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Original Article

Management and Outcome of Ruptured Hepatocellular Carcinoma

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Abstract **This study reviewed 84 patients with ruptured hepatocellular carcinoma (HCC) who were treated at Chonburi Hospital during 2006-2012. There were 72 males and 12 females. In acute management, 52 were treated conservatively, 23 were treated by transarterial embolization (TAE), 5 were treated by surgery followed by TAE and 4 were treated by surgery alone. Overall 30-day mortality was 61.9%. Factors related to early mortality are Child's classification, MELD score and age. Four patients underwent delayed hepatectomy as a definitive treatment. The median survival after hepatectomy was more than 34 months. The longest follow up was a patient who underwent delayed hepatectomy as a definitive treatment and remained disease-free after 60 months. Hepatectomy should be considered as a definitive treatment for ruptured HCC in delayed phase. A suitable candidate for hepatectomy is a patient who has good performance status and normal liver function.**

Keywords: **Ruptured, hepatocellular carcinoma, management, outcome**

Introduction

Hepatocellular carcinoma (HCC) usually develops in cirrhosis. Most patients have no symptom of tumor but cirrhosis. A few patients have symptoms related to tumor including mass effect and rupture of tumor. Ruptured HCC can lead to massive blood loss, hypovolemic shock, and eventually death. The rate of ruptured HCC varied between 3-26%[1-8]. These patients have very high mortality rate of 20-71%[1-3,6,7,9-12]. The initial treatments aim to control bleeding of the rupture site. The most common method to control bleeding is trans-arterial embolization (TAE) with success rate of

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bleeding control around 30-100%[8,13,14] whereas surgery has a role in control bleeding in selected situation, with success rate lower than TAE. Surgery in acute management includes packing, hepatic artery ligation and wedge resection or anatomical hepatectomy. Definite hepatectomy is not recommended in acute situation[15]. Patients who survive after acute bleeding should be considered for a definitive treatment same as patients who never have rupture. The best choice for definitive treatment is hepatectomy. The alternative treatments are trans-arterial chemoembolization (TACE) and radiofrequency ablation (RFA). Liver transplantation which is the best definitive treatment for non-ruptured HCC has no role for ruptured HCC at the present time.

The present study reviewed series of patients with ruptured HCC at the Chonburi Hospital during 2006 to 2012. Outcomes of different treatment strategies were reviewed and analyzed.

Methods

Medical records of patients with HCC during 2006-2012 at Chonburi Hospital were reviewed. There were 748 patients who admitted for treatment of hepatocellular carcinoma. Ninety five charts with additional record of hemoperitoneum were reviewed. The patients who had been confirmed to have ruptured hepatocellular carcinoma were included in this study. The diagnosis of ruptured HCC was confirmed by imaging studies plus one of the following evidences: 1) abdominal tapping showed unclotted bloody fluid, 2) imaging demonstrated disruption of the peritumoral liver capsule with enhanced fluid collection in the perihepatic area adjacent to the tumor. Eleven patients were excluded because they were not confirmed for ruptured HCC. Eighty four cases with ruptured HCC were included in the analysis. Details of patient characteristics including cirrhosis classifications, tumor characteristics, early and late treatment, early and late survival and results of hepatectomy were recorded. The longest follow up was 60 months. This study was approved by the hospital research committee.

Results

There were 72 males and 12 females. The mean age was 56.1 year (range 34-87). Eighty three patients (98.8%) had hemodynamic or were clinically unstable. The mean systolic blood pressure was 107 mmHg (range 0-180). The mean hematocrit level was 25.6% (range 7.4-40.1). The mean MELD score was 18.3 (range 6-47). 30-day mortality was 61.9% (Figure 1). Trans-arterial embolization (TAE) was performed in

