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ORIGINAL ARTICLE

Quality of life can be improved by surgical management of giant hepatic haemangioma with enucleation as the preferred option

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Abstract

Objectives: Surgical resection represents the main curative treatment for giant hepatic haemangioma (GHH). The aim of this study was to compare the respective outcomes of hepatic enucleation (HE) and hepatic resection (HR) for GHH.

Methods: Giant hepatic haemangioma was defined as haemangioma of 5–15 cm in size. A prospectively maintained database consisting of a series of consecutive patients who underwent HE or HR of GHH from January 2004 to December 2013 was analysed.

Results: Hepatic enucleation was performed in 386 (52.9%) patients and HR in 344 (47.1%) of a final cohort of 730 patients. The median size of GHH was similar in the HR and HE groups (9.8 and 10.6 cm, respectively; $P = 0.752$). The HE group had a shorter median operative time (150 min versus 240 min; $P = 0.034$), shorter median hospital stay (5.7 days versus 8.6 days; $P < 0.001$), lower median blood loss (400 ml versus 860 ml; $P < 0.001$), and fewer complications (17.6% versus 28.2%; $P < 0.001$) than the HR group. Quality of life scores in both the HR and HE groups significantly improved compared with preoperative levels and were similar to those found in healthy Chinese individuals following surgery, confirming the efficacy of both treatments.

Conclusions: Hepatic enucleation was associated with favourable operative outcomes compared with HR and is a safe and effective alternative to partial hepatectomy for GHH.

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Introduction

Hepatic haemangioma is the most frequent benign hepatic tumour. It shows a female predominance in all age groups and is increasingly found incidentally on abdominal ultrasonography or computed tomography examinations.[1–3] The overwhelming majority of haemangiomas are asymptomatic and do not require intervention. However, large haemangiomas can produce a variety of symptoms, including abdominal, shoulder and back pain, nausea, vomiting, jaundice, abdominal distension and dyspnoea. In addition, thrombocytopoenia, fever and compression of adjacent structures, rupture and consumptive coagulopathy (Kasabach–Merritt syndrome) have been reported.[4–6]

Indications for surgery include severe progressive symptoms, increase in size, inability to exclude malignancy, and a high risk for hepatic injury and complications.[7,8] Size alone is not, however, an indication for surgery.[9]

Giant hepatic haemangioma (GHH) is defined as haemangioma of ≥5 cm in size. Treatment modalities for symptomatic GHH, such as medical therapies, arterial ligation, transcatheter arterial embolization (TAE), radiofrequency ablation and liver transplantation, have been applied with variable success.[10–14] Surgical resection or transplantation remain the only consistently curative methods of treatment for symptomatic GHH. Hepatic enucleation (HE) and hepatic resection (HR) have both been described; however, it is unclear which of these treatments is superior. The aim of this study was to compare the outcomes of patients undergoing HE or HR for the management of GHH with the purpose of identifying an optimal treatment strategy.

Materials and methods

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Clinical

Trial Ethics Committee of West China Hospital. Written informed consent was obtained from each participant before surgery. A prospective database comprising demographic information, perioperative parameters and complications in all patients with hepatic haemangioma who underwent surgical intervention has been maintained since 2004. Inclusion criteria for this study required patients to demonstrate hepatic haemangioma of 5–15 cm in diameter, along with indications for surgery that included the presence of progressive symptoms, increasing size, inability to exclude malignancy, or complications following a period of observation. Exclusion criteria denied the participation of patients with cirrhosis or another significant comorbidity. Patients who refused to participate were not included. Patients with GHH of >15 cm in size were excluded because the preferred treatment option in these cases was TAE followed by HE and thus their inclusion would have biased the comparison of HE with HR.

The choice of surgical technique was left to the individual surgeon. A total of nine surgeons contributed patients to the study. For both HE and HR, the surgical procedure was performed using a Chevron incision. Surgery was performed under low central venous pressure anaesthesia. Intermittent vascular inflow control was used as required. Transection of the liver parenchyma was undertaken using a water-jet dissector and/or an ultrasonic dissector (Cavitron Ultrasonic Surgical Aspirator; Tyco Healthcare Group, Mansfield, MA, USA). In patients treated with HR, the aim was to achieve a tumour-free resection margin of 0.5–1.0 cm as estimated by visual inspection and to avoid peritumoural vessels. Hepatic enucleation was performed under vascular inflow control with the tumour dissected from normal hepatic parenchyma by meticulous dissection of the surgical plane, ligating or clipping feeding vessels as exposed.[15] All excised specimens were submitted for histopathological analysis. Massive haemorrhage was defined as intraoperative blood loss of >1000 ml. Bile leak was defined as external drainage or intra-abdominal collection of fluid characterized as bile. Perioperative morbidity and mortality included complications or death occurring during the hospital stay or within the 30 days after the operation. Perioperative morbidity was categorized according to the Clavien–Dindo system of classification.[16]

The 36-item Short-Form Health Survey (SF-36) questionnaire was administered to all patients in both groups before surgery and at 1, 3 and 6 months after surgery. The SF-36 is a well-validated questionnaire that measures eight areas of health: physical functioning; role–physical; role–emotional; bodily pain; vitality; mental health; social functioning, and general health.[17] The summary score is derived from a total of scores on all items, with the worst score being 0 (poor health) and the best score being 100 (good health). Scores on the SF-36 were compared between the HE and HR groups and with established scores of healthy persons in China.[18]

Statistical analysis

Discrete variables were assessed for statistical significance using the chi-squared test. Continuous data are expressed as the median (range). Two-tailed Mann–Whitney *U*-tests and log rank tests were used to compare outcomes between the HE and HR groups as appropriate. A *P*-value of ≤ 0.05 was considered to indicate statistical significance. All analyses were performed using SPSS for Windows Version 16.0 (SPSS, Inc., Chicago, IL, USA).

Results

A total of 2865 patients in whom a diagnosis of haemangioma of the liver was documented between January 2004 and December 2013 were identified. Of these, 1003 (35.0%) patients were identified with GHH.

Of the 1003 patients, 200 (19.9%) were identified as having GHH of >15 cm in largest diameter and were therefore excluded. Seventy-three patients were deceased at the time of the survey and thus were excluded from analysis because the available data were insufficient. A total of 730 (25.5% of the full cohort) patients were included in the current study. Of these, 386 patients (52.9%) underwent HE and 344 patients (47.1%) underwent HR. The clinical characteristics of all included patients are summarized in Table 1.

Operative data and morbidity for the two groups are shown in Tables 2 and 3, respectively. Overall, 352 (91.2%) of the 386 patients in the HE group and 308 (89.5%) of the 344 patients in the HE group completed the SF-36 assessment at their 1-, 3- and 6-month follow-ups. Preoperative SF-36 scores did not differ significantly between the HE and HR groups on any of the eight domains (Table 4), but were significantly lower in all eight domains than those recorded for healthy Chinese individuals. At 6 months after surgery, SF-36 scores in both the HE and HR groups were comparable with those in Chinese normal individuals.

Discussion

Haemangioma is the most common neoplasm of the liver, affecting 3–20% of the general population.[19] Most hepatic haemangiomas are small and stable, and are usually managed expectantly in the absence of symptoms or complications. The natural history of hepatic haemangioma remains unclear. Although spontaneous rupture of GHH has been reported in the literature, it is rare and prophylactic resection is not recommended.[13,20,21] Schnelldorfer *et al.*[22] demonstrated that non-operative management of GHH of the liver is safe, even in patients with extremely large hepatic haemangiomas. Therefore, although resection or enucleation of haemangiomas can be performed with low morbidity, operative intervention should be recommended only in patients with symptoms that are sufficiently severe to affect lifestyle and to justify operative risk. In

Table 1 Clinical characteristics of patients undergoing hepatic resection (HR) or hepatic enucleation (HE) for giant hepatic haemangioma

