characteristics

Demographics/Characteristics	All Patients (n = 86)	Enucleation (n = 47)	Resection (n = 39)	*P*-Value
Median age, year (range)	47 (26–65)	46 (29–63)	48 (26–65)	0.250
Female gender (%)	59 (68.6)	34 (72.3)	25 (64.1)	0.413
Reason for evaluation				0.433
Asymptomatic (%)	18 (20.9)	11 (23.4)	7 (17.9)	
Symptomatic (%)				
Upper abdominal discomfort, indigestion	30 (34.9)	16 (34.0)	14 (35.9)	
Right or left quadrant pain	24 (24.4)	14 (29.8)	10 (25.6)	
Abdominal mass	3 (3.5)	2 (4.3)	1 (2.6)	
Rapid growth (%)	10 (11.6)	5 (10.6)	5 (12.8)	
Rupture (%)	1 (1.2)	1 (2.1)	0 (0)	
Accompany gastrointestinal disease (%)	42 (48.8)	22 (46.8)	20 (51.3)	0.679
Gastroesophageal disease (%)	15 (17.4)	10 (21.3)	5 (12.8)	
Hepatitis/liver disease (%)	16 (18.6)	8 (17.0)	8 (20.5)	
Disease of biliary system (%)	7 (8.1)	1 (2.1)	6 (15.4)	
Colorectal disease (%)	4 (4.7)	3 (6.4)	1 (2.6)	
Size of the largest lesion, mean ± SD, cm	14.1 ± 5.0	13.1 ± 3.6	15.2 ± 6.1	0.381
<15 cm, n (%)	60 (70.0)	35 (74.5)	25 (64.2)	
15–20 cm, n (%)	17 (19.6)	10 (21.3)	7 (17.9)	
>20 cm, n (%)	9 (10.4)	2 (4.2)	7 (17.9)	
Location				
Right liver (%)	43 (50.0)	32 (68.1)	11 (28.2)	**0.000**
Left liver (%)	30 (34.9)	6 (12.8)	24 (61.5)	
Bilateral (%)	13 (15.1)	9 (19.1)	4 (10.3)	
Number				
Single lesion (%)	58 (67.4)	31 (66.0)	27 (69.2)	0.747
Multiple lesion (%)	28 (32.6)	16 (34.0)	12 (30.8)	
Median number of lesions (range)	1 (1–4)	1 (1–4)	1 (1–3)	0.615

The bold used in the table mean that the difference is significant ($p < 0.05$).

final diagnosis of hemangioma was supported by findings from 2 imaging techniques and in 4 (4.6%) patients by findings from 3 techniques. The mean number of studies performed in all patients was 2.0. No cases were suspected of malignancy. No patients underwent percutaneous or intraoperative biopsy to establish a definitive diagnosis.

Sixteen (18.6%) patients had hepatitis or liver disease. Among them, 13 patients had hepatitis B, 2 had hepatitis C, and 1 had a liver cyst. The mean hemangioma size was 14.1 (range, 10–35) cm. Lesions were located in the right liver in 43 (50.0%) patients, in the left liver in 30 (34.9%) patients and in the bilateral liver in 13 (15.1%) patients. Fifty-eight (67.4%) patients had a single hemangioma and 28 (32.6%) patients had multiple hemangiomas (Table 1). All resected specimens were confirmed as cavernous hemangioma. As shown in Figure 1, cavernous hemangioma is typically composed of varying sized blood-filled vascular channels, and lined by single layer of flat endothelia without any cellular atypia.

Surgical Treatment

The surgical procedure was either enucleation (n = 47) or liver resection (n = 39). In the liver resection group, the following procedures were performed: left lateral sectionectomy in 14 patients; left hepatectomy in 8 patients; left trisectionectomy in 1 patient; right hepatectomy in 7 patients (Figure 2); right trisectionectomy in 3 patients; and nonanatomic liver resection in 6 patients. Right-liver lesions were more frequently treated using enucleation and left-liver lesions using resection ($P = 0.000$; Table 1).

Taking into consideration the nonequal anatomical distribution between the enucleation and resection groups, patients were stratified in terms of the location of their hemangiomas. In the patients with right-liver hemangiomas, preoperative variables were similar between the resection and enucleation groups. No statistically significant relationship between the surgical approach and blood loss, or blood product use, was observed. Operation time, hepatic vascular occlusion time and

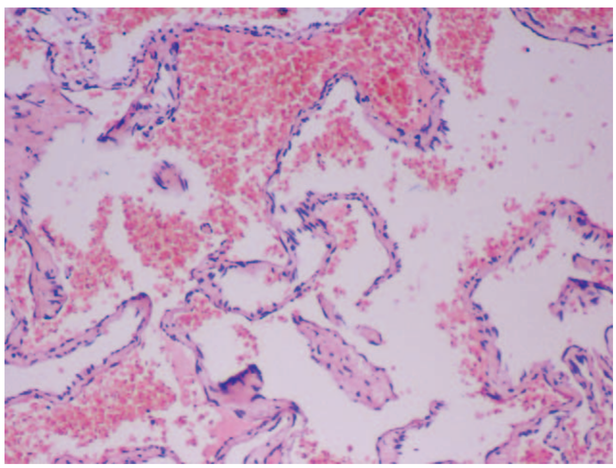


FIGURE 1. Typical cavernous hemangioma with multiple vascular channels filled with blood.

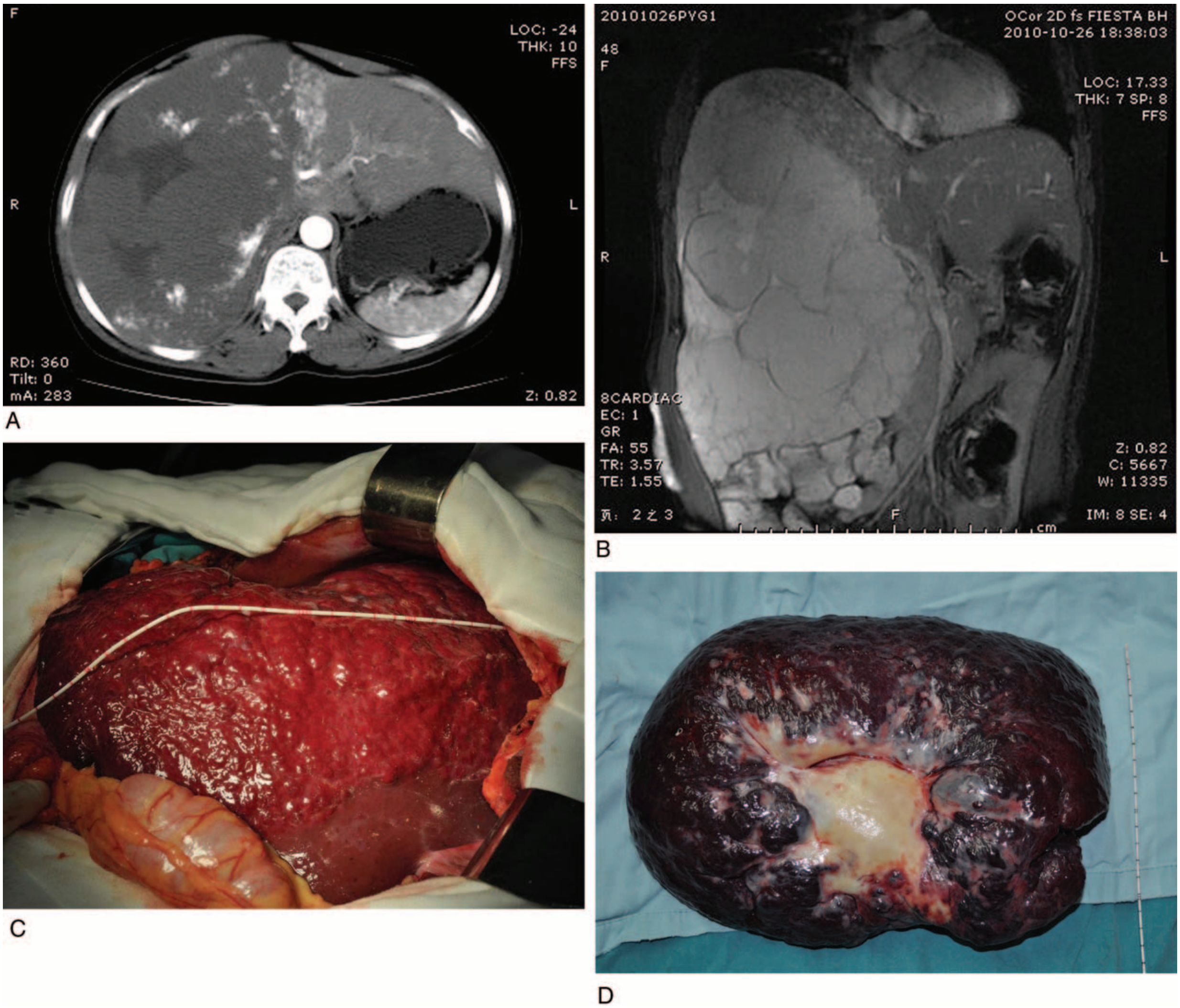


FIGURE 2. A symptomatic hemangioma of 28 cm × 22 cm in the right liver submitted treated with right hepatectomy. (A) Abdominal computed tomography showing the characteristic peripheral enhancement with hypodense center after the administration of contrast medium. (B) T2-weighted magnetic resonance image showing a mass markedly hyperintense relative to liver parenchyma. (C) Intraoperative photo of a giant liver hemangioma. (D) Giant liver hemangioma specimen.

frequency, postsurgical hospital stay and complications were also similar for both groups (Table 2). In the patients with left-liver hemangiomas, the median number of lesions in the enucleation group was higher than in the resection group ($P = 0.034$). Surgical outcomes demonstrated that operation time, hepatic vascular occlusion time and frequency, blood loss, complications and postsurgical hospital stay were similar for both surgical techniques.

Bilateral liver hemangiomas included the centrally located lesion (in segments I, IV, V, and VIII) and the lesion occupying 3 hepatic sections. Nine centrally located lesions were treated using enucleation and the 4 lesions occupying 3 hepatic sections were treated using resection (left or right trisectionectomy).

Twenty-eight (32.6%) patients had complications, but none died. The most common complication was pleural effusion, which occurred in 22 (25.6%) patients. Other complications included diaphragmatic injury (1), hemorrhage (3), pneumonia (1), and bile leak (1).

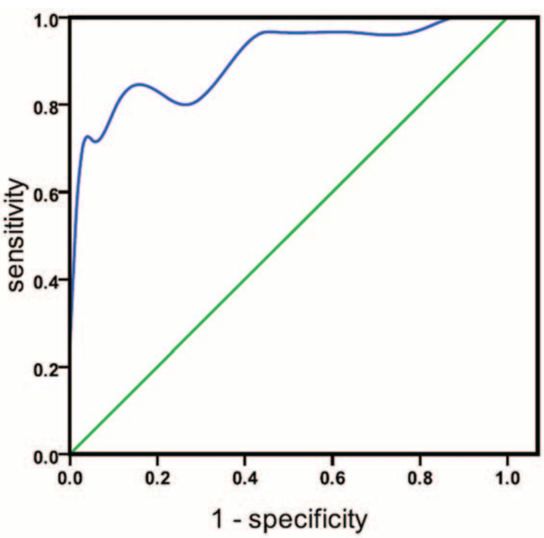
Parameters Associated With Estimated Blood Loss

Mean and median blood loss were 526.1 ± 468.8 mL and 400 (range, 100–3000) mL, respectively. Ten (11.6%) patients lost >1 L of blood intraoperatively. Twenty-four (27.9%) patients received a blood transfusion; the median volume of the red cell transfusion was 3 (range, 2–14) U. According to the ROC analysis, the predictive value of blood loss in patients who received a red cell transfusion was 550 mL (Figure 3). Table 3 details the results of a univariate analysis between various parameters and blood loss (>550 mL). Patients with larger hemangiomas experienced significantly greater blood loss ($P = 0.000$). Blood loss >550 mL was significantly more common in patients with right or bilateral liver hemangiomas, and hemangiomas adjacent to major vascular structures ($P = 0.013$ and $P = 0.000$, respectively). In terms of preoperative liver function and surgical records, shorter prothrombin time and a

TABLE 2. Preoperative Variables, Operative and Hospital Course

	Right Liver			Left Liver		
Variables	**Enucleation (n = 32)**	**Resection (n = 11)**	***P*-Value**	**Enucleation (n = 6)**	**Resection (n = 24)**	***P*-Value**
Age (year)	42.1 ± 9.5	45.8 ± 9.6	0.272	44.5 ± 6.7	50.2 ± 8.2	0.124
Female gender (%)	24 (75.0)	10 (90.9)	0.407	5 (83.3)	12 (50.0)	0.196
Size of the largest lesion (cm)	13.0 ± 3.3	17.5 ± 8.1	0.063	14.8 ± 5.4	12.8 ± 3.8	0.281
Median number of lesions (range)	1 (1–4)	1 (1–2)	0.902	2 (1–3)	1 (1–3)	**0.034**
Hemoglobin (g/L)	121.5 ± 21.2	112.5 ± 15.3	0.203	113.2 ± 23.9	127.3 ± 14.7	0.075
Platelet ($\times 10^9$/L)	182.3 ± 64.3	178.6 ± 52.5	0.864	163.7 ± 52.6	178.5 ± 47.9	0.369
Prothrombin time (s)	10.9 ± 1.1	11.4 ± 1.4	0.282	11.4 ± 2.0	10.8 ± 0.7	0.499
ALT (IU/L)	18.4 ± 8.7	14.9 ± 8.1	0.254	13.0 ± 8.0	17.0 ± 9.9	0.362
AST (IU/L)	15.9 ± 8.2	13.8 ± 11.4	0.509	11.0 ± 6.3	12.8 ± 6.5	0.558
TB (μmol/L)	12.1 ± 6.8	17.1 ± 11.9	0.093	14.7 ± 4.8	13.4 ± 4.4	0.532
Surgical time (minutes)	201.1 ± 63.5	237.1 ± 49.0	0.095	221.0 ± 46.2	215.8 ± 64.7	0.854
Hepatic vascular occlusion						
No. (%) of patients	31 (96.9)	11 (100)	1.000	4 (66.7)	11 (45.8)	0.651
Duration (minutes)	13.5 ± 5.2	17.5 ± 8.5	0.070	14.0 ± 2.2	11.5 ± 3.2	0.169
Blood loss (mL)	400 (100–3000)	500 (200–1000)	0.491	175 (100–1000)	300 (100–1600)	0.48
Blood transfusion						
No. (%) of patients	9 (28.1)	4 (36.3)	0.608	2 (33.3)	4 (16.7)	0.361
Median, no. of units	3 (2–14)	2.5 (2–4)	0.683	3 (2–4)	3.75 (2–6)	0.634
Complication, no. (%)	12 (37.5)	4 (36.4)	0.946	2 (33.3)	5 (20.8)	0.914
Diaphragmatic injury	0	0		0	0	
Postoperative hemorrhage	1	1		0	0	
Pneumonia	0	0		0	0	
Bile leak	1	0		0	0	
Pleural effusion	10	3		2	5	
Postsurgical hospital stay (days)	12.2 ± 3.8	12.0 ± 3.3	0.503	10.8 ± 1.9	12.0 ± 2.7	0.326
Mortality	0	0	—	0	0	—

The bold used in the table mean that the difference is significant ($p < 0.05$).



Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval: Lower Bound	Asymptotic 95% Confidence Interval: Upper Bound
.901	.037	.000	.828	.975

FIGURE 3. ROC curve for estimated blood loss in patients who received red cell blood transfusion.

longer operation time were associated with blood loss >550 mL ($P = 0.019$ and $P = 0.03$, respectively). Hepatic vascular occlusion and complications were significantly more common in patients whose blood loss was >550 mL ($P = 0.01$ and $P = 0.001$, respectively). The surgical method (liver resection or enucleation) was not significantly associated with blood loss.

On multivariate analysis, adjacency to major vascular structures, and right or bilateral liver hemangiomas were independently associated with blood loss >550 mL ($P = 0.000$ and $P = 0.042$, respectively; Table 4).

Follow-Up

Data regarding clinical follow-up was available for 82 patients. The median interval between the operation and the final evaluation was 43 (range, 7–98) months. Fifty-seven patients were symptomatic before surgery. Complete resolution or significant amelioration was achieved for 94.7% of the patients. Three of the 57 patients had persistent or recurring preoperative symptoms. Two patients had a long history of erosive gastritis and duodenal ulcer, and still had recurrent upper abdominal discomfort or pain. Another patient with a history of hepatitis had upper quadrant discomfort at 12 months after their operation. No significant abnormalities were detected in the liver function test in any of the patients. Ultrasonography revealed that no patients developed new hemangiomas at a different site within the liver.