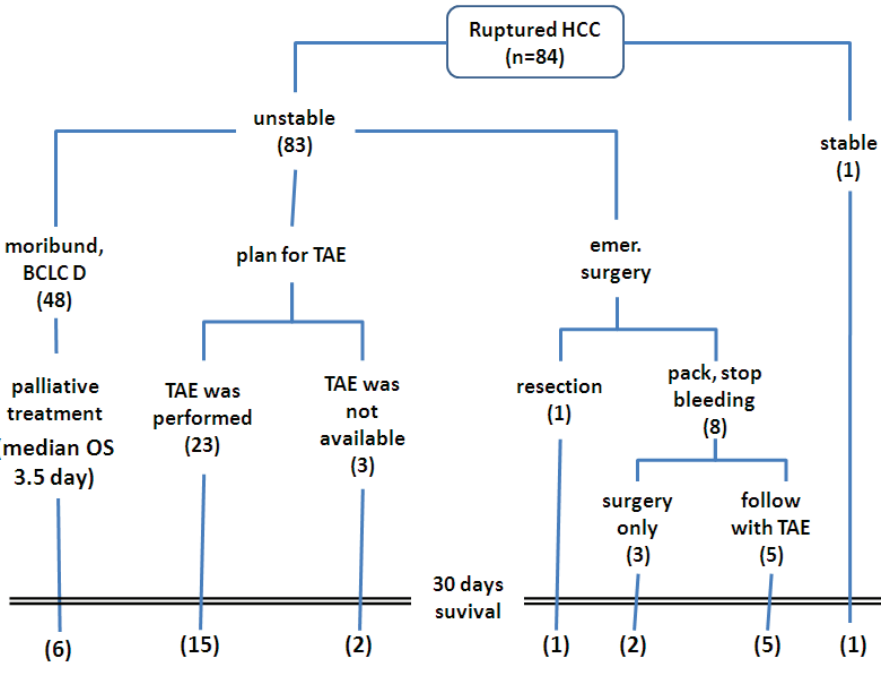

Figure 1 Flow chart depicting acute management of patients with ruptured HCC. (TAE, transcatheter arterial embolization ; numbers in parenthesis are numbers of patients)

28 patients with success rate of 85.7% (24 in 28). Other treatments were perihepatic packing (N=5), surgical hemostasis (N=3) and wedge hepatectomy (N=1). Success rate of overall surgical control of bleeding was 66.7% (6 in 9).

Most patients had hemodynamic unstable and 57.8% were not candidates for any treatment because they were moribund or had very poor liver status. Among those who had treatment, TAE was the most frequently used modality. Surgery was performed to control bleeding in acute phase for 10.7%. In later management, BCLC classification was applied in order to determine the opportunity of definitive treatment. Four hepatectomies were performed for definitive treatment.

According to analysis of factors effecting early survival, Child Classification, MELD score and younger age were significantly related with survival (Table 1). Other potential factor was tumor size but the level of significance was not reached. Hematocrit and blood pressure were not related with survival. Treatment methods were significantly related to survival because potential survivors were usually selected for TAE or surgery whereas moribund cases were usually chosen for conservative treatment. There were 32 patients who survived until subsequent evaluation for definite treatment. BCLC classification was used as a strategy

Table 1 Characteristics of survivors and non survivors in 30 days of ruptured HCC

	Survivor (n=32)	Non survivor (n=52)	*P* value
Age (range)	59.3 ± 11.8 (34-87)	54.1 ± 11.2 (36-87)	0.04
Gender male (%)	25 (78%)	47 (90%)	0.2
Child-Pugh classification (%)			
A	12 (37.5)	0	
B	18 (56.3)	23 (44.2)	<0.0001
C	2 (6.2)	29 (55.8)	
HBsAg +(%)	48.1	59.5	0.52
AntiHCV+ (%)	27.3	26.5	0.8
Chronic Alcoholic (%)	65.6	76.5	0.41
SBP (mmHg)	109 ± 26	106 ± 32	0.67
Hct (%)	27.3 ± 6.1	24.6 ± 7.5	0.08
MELD score	13.0 ± 7.1	21.5 ± 9.4	<0.0001
Tumor size (cm.)	8.6 ± 4.2	10.4 ± 3.9	0.05
> 3 tumors (%)	31.3%	52.9%	0.09
Tumor location			
Right	17	20	
Left	6	6	0.11
Both	8	25	
Treatment			
TAE	15	8	
Surgery only	3	1	<0.0001
Surgery plus TAE	5	0	
Conservative	9	43	
Median Survival (Days)	109	3.5	NA