Clinical characteristics	HE group (*n* = 386)	HR group (*n* = 344)	*P*-value
Gender, male, *n* (%)	224 (58.0%)	205 (59.6%)	0.764
Age, years, median (range)	45 (20–70)	46 (21–68)	0.455
ASA status (I/II/III), *n*	267/111/8	245/92/7	0.327
Surgical indications, *n* (%)			
Symptomatic	222 (57.5%)	197 (57.3%)	0.234
Progressive increase in size	89 (23.1%)	80 (23.3%)	0.542
Haemangioma related complications	42 (10.9%)	37 (10.8%)	0.324
Uncertain diagnosis	24 (6.2%)	22 (6.4%)	0.265
Other	9 (2.3%)	8 (2.3%)	0.321
Tumour location (segment), *n*			
I	3	5	0.132
II, III	44	39	0.228
IV	98	88	0.176
V, VI	166	147	0.253
VII, VIII	75	65	0.154
Largest tumour size, cm, median (range)	9.8 (1.5–5.7)	10.6 (1.8–4.4)	0.752
Solitary haemangioma, *n* (%)	304 (78.8%)	276 (80.2%)	0.541

ASA, American Society of Anesthesiologists.

Table 2 Operative data for patients with giant hepatic haemangioma undergoing hepatic enucleation (HE) or hepatic resection (HR)

Parameters	HE group (*n* = 386)	HR group (*n* = 344)	*P*-value
Operative time, min, median (range)	150 (30–275)	240 (50–400)	<0.001
Blood loss, ml, median (range)	400 (150–600)	860 (300–1250)	<0.001
Units of auto-transfusion, units, median (range)	1.5 (0.5–2.0)	3.5 (1.5–6.0)	<0.001
Specimen weight, g, median (range)	385.5 (45–125)	355.7 (40–130)	0.037
Hospital stay, days, median (range)	5.7 (6–11)	8.6 (7–20)	<0.001

Table 3 Postoperative morbidity and mortality in patients undergoing hepatic enucleation (HE) or hepatic resection (HR) for giant hepatic haemangioma

Parameters	HE group (*n* = 386) *n* (%)	HR group (*n* = 344) *n* (%)	*P*-value
Patients with complications	68 (17.6)	97 (28.2)	<0.001
Major complication (≥Grade III)	57 (14.8)	70 (20.3)	0.065
Bile leak (Grade III)	33 (8.5)	55 (15.9)	0.002
Acute hepatic failure (Grade IV)	3 (0.8)	4 (1.2)	0.603
Ascites (Grade I)	34 (8.8)	51 (14.8)	0.010
Perihepatic abscess (Grade III)	7 (1.8)	6 (1.7)	0.473
Postoperative haemorrhage (Grade IV)	5 (1.3)	6 (1.7)	0.620
Reoperation	3 (0.8)	5 (1.5)	0.391
Mortality	0	0	1.000

Complications are graded according to Dindo *et al.*[16] Grade I complications require variation without necessitating operative or medicinal treatment. Grade II complications need medicinal therapy. Grade III complications need operative, endoscopic or radiologic assistance. Grade IV complications are life-threatening additional complications which include central nervous system, solitary body organ malfunction, and multi-organ malfunction necessitating intensive care unit treatment. Grade V complications involve the death of the affected individual. In the existing analysis, complications of Grades I and II are categorized as minor and those of Grades III–V are considered to be major complications.

Table 4 Preoperative and postoperative scores on the Short-Form (36-item) Health Survey (SF-36)

SF-36 items	SF-36 score, median (range)								
	Patients with giant hepatic haemangioma								Chinese healthy subjects
	Preoperative		1 month		3 months		6 months		
	HE group	HR group	HE group	HR group	HE group	HR group	HE group	HR group	
Physical functioning	44 (35–65)[a]	43 (37–68)[a]	63 (55–74)[a]	63 (54–72)[a]	75 (60–83)[a]	79 (62–85)[a]	87 (78–94)	85 (80–95)	90 (75–99)
Role–physical	47 (38–62)[a]	45 (40–59)[a]	63 (51–69)[a]	62 (54–68)[a]	75 (65–81)[a]	75 (58–82)[a]	79 (70–92)	78 (71–89)	79 (72–97)
Role–emotional	45 (38–57)[a]	46 (35–62)[a]	66 (55–72)[a,b]	52 (48–65)[a]	74 (68–83)[a]	75 (67–87)[a]	76 (72–84)	75 (69–83)	76 (70–94)
Bodily pain	60 (55–75)[a]	57 (50–72)[a]	59 (53–71)[a]	61 (55–72)[a]	79 (74–90)[a]	79 (68–86)[a]	81 (76–92)	80 (75–90)	85 (74–95)
Vitality	50 (45–65)[a]	52 (44–66)[a]	65 (57–70)[a]	63 (55–71)[a]	66 (60–75)[a]	67 (65–72)[a]	69 (66–82)	69 (65–85)	70 (67–87)
Mental health	63 (55–71)[a]	61 (54–68)[a]	68 (60–71)[a]	69 (60–72)[a]	71 (65–79)[a]	70 (62–81)[a]	72 (64–84)	70 (66–82)	73 (68–86)
Social functioning	52 (47–72)[a]	50 (46–71)[a]	62 (51–75)[a]	63 (53–77)[a]	76 (65–86)[a]	76 (66–85)[a]	83 (70–96)	82 (71–95)	86 (69–99)
General health	56 (50–65)[a]	51 (50–60)[a]	59 (55–67)[ab]	51 (46–57)[a]	61 (55–70)[a]	61 (55–71)[a]	65 (57–75)	64 (58–76)	69 (60–88)

[a]$P < 0.05$ versus Chinese normal individuals.
[b]$P < 0.05$ for HE versus HR.
HE, hepatic enucleation; HR, hepatic resection.

the present series, all patients submitted to surgery had significantly reduced SF-36 scores in all domains in comparison with scores in healthy Chinese individuals (Table 4), which indicates that this cohort represents a well-selected patient group.

In this large series, patients were managed by either HE or HR. Although the technique selected was left to the discretion of the individual surgeon, there was no evidence that the groups were fundamentally different in terms of preoperative risk factors or extent of disease. Perioperatively, HE was associated with significant reductions in blood loss, operative time, hospital stay and complications. Not unexpectedly, there were no differences in postoperative quality of life (QoL) scores between the two techniques and by 6 months QoL scores in both groups had significantly improved compared with preoperative levels and were similar to those found in healthy Chinese individuals, confirming the efficacy of both treatments.

The results of the current study demonstrate that HE was associated with significantly less operative blood loss, a shorter hospital stay, fewer complications and shorter operative time compared with HR in patients with GHH.

Major intraoperative haemorrhage can be a significant problem during surgical treatment for GHH. Severe blood loss is a contributing factor to the occurrence of complications.[23] Vascular inflow control and low central venous pressure anaesthesia are standard procedures employed to reduce blood loss during liver resection. In the current series, vascular inflow control was used in both groups. When bleeding occurs during HE, it can be controlled by extrahepatic ligation of the right or left hepatic artery. After the relevant hepatic artery has been ligated, there is a gradual reduction in the size of the haemangioma, which may be augmented by gentle pressure. However, for segment IV lesions, more selective dissection controlling the relevant feeding vessels may be necessary.

Hanazaki *et al.*[9] previously reported that patients with tumours of ≥10 cm in size required a mean of 15 units of blood, 5.3-fold more than that required for patients with tumours of <10 cm, and experienced higher rates of postoperative complications and mortality because of the risk for haemorrhage and the need for abundant intraoperative transfusions. These results may explain why the incidence of morbidity was higher in the HR group (28.2%) than in the HE group (17.6%), although no operative mortality occurred in either group.

Conclusions

Liver enucleation combined with inflow occlusion was associated with favourable operative outcomes compared with conventional hepatectomy. Therefore, enucleation should be considered a viable and preferable option in the treatment of patients with GHH.

Conflicts of interest

None declared.

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