

## Surgical Outcomes in Patients with Ruptured Hepatocellular Carcinoma

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Ruptured hepatocellular carcinoma (HCC) causes acute hemorrhage, and requires emergency procedures. The condition is therefore involves the risk of peritoneal dissemination and is associated with poor prognosis. There have been few reports concerning the outcome after ruptured HCC resection. Methods: We compared the outcomes in 23 patients with ruptured HCC clinicopathologically with those in 589 patients with non-ruptured HCC. Ruptured HCC cases were divided into two types according to the extent of bleeding. Type I: extended intraperitoneal bleeding, Type II: bleeding blocked by the surrounding organs. Results: Vascular invasion, and intrahepatic metastasis rate were significantly greater in the ruptured HCC group. The outcome of resection was poor in the Type I group, as opposed to in the Type II group.

The cumulative survival rates were significantly better in the non-ruptured HCC group than in the ruptured HCC group. The rate of peritoneal dissemination after surgery was significantly higher in the ruptured HCC group than in the non-ruptured HCC group. Conclusion: The rate of vascular invasion, intrahepatic metastasis and peritoneal dissemination after surgery were significantly higher in the ruptured HCC group. We believe that the ruptured HCC group had high grade malignancy. And we have to treat ruptured HCC thinking that.

**Key words:** ruptured hepatocellular carcinoma, peritoneal dissemination, acute hemorrhage, intraperitoneal bleeding, emergency procedures

### Introduction

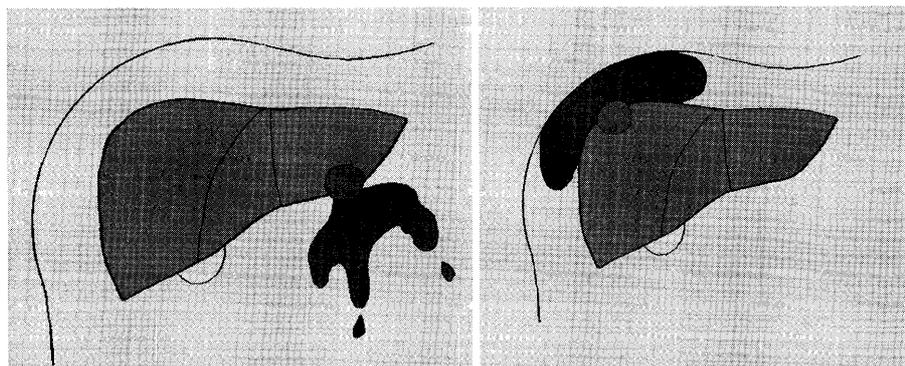
Ruptured hepatocellular carcinoma (HCC) causes acute hemorrhage<sup>1)</sup>, and requires emergency procedures. The procedures are hepatic resection<sup>2)</sup>, transcatheter arterial embolization (TAE)<sup>3)</sup>, hepatic artery ligation, and intermittent hepatic artery occlusion with chemotherapy<sup>4)</sup>. The condition therefore involves the risk of peritoneal dissemination and is associated with poor prognosis. There have been few reports<sup>5)</sup> concerning the outcome after ruptured HCC resection. In the present study, we clinicopathologically examined 23 patients with ruptured HCC.

### Patients and Methods

From 1987 to 1995, 612 patients with HCC underwent hepatic resection at the Institute of Gastroenterology, Tokyo Women's Medical University Hos-

pital. We divided these 612 patients into a ruptured HCC group (23 patients) and a non-ruptured HCC group (589 patients). We further divided the ruptured HCC group into two types according to the extent of extension (Fig. 1), Type I (12 patients): free bleeding into the peritoneal cavity, causing a free flow of blood into the peritoneal cavity, Type II (11 patients): bleeding was blocked by the surrounding organs. The sites of rupture (bleeding) were close to the diaphragm, colon or fibrous capsule.

Gender, age, hepatitis B surface antigen, anti-hepatitis C,  $\alpha$ -fetoprotein level (AFP), liver cirrhosis, indocyanine green retention at 15 min (ICGR15), pathological features, surgical outcomes and peritoneal dissemination were compared between the ruptured and non-ruptured HCC groups. Cumula-



**Fig. 1** Two types of ruptured HCC group

Left: Type I, free bleeding into the peritoneal cavity, causing a free flow of blood into the peritoneal cavity

Right: Type II, bleeding blocked by the surrounding organs

The sites of rupture (bleeding) were close to the diaphragm, colon or fibrous capsule.