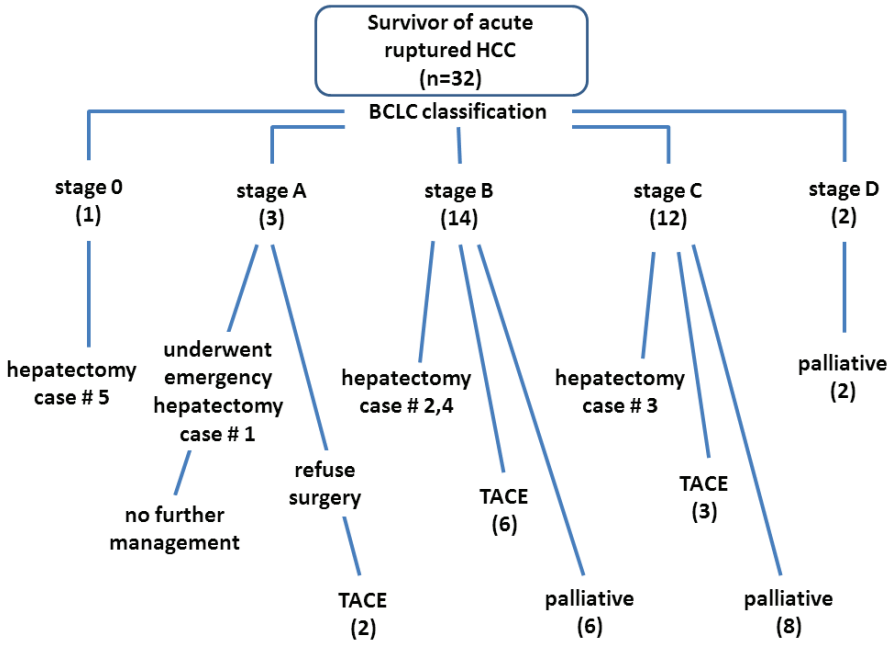

Figure 2 Flow chart of late management of patients with ruptured HCC according to BCLC classification. (Numbers in parenthesis are numbers of patients.)

for determination of treatment (Figure 2). Four of them had hepatectomy as definitive treatment. The others were offered transarterial chemoembolization (TACE) if deemed suitable or best supportive care for palliative treatment. Fourteen patients underwent TACE as palliative treatment. The result of TACE were partial response (3 in 14), stable disease (6 in 14) and no response (5 in 14). None of them had complete response. Median survival of TACE group was 15.5 months. Table 2 showed characteristic of patients classified by treatment. Three patients underwent hepatectomy after TACE (Table 3, case #2, 3 and 5). The detail and result of five patients who underwent hepatectomy was shown in Table 3. The other 17 patients who did not undergo any definite treatment received palliative treatment because of poor performance status, advanced cirrhosis, bilateral tumor or metastatic disease. These patients had very poor median survival of 2.5 months. Survival of each treatment was shown in Figure 3.

Table 2 Late management of ruptured HCC patient

	TACE (n=11)	Hepatectomy (n=4)	Palliative (N=17)
Age	62.3 ± 14.3	50.5 ± 14.8	59.5 ± 8.8
Gender male (%)	10 (91%)	3 (75%)	12 (71%)
Child-Pugh Classification (%)			
A	6 (54.5)	4 (100)	2 (11.8)
B	5 (45.5)	0	13(76.4)
C	0	0	2(11.8)
Tumor size (cm.)	9.2 ± 4.5	6.7 ± 3.7	8.6 ± 4.2
Tumor Location			
Right	5	3	9
Left	2	1	3
Both	4	0	5
Extrahepatic disease	3 (2 lung metastasis, 1 LN metastasis)	1 (peritoneal seeding)	4 (3 lung metastasis, 1 lung & bone metastasis)
Previous treatment			
TAE / TACE	9	3	8
Emer. Surgery	1	2	3
None	1	-	7
Median survival (months)	15.5	not reach (>34)	2.5

Table 3 Characteristics of five patients who underwent hepatectomy

Case #	Characteristic	Tumor	Previous Treatment	Operation	Survival (months)
1	M, 59 yrs, alcoholic cirrhosis	5 cm. Segment 4	none, emergency surgery	wedge hepatectomy	33 months, dead from massive variceal bleeding
2	M, 43 yrs, HBVcirrhosis	7 cm. segment 5,8	**Acute phase :** liver packing follow by TAE **Secondary Phase :** TACE × 1	extended right hepatectomy **pathology result showed complete tumor necrosis by effect of TACE	60 months, alive, disease free, regularly follow up
3[16]	M,34 yrs, HBVcirrhosis	10 cm. Rt.lobe + 30 cm seeding tumor at Lt.lower abdomen	**Acute phase :** TAE **Secondary Phase :** TACE × 4	1. Right hepatectomy + Enbloc resection of tumor seeding 2. Re-resection of recurrence seeding 3. Re-resection of recurrence seeding	34 months, dead from tumor recurrence at peritoneum seeding
4	M,67 yrs, HBVcirrhosis	8 cm. Rt.lobe	**Acute phase :** conservative (stable VS., bleeding stop spontaneously)	Right hepatectomy	32 months, alive, disease free, regularly follow up
5	F,58 yrs	1.5 cm. segment 2	**Acute phase :** TAE **Secondary Phase:** TACE × 1	Left hepatectomy	40 months, alive, disease free, regularly follow up

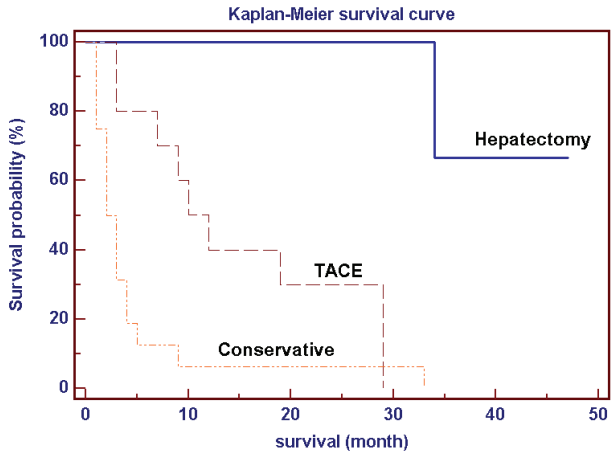

Figure 3 Kaplan-Meier survival curve of late management of ruptured HCC patients

Conclusion

Ruptured hepatocellular carcinoma is a lethal presentation of hepatocellular carcinoma. The mortality is likely related to liver status more than the tumor status (Child-Pugh classification and MELD score rather than tumor size). Secondary treatment was selected according to patient's condition. Patients who have tolerable liver status deserve better chance of survival and opportunity for definitive treatment, even though survival after hepatectomy in ruptured HCC is not as good as in non-ruptured HCC[2,17]. Hepatectomy is still the most appropriate definitive treatment available so far[8,10,18,19]. BCLC classification which includes liver status, tumor status and patient performance status for grading is a good prognosis predictor in long term. BCLC classification is also a good strategy to determine treatment. Hepatectomy should be offered for BCLC grade 0-B in order to meet a long term survival in these patients. Patient with peritoneal seeding (BCLC grade C) could meet a long term survival if resection could be performed.

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