Spontaneous Ruptured Hepatocellular Carcinoma

An Appraisal of Surgical Treatment

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Spontaneous rupture with bleeding is not an infrequent complication of hepatocellular carcinoma (HCC). From May, 1972 to January, 1987, 56 symptomatic patients with ruptured HCC were managed by plication of the lesion (2 patients), ligation of either the common hepatic artery, CHAL, (39 patients), or selectively, the arterial branch supplying the tumor-bearing lobe of liver, SHAL, (8 patients), and hepatic resection, HR, (7 patients). Effective hemostasis was achieved in 68.1% of patients with the use of hepatic artery ligation (HAL). SHAL provides a comparable control of bleeding but no demonstrable reduction of postoperative organ failure when compared with CHAL. The operative treatment employed had no influence on either the postoperative rates of morbidity, mortality, or survival. However, the rate of hospital mortality was high among the four patients who had emergency anatomical lobectomy, despite the absence of severe cirrhosis. Hepatic artery ligation, either CHAL or SHAL, is a satisfactory definitive hemostatic measure for unresectable HCC when it ruptured. SHAL is probably preferred to routine emergency HR for patients with potentially resectable lesions. Nonetheless, for selected patients with easily accessible lesions, segmentectomy or subsegmentectomy could still be contemplated in the absence of severe cirrhosis.

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S PONTANEOUS RUPTURE IS one of the catastrophic presentation of hepatocellular carcinoma (HCC). In prevalent areas, the reported incidences ranged from 10.2% to 14.5%.[1-3] Accurate diagnoses of the condition are often difficult because pathonognomic signs are few. Hence many patients were explored for their acute abdominal conditions without adequate preoperative investigations. This report reviewed our experience with the surgical treatment of this potentially fatal complication during the past 15 years.

Patients and Methods

The clinical records of all patients with hepatocellular carcinoma (HCC) managed in the Department of Surgery,

University of Hong Kong at Queen Mary Hospital were retrospectively reviewed. The diagnosis of ruptured HCC was based on either the operative findings or the presence of hemoperitoneum on abdominal paracentesis when the patient was managed conservatively. In the absence of a history of severe abdominal injury, percutaneous liver biopsy or peritoneoscopic examination, the rupture was considered spontaneous.

The cirrhotic state of the liver was classified into mild, moderate, or severe according to the macroscopic assessment described in the operative records. Using the Pugh's modification of the Child's criteria,[4] hepatic reserve was evaluated by a combination of clinical and laboratory parameters. Persistent or recurrent intra-abdominal bleeding was diagnosed when blood measuring one or more liters was found at either re-exploration or postmortem examination performed within the same hospitalization. Hepatic failure after surgery was diagnosed when the postoperative serum total bilirubin exceeded 100 μmol/l among nonicteric patients (serum total bilirubin $\leq$ 26 μmol/l) and for patients who had impaired liver function before surgery (total bilirubin > 26 μmol/l), an increase of 80 μmol/l over their respective preoperative values. For patients with normal preoperative renal function (serum creatinine $\leq$ 0.13 μmol/l), the diagnosis of renal failure following surgery was made when the postoperative value doubled its preoperative value or exceeded 0.18 μmol/l or in the presence of deranged renal function (serum creatinine > 0.13 μmol/l) before exploration, an increase of serum creatinine by 0.10 μmol/l over the preoperative result.[5] The cause of death would be attributed to bleeding secondary to the ruptured tumor when the patients succumbed within 24 hours after surgery in the absence of other obvious contributable causes.

Between May, 1972 and January, 1987, a total of 1338 patients with HCC were managed in our institution. During this period of 15 years, 60 patients (4.5%) presented with spontaneous rupture of their tumors. There were 49 men and 11 women. The mean age was 54.5 ± 12.2 (SD) years with a range of 26 to 78 years. Emergency surgery was performed on 56 patients. Conditions of the remaining four patients, one of whom had recurrent HCC, were moribund at presentation and succumbed before any active intervention could be undertaken.

Because ruptured HCC is a fatal condition, 7-day and 30-day mortality rates were reported. Determination of these results as well as survival analysis, which was calculated as described by Kaplan and Meier,[6] were done with reference to the date of operation. Chi-square test with Yate's correction, Fisher's exact test, and Mann-Whitney test were employed where appropriate. All statistical calculations were done using standard computer programs. Statistical significance was assumed when p<0.05.

Results

Clinical Features

All 60 patients were symptomatic with peritonism (65.5%), hypotension (63.3%), and abdominal distension (64.8%), alone or in combination, at presentation. Based on the intraoperative findings determined by the surgeon, 34 of the 56 patients (64.1%) explored had severe macroscopic cirrhosis. The cirrhotic state in 19 patients (33.9%) was considered mild but indeterminated in three of them. Using the Pugh's modification of the Child's

TABLE 2. *Treatment of Ruptured Hepatocellular Carcinoma*

	Treatment	Number of Patients
I	Hepatic resection	
	Right hemihepatectomy	2
	Left hemihepatectomy	2
	Left lateral segmentectomy	3
II	Hepatic artery ligation	
	Common trunk	39
	Selective	8
III	Plication	2
IV	Conservative	4
	Total	60

criteria,[5] there were 9 Child's A patients, 17 Child's B patients, and 16 Child's C patients. The remaining patients had incomplete data for evaluation. Biochemical data and macroscopic assessment of the concomitant cirrhosis are shown in Table 1.

Operative Treatments

Hepatic resection (HR) of different extent was carried out in seven patients (Table 2). In 47 patients, hepatic artery ligation (HAL) was used as the hemostatic measure. Ligation of the common hepatic artery (CHAL) was done in 39 patients, while selective interruption of the branch supplying the tumor-bearing lobe of the liver (SHAL) was performed in eight patients. Two patients had simple plication of their HCC for the control of bleeding. The presence of severe macroscopic cirrhosis among patients who

TABLE 1. *Laboratory Data of Patients with Ruptured Hepatocellular Carcinoma Who Were Operated On*

Transpeptidase	Overall (n = 56)	Hepatic Resection [HR] (n = 7)	Hepatic Artery Ligation [HAL]			Plication (n = 2)
			All (n = 47)	Common (n = 39)	Selective (n = 8)	
Hemoglobin (g/%)	11.8 ± 1.2	11.5 ± 1.0	11.9 ± 1.5	10.2 ± 0.5	12.2 ± 3.1	10.5 ± 3.5
Platelet (10⁹/ml)	154.7 ± 30.6	93.0 ± 30.3	171.7 ± 36.4	144.2 ± 19.0	163.0 ± 48.7	21.0
Creatinine (mmol/l)	0.32 ± 0.17	0.11 ± 0.01	0.34 ± 0.20	0.37 ± 0.24	0.21 ± 0.09	0.33 ± 0.18
Total bilirubin (μmol/l)	70.7 ± 18.4	28.3 ± 12.1*	79.6 ± 21.8	80.8 ± 25.4	74.25 ± 39.6	23.0
Alkaline phosphatase (μmol/min · l)	255.9 ± 49.0	68.0 ± 18.9*	287.9 ± 56.8	256.6 ± 39.6	424.8 ± 359.8	133.5 ± 68.5
γ-glutyl transpeptidase (μmol/min · l)	165.9 ± 3.4	73.3 ± 18.9	183.4 ± 39.5	158.8 ± 30.2	250.1 ± 125.1	78.0 ± 46.0
Aspartate transaminase (μmol/min · l)	354.0 ± 87.4	348.6 ± 210.9	367.9 ± 100.7	302.4 ± 96.4	646.2 ± 334.6	80.5 ± 22.5
Alanine transaminase (μmol/min · l)	176.6 ± 43.5	51.8 ± 10.4	205.2 ± 52.3	158.7 ± 49.9	391.2 ± 160.9	40.5 ± 8.5
Albumin (g/l)	34.5 ± 1.1	35.7 ± 3.2	35.4 ± 1.2	34.1 ± 1.2	40.8 ± 3.5	36.5 ± 6.5
Prothrombin time (sec. over control)	3.74 ± 0.62	4.5 ± 3.3	3.9 ± 0.5	4.2 ± 0.6	2.7 ± 0.88	0.5 ± 0.5
Macronodular cirrhosis (%)	64.2	42.8	68.1	75.0	37.5	50.0

* p < 0.05, HR *versus* HAL.

TABLE 3. *Postoperative Morbidities and Mortalities of Patients with Ruptured Hepatocellular Carcinoma*

	Overall (n = 56)	Hepatic Resection [HR] (n = 7)	Hepatic Artery Ligation [HAL]			
			All (n = 47)	Common (n = 39)	Selective (n = 8)	Plication (n = 2)
Intra-abdominal bleeding (%)	17 (30.4)	2 (28.5)	15 (31.9)	11 (28.2)	4 (50)	0 (0)
Liver failure (%)*	10 (28.5)	1 (16.6)	8 (29.6)	5 (22.7)	3 (60)	1 (50)
Renal failure (%)*	12 (33.3)	2 (40.0)	10 (34.5)	7 (29.1)	3 (60)	0 (0)
7-day mortality (%)	29 (51.8)	2 (28.5)	27 (57.4)	23 (58.9)	4 (50)	0 (0)
30-day mortality (%)	39 (71.4)	3 (42.8)	36 (76.6)	30 (76.9)	6 (75)	1 (50)
Hospital mortality (%)	42 (75.0)	5 (71.4)	36 (76.6)	30 (76.9)	6 (75)	1 (50)

* Incomplete data.

had HR (42.8%), HAL (68.1%), and plication (50%) was not statistically different. All of the four patients who underwent anatomical liver resection had mild cirrhosis.

Morbidity and Mortality

Intra-abdominal hemorrhage was the most frequent postoperative complications (Table 3). Among the 17 patients (30.4%) with postoperative bleeding, 2 patients (28.5%) had HR, 11 patients (28.2%) had CHAL, and 4 patients (50%) had SHAL. Re-exploration was carried out in four patients. While postoperative bleeding was significantly more frequent among patients with severe macroscopic cirrhosis (p< 0.05), the incidence was comparable with respect to the operative treatment received.

Among the 35 patients with complete pre- and postoperative data, liver failure developed in 10 (28.5%) of them. Renal failure, on the other hand, was detected in 12 of the 36 patients (33.3%) with detailed information. The incidence of liver and kidney failures were comparable among patients who had different surgical treatments for their ruptured HCC.

The overall 7-day, 30-day and hospital mortality rates (51.8%, 71.4%, and 75%, respectively) were comparable among different treatment groups (Table 3). Severity of the underlying cirrhosis was the most important determinant of the postoperative course of these patients. Both the 7-day (p<0.05) and 30-day (p<0.02) mortality rates were significantly higher among patients with severe mac-

TABLE 4. *Causes of Death Among Patients with Ruptured Hepatocellular Carcinoma*

Cause	Number of Patients
Bleeding	20
Malignant cachexia	15
Liver failure	4
Multi-organ failure	12
Bronchopneumonia	5
Lost	4
Total	60

ronodular cirrhosis. Patients with Child-Pugh class 'C' status also had a higher 7-day mortality rate (p<0.05).

The relationship between postoperative mortality rates and the operative procedures employed was not apparent. However, despite the absence of severe cirrhosis among all four patients with anatomical lobectomy, three of them succumbed within the same hospitalization period. Individual parameters including hemoglobin, hematocrit, creatinine, total bilirubin, alkaline phosphatase, gamma glutyl transpeptidase, transaminases, and the clotting profile sampled before operation all failed to predict the postoperative course of these patients. The causes of death for the 60 patients were as shown in Table 4.

Survival

The operative procedure employed, including liver resection, did not affect the duration of survival for these patients with ruptured HCC (Fig. 1). Patients who had severe macroscopic cirrhosis (p=0.075) or Child-Pugh status (p<0.004) had worse long-term prognoses. The median survival for these 56 patients who had surgery was ten days. When patients who died within the first postoperative week were excluded, the overall median survival was 48 days.

Discussion

Spontaneous rupture is a comparatively common presentation of HCC. In the earlier report of 207 patients from our institution, the incidence was 14.5%.[1] The reasons responsible for the recent decline of our local incidence to 4.5% was not apparent.[1] While prognosis remains grave despite active treatment, early aggressive intervention provides the only chance of salvaging these patients. Bleeding from the tumor[2] or its overlying hepatic tissue[7] carried a mortality rate of 84.6% when patients were managed conservatively.[2]

When confronted with this life-threathening condition, hemostatis is the prime concern. The best operative procedure, particularly when the tumor is deemed resectable,

remains unsettled. At exploration, control of bleeding by direct plication of the overlying capsule might be attempted as a temporizing measure. Control of bleeding by plication was, however, not uniform because of the friable nature of the liver neoplasm.[7] Although occasional success had been noted by different investigators,[3,8] our experience with plication as the sole hemostatic measure was disappointing and therefore rarely practiced. Other local measures such as packing of the bleeding site followed by its removal in the subsequent 24 to 48 hours had been advocated in the past.[9] Accumulated experiences have shown that recurrent bleeding was frequent even with the pack *in situ* or after its removal.[1] Nevertheless, these local measures serve as useful adjuncts to allow completion of definitive hemostatic procedures during emergency exploration or transportation of patients to larger centers for appropriate therapy.

When the tumor ruptures, bleeding is from the hepatic artery as it provides the major blood supply to HCC.[1,10] Hepatic artery ligation (HAL) is a satisfactory emergency hemostatic measure, although its role as an elective definitive treatment is limited even for unresectable lesions.[11] Experiences reported in the past with the procedure were encouraging. Among the 38 patients with ruptured HCC reported from Thailand and Hong Kong, bleeding was successfully controlled in almost all of them when judged on a clinical basis.[1,2] Liver failure was the principle cause of death after surgery, which occurred in five of the 12 patients managed by Ong and Taw.[1] Among our 47 patients with HAL, successful hemostatis was achieved only in 68.1%, which probably reflected the strict objective definition used in the present report. When measured against CHAL, SHAL had similar effectiveness for securing hemostasis. On the other hand, preservation of the arterial supply to one lobe of the liver by SHAL had not resulted in a significant reduction of the incidence of postoperative hepatic failure. The drastic hemodynamic disturbances associated with ruptured HCC is perhaps adequate to precipitate decompensation of the cirrhotic liver. When a clearly unresectable lesion was found during surgery, interruption of either the common trunk or the appropriate branch supplying the lesion could be safely used. The choice perhaps depends on localization of the bleeding tumor and technical ease of isolating the vessel. When resection is possible, SHAL is probably the preferred operation because the chance for any subsequent potential hepatic resection would not be jeopardized.

Hepatic resection provides the only hope of cure for patients with HCC. Besides the extent of disease, resectability depends on severity of the concomitant cirrhosis. In Hong Kong and other Asian countries, cirrhosis occurred in 77% to 89% among patients with HCC.[11-14] At the time of emergency exploration, information on the liver function is seldom available because of the acute
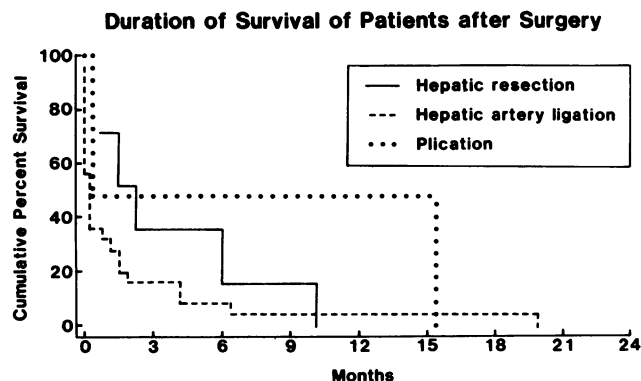

Duration of Survival of Patients after Surgery

FIG. 1. Survival among patients who had different surgical treatments for their ruptured hepatocellular carcinoma (p=0.13).

presentation. The current data established that decisions concerning the extent of hepatic resection (when it is necessary) could be adequately made by evaluating the macroscopic appearance of the liver. Both 7-day and 30-day mortality rates correlated significantly with the visual evaluation of the hepatic cirrhosis. Besides assessment with the Child-Pugh classification, no other parameters that were analyzed affect the immediate postoperative course of these patients.

When a resectable lesion is found at surgery, the role of emergency hepatectomy is debatable. In the presence of venous permeation,[2,8] a delay from staging the operation after initial hemostasis might compromise the chance of a curative resection.[1] Although long-term survival had been reported after emergency hepatectomy,[1] early recurrent tumor was not an infrequent cause of failure after a successful extensive operation.[3] When compared with results of elective liver resection,[15] the overall rates of mortality were high, particularly after anatomical lobectomy.[1,3,8] Furthermore, the present results failed to demonstrate any significant benefit to the survival of these patients with ruptured tumor. Judging from the information available, it is apparent that routine emergency anatomical liver resection is probably not justified.

In summary, routine exploration for all symptomatic patients with ruptured HCC is advisable because results of conservative management were poor. At laparotomy, location of the lesion and severity of the concomitant cirrhosis should be determined as a preliminary assessment of resectability after initial temporary control of bleeding with local measures. Depending on the lateralization of the tumor, ligation of either the common hepatic artery or its branch supplying the tumor-bearing lobe of the liver is the preferred hemostatic and definitive treatment for an obviously unresectable lesion. When the lesion is potentially resectable, selective interruption of arterial supply should be done. Evaluation of the hepatic tumor could then be carried out in the immediate postoperative period

for the consideration of an early elective resection. Segmentectomy or sub-segmentectomy might be contemplated in selected patients with relatively normal livers and easily accessible lesions. While the use of nonoperative measures such as transcatheter arterial embolization is appealing,[16] its role in the management of ruptured HCC remains to be determined by further studies.

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