**Table 1** Patient characteristics in ruptured and non-ruptured HCC

	ruptured	non-ruptured	p-value
Number	23	589	
Mean age	56.9 ± 8	63.2 ± 9	0.186
Sex Male	18 (78%)	479 (81%)	0.923
HBsAg positive	8 (34.8%)	91 (15.4%)	0.721
Anti-HCV positive	10 (43.5%)	428 (72.7%)	0.0023
Liver cirrhosis	8 (34.8%)	360 (61.1%)	0.0207
ICGR15 (%)	20.5 ± 13.1	17.9 ± 10.7	0.306
AFP (ng/ml)	78,990 ± 301,949	5,377 ± 50,195	< 0.001

ICGR15: indocyanine green retention at 15 min, AFP:  $\alpha$ -fetoprotein.

Values are mean ± SD, Chi-squared test and t-test were used to compare.

tive patient survival rates were calculated with the Kaplan-Meier method. Survival duration was defined as the time from liver surgery to the date of death or last contact. The chi-square test, Fisher's exact test, and t test were used to compare cases with ruptured HCC and cases with non-ruptured HCC. Differences were considered significant when  $p < 0.05$ .

## Results

### Patient characteristics in the ruptured and non-ruptured HCC groups clinical findings

The rate of anti-hepatitis C, liver cirrhosis were significantly higher in the non-ruptured HCC group than in the ruptured HCC group. AFP were significantly higher in the ruptured HCC group than in the non-ruptured HCC group (Table 1).

### Pathological findings

Tumor size in macroscopic greatest diameter and

tumor number were significantly greater in the ruptured HCC group than in the non-ruptured HCC group. Vascular invasion (portal vein), intrahepatic metastasis rate were significantly greater in the ruptured HCC group than in the non-ruptured HCC group (Table 2).

### Patient characteristics and outcomes in the Type I and Type II groups

Emergency operation were performed in 4 cases in the Type I group and 1 case in the Type II group. Sudden-onset shock was seen in 2 cases in the Type I group. The outcome of resection was poor in the Type I group, with an average survival of 27 weeks, as opposed to 86 weeks in the Type II group (Table 3).

### Survival rates after surgery

In the ruptured HCC group mortality was 3 cases (13%), and 5 cases (21.8%) had non-curative resec-

**Table 2** Macroscopic and microscopic findings in ruptured and non-ruptured HCC

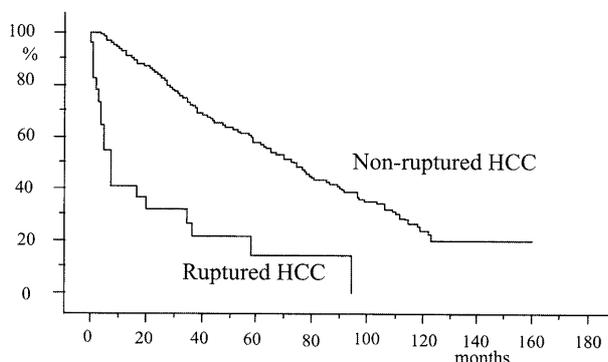
	ruptured	non-ruptured	p-value
Number	23	589	
Solitary	10 (43.5%)	461 (78.3%)	< 0.001
Multiple	13 (56.5%)	128 (42.1%)	
Vascular invasion			
Portal vein	14 (60.9%)	49 (8.3%)	< 0.001
Hepatic vein	2 (8.3%)	17 (2.9%)	0.335
Intrahepatic metastasis	12 (52.1%)	142 (24.1%)	0.0023
Size (cm) (mean $\pm$ SD)	8.53 $\pm$ 5.54	3.98 $\pm$ 3.25	0.018

Chi-squared test, Fisher's exact test, and t-test were used to compare.

**Table 3** Patient characteristics in Type I and Type II ruptured HCC

	Type I	Type II	p-value
Number	12	11	
Symptom of shock	2 (16.7%)	0 (0%)	0.156
Emergency operation	4 (33.3%)	1 (9.1%)	0.159
Solitary	6 (50%)	4 (36.3%)	0.812
Multiple	6 (50%)	7 (63.7%)	
Vascular invasion	7 (58.3%)	9 (81.8%)	0.370
Postoperative dissemination	5 (41.7%)	2 (18.2%)	0.221
Average weeks of survival	27	86	0.481

Chi-squared test and Fisher's exact test were used to compare.

**Fig. 2** Cumulative survival curve of non-ruptured HCC patients and ruptured HCC patients

tion. The cumulative survival rates were better in the non-ruptured HCC group than in the ruptured HCC group (Fig. 2). The rate of peritoneal dissemination after surgery was significantly higher in the ruptured HCC group than in the non-ruptured HCC group (Table 4).

### Discussion

In Europe and America few ruptured HCC cases have been reported<sup>(6-8)</sup>. However, in Southeast Asia, the incidence of spontaneous rupture of HCC

**Table 4** Postoperative peritoneal dissemination in non-ruptured and ruptured HCC

	ruptured	non-ruptured
Postoperative peritoneal dissemination	7 (30.4%)	5 (0.85%)

Chi-squared test, p-value < 0.0001.

is 12-15%<sup>(9,10)</sup>. There have been few reports<sup>(5)</sup> concerning the outcome after ruptured HCC resection. One of the reasons is the low rate of resectable cases of ruptured HCC. A wide variety of treatment modalities have been performed for ruptured HCC cases. Yamagata et al<sup>(11)</sup> reported that TAE was performed in 33%, one-stage hepatectomy in 18%, suture and/or packing in 17%, two-stage hepatectomy in 12%, conservative therapy in 8%, and hepatic artery ligation in 6% of cases.

Ruptured HCC causes intraperitoneal hemorrhage precipitating hemorrhagic shock, is frequently complicated by liver cirrhosis, and occurs most frequently in advanced HCC. In Type II (11 patients) of our classification of ruptured HCC, bleeding was blocked by the surrounding organs

without sudden epigastralgia, pain in the right hypochondrium or hemorrhagic shock. In this type, emergency operation was lower frequently and we therefore have to consider different types of ruptured HCC. The bleeding type of ruptured HCC was associated with surgical outcome, although the difference was not statistically significant.

The possible dissemination of cancer cells at the time of rupture of a HCC has been a matter of concern. Ong et al<sup>8)</sup> reported that the spread of tumors was rapid and a delay of 2-3 weeks may render the tumor unresectable. We encountered 7 cases with postoperative peritoneal dissemination. We consider some special care is required during the operation to prevent peritoneal dissemination.

Previous Japanese<sup>11)</sup> and Italian<sup>12)</sup> studies have demonstrated that emergency hepatic resection for ruptured HCC may achieve a long-term outcome comparable with that of elective surgery in selected cases. Besides, a report by Yeh et al<sup>5)</sup> confirms comparable overall survival of patients with ruptured HCC who underwent hepatic resection compared with the non-ruptured HCC group. However, in the present report the cumulative survival rates were significantly better in the non-ruptured HCC group than in the ruptured HCC group. In the ruptured HCC group mortality was 3 cases (13%), and 5 cases (21.8%) had non-curative resection. Also, the tumor size and tumor number were significantly greater in the ruptured HCC group than in the non-ruptured HCC group. Vascular invasion, intrahepatic metastasis rate were significantly greater in the ruptured HCC group than in the non-ruptured HCC group. Yamagata et al<sup>11)</sup> claimed that raised in-

tratumoral pressure with a high incidence of venous invasion was the main reason for recurrence in the ruptured HCC group. We believe that the ruptured HCC group had high grade malignancy. And we have to treat ruptured HCC thinking that.

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## 破裂肝細胞癌切除症例の検討

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[目的]肝細胞癌破裂は、腹腔内出血という緊急の病態を引き起こし、また癌細胞の播種の危険に曝され予後不良とされている。しかし実際の破裂切除例での術後経過が観察された報告は少ない。そこで破裂切除例の臨床病理像、術後経過を検討した。

[方法]対象は1987～1995年の期間に切除された肝細胞癌612例中の破裂例23例である。その臨床像、病理像を検討した。手術所見での腹腔内出血の型から、I型：腹腔内に開放性に出血した型、II型：出血が周囲臓器および被膜に被包され限局した型、に分類した。

[結果]破裂肝癌例は肉眼的血管侵襲、肝内転移が有意に多く、生存率は非破裂肝癌例が破裂例に比し良く、術後腹膜播種は破裂例に有意に多かった。破裂例の腹腔内出血の型別では、I型の生存期間が短かった。

[結語]破裂肝癌切除例では、進展因子、術後腹膜播種は有意に多く予後は不良であった。破裂する肝癌例は生物学的に悪性度が高いことが想定され、それを念頭においた治療が必要である。