TABLE 3. Univariate Analysis of Associations Between Intraoperative Blood Loss and Various Parameters

Variable	≤550 mL (n = 60)	>550 mL (n = 26)	*P*-Value
Gender			
Male	19	8	0.934
Female	41	18	
Age			
≤45	29	14	0.639
>45	31	12	
Reason for evaluation			
Asymptomatic	13	5	0.966
Symptomatic	40	18	
Rapid growth	7	3	
Underlying chronic hepatitis			
Presence	29	13	0.887
Absence	31	13	
Size (cm)			
≤15	49	11	**0.000**
>15	11	15	
Number			
Solitary	39	19	0.463
Multiple	21	7	
Location			
Left	26	4	**0.013**
Right/bilateral	34	22	
Adjacency to major vascular structures			
Yes	16	22	**0.000**
No	44	4	
Platelet ($\times 10^9$/L)			
≤173	27	16	0.159
>173	33	10	
Prothrombin time (s)			
≤11	35	8	**0.019**
>11	25	18	
Operative time (min)			
≤210	36	9	**0.03**
>210	24	17	
Operative method			
Liver resection	29	10	0.398
Enucleation	31	16	
Hepatic vascular occlusion			
Yes	43	25	**0.01**
No	17	1	
Complication			
Presence	14	16	**0.001**
Absence	46	10	
Postsurgical hospital stay (day)			
≤12	33	10	0.159
>12	27	16	

The bold used in the table mean that the difference is significant ($p < 0.05$).

DISCUSSION

Management of liver hemangiomas ranges from observation to a variety of radiological and surgical interventions.[26,27] A large majority of hemangioma should not receive any treatment as hemangioma usually follows a benign course. Surgical intervention is the only radical treatment for liver hemangiomas. Indication for surgery has traditionally been the presence of symptoms.[28,29] Abdominal pain or discomfort associated with liver hemangioma is the most common indication for surgical excision. Increasing size or intratumoral thrombosis or hemorrhage can cause pain, as a result of liver capsule distension. Abdominal fullness and palpable masses are associated with space occupation or compression caused by the lesion.[27] However, not all patients with symptoms are good candidates for resection. The symptoms of some patients persist despite liver resection.[16] Etemadi et al[30] reported that pain was attributed to hemangioma in only 12.6% of patients. Therefore, it is important to recognize extraneous causes of symptoms before considering surgical treatment for liver hemangioma. Large hemangiomas were more likely to cause persistent symptoms during follow-up.[31] In our series, 57 of 86 (66.3%) patients presented with abdominal discomfort, pain, or a palpable mass.

The size of the hemangioma alone is not a formal indication for surgical intervention, although pain was more frequently observed in patients with larger lesions. Some authors[19,28,32,33] have emphasized that hemangiomas >10 cm in size may have a greater potential for internal bleeding, further growth or rupture, which justified the prophylactic excision of asymptomatic large lesions. Choi et al[34] has suggested that earlier intervention should be considered for liver hemangiomas adjacent to major vascular structures. However, in another author's experience, size alone was found to be a poor predictor of the subsequent behavior of hemangiomas and should not be an absolute indication for surgery.[35] Prophylactic surgical intervention is not broadly applicable, even in patients with extremely large hepatic hemangiomas (>10 cm).[36] Thus, the topic remains open to debate. The reported percentage of asymptomatic hemangiomas in the surgical group has been reported to range from 16% to 39.8%.[18,29,36] In our series, 18 of the 86 (20.9%) patients were asymptomatic. In our opinion, reasons for deciding in favor of surgically treating asymptomatic hemangiomas >10 cm in size include: a greater potential for spontaneous or traumatic rupture; the patient's willingness to have surgery because of the undesirable feeling of living with a large liver lesion and the decompensated fear of complications.[18]

There are 2 common surgical procedures for the treatment of liver hemangioma, namely enucleation and resection. Some authors advocate formal liver resection[15–18] while others advocate enucleation.[25,29,37] Comparative studies between liver resection and enucleation of the hemangioma have reported that enucleation is associated with less intraoperative bleeding, shorter operation times, lower morbidity, and a shorter hospital stay.[11–14] These comparative studies have several limitations: the mean size of lesions reported was seldom >10 cm; the study population sizes in these studies were small; and the influence of hemangioma location on the selection of the surgical technique was not analyzed individually.

Liver hemangioma is a benign disease. Avoiding unnecessary loss of healthy liver parenchyma is one of the basic principles that should be born in mind when selecting a surgical procedure.[38] Therefore, enucleation is still the preferred surgical procedure for giant liver hemangioma. In our series, 47 of 86 (54.7%) liver hemangiomas were treated using enucleation. We found that surgical time, hepatic vascular occlusion time and frequency, blood loss, complications, and postsurgical hospital stay did not differ between the liver resection and enucleation groups, for either right or left liver hemangiomas. A recent study has reported similar outcomes.[39] Consequently, under the premise of keeping the removal of the

TABLE 4. Multivariate Analysis of Associations Between Intraoperative Blood Loss and Various Preoperative Parameters

Variables	Odds Ratio	95% Confidence Interval	*P*-Value
Hemangioma size			
>15 cm, ≤15 cm	2.494	0.687–9.049	0.165
Hemangioma location			
Right/bilateral, left	3.980	1.05–15.091	**0.042**
Adjacency to major vascular structures			
Yes, no	14.74	4.26–50.999	**0.000**
Prothrombin time (seconds)			
>11, ≤11	1.252	0.321–4.885	0.747

The bold used in the table mean that the difference is significant ($p < 0.05$).

normal liver parenchyma to a minimum, liver resection is a useful alternative surgical procedure. For giant liver hemangiomas occupying the hemiliver or left lateral sections, few normal liver parenchyma remain on the affected side. In this situation, anatomical liver resection will not result in excessive sacrifice of healthy liver parenchyma. In addition, if it is not feasible to preserve the normal liver parenchyma located around a liver hemangioma, such as in deeply located or multiple liver hemangiomas, liver resection is the preferred technique.

Surgical treatment for extremely large hemangiomas (>10 cm) carries a significant risk of torrential intraoperative bleeding.[15,19,21] In the experience of the Memorial Solan Kettering Cancer Center, 10 (19.2%) patients experienced blood loss of ≥1 L.[29] In our series, the percentage of patients with blood loss exceeding 1 L was 11.6%. A univariate analysis of our study data showed that the size and location of the liver hemangioma, its relationship to major vascular structures, prothrombin time, operation time, hepatic vascular occlusion, and complications were associated with increased blood loss. The association between size of the liver hemangioma and blood loss has been reported previously.[19,39] Involvement of hepatic vessels and tumor location might be strongly related to increased blood loss during resection of hepatocellular carcinoma (HCC).[40] Fu et al[41] found that enucleation of centrally located liver hemangiomas was associated with greater blood loss, and an increased need for additional blood transfusions, than peripherally located lesions. Prothrombin time can directly affect hemostatic functions. Previous reports have shown a significant relationship between coagulation activity and blood loss during hepatectomy.[42] Prolonged operation time and more frequent hepatic vascular occlusion are most likely the consequence of increased intraoperative blood loss in association with greater size, and are more technically demanding regarding the surgical removal of liver hemangioma. Multivariate analysis indicated that the risk of intraoperative blood loss was more closely related to adjacency to major vascular structures than to the size of the hemangioma. Effective hemostatic strategies including hepatic inflow and/or outflow occlusion, lowering of the CVP, the liver hanging maneuver, and a variety of hemostatic devices should be adopted for patients at a higher risk of intraoperative blood loss.

Previous studies have demonstrated that the blood supply of hemangiomas is primarily from the corresponding hepatic artery. Baer et al[25] reported that ligation of a branch of the hepatic artery before enucleation of liver hemangiomas reduced blood loss. We controlled the corresponding hepatic artery, or any aberrant arteries from the left gastric artery or the superior mesenteric artery, before extracapsular resection of hemangioma. Occlusion preparation for bleeding from inflow vessels was performed routinely. If the hemangioma was attached to the main trunk of the hepatic veins and/or retrohepatic IVC, preparation for infrahepatic IVC occlusion was also undertaken. In our experience, portal triad clamping (PTC) combined with infrahepatic IVC clamping has proved more efficacious in controlling bleeding, and has caused fewer hemodynamic changes during complex hepatectomy than PTC with low CVP.[24]

The main limitations of our study were its retrospective nature and the nonrandomized selection of patients. We cannot exclude potential selection bias. The types of surgical procedures were selected in accordance with the surgeon's preference, and these choices were influenced by the features of the lesion and the experience of the surgeons. Because of the nonequal anatomical distribution between the resection and enucleation groups, we stratified patients in terms of the location of hemangiomas. Second, this study was performed in a single institution and the results obtained might not be comparable to those in other centers. Single center studies carried out in a relatively short period (7 years), however, have the advantage of reducing the possible differences in indication for surgery, surgical technique, and transection devices. Additional external validation is required to confirm that our findings would be applicable to other surgical teams.

To the best of our knowledge, the present study is the largest to date reporting on hepatic hemangioma of size >10 cm. We found that both enucleation and liver resection are safe and effective surgical treatments for liver hemangiomas >10 cm. There were no major differences in outcomes when using enucleation and liver resection for liver hemangioma in different regions of the liver. Adjacency to major vascular structures and right or bilateral liver hemangiomas were found to be independent preoperative predictor factors regarding increased intraoperative blood loss.

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