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Original Article

Emergency Transcatheter Arterial Embolization in Ruptured Hepatocellular Carcinoma in Siriraj Hospital

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Abstract

Objective: To review the outcome of the patients who had ruptured hepatocellular carcinoma after receiving TAE and to identify prognostic indicators in Siriraj Hospital

Patient and Method: Retrospectively reviewed the outcome of patients who had undergone TAE for rupture of HCC during March 2003 - December 2006,. Angiographic finding, arterial embolization, size of tumor, tumor location, agents used for embolization were recorded. The final outcome in terms of technical success, 0-3 day clinical success, 30 days mortality rate, overall mean survival time and complication were recorded. Correlation between portal vein patency with incidence of liver failure was calculated. We also compared their survival time in each child-Pugh classification and with respect to different prognostic indicators.

Results: Adult: 35 men and 3 women. (ranges 17-89 years and mean age 53.11 years. At the time of ruptured tumor) 2 patients had Child's A, 13 Child's B and 23 of Child's C disease. The most common presentation was abdominal pain (17 patients). Bleeding was successfully immediate arrested in all 38 patients. The most tumor location was detected at right lobe of liver (20 patients). The overall mean survival was 61.92 days. We found that survival time between Child B and C classification had statistically significant difference. Twenty four patients died within 30 days after TAE, the major cause of death was liver failure, which occurred in 7 patients. In addition, we had also postulated several prognostic indicators for patients' survival. The results showed that only those with a bilirubin level more than 3 mg/dl had a poor outcome. (P=0.05)

Conclusion: TAE should be considered in management of patients with ruptured HCC. It is effective in arresting tumor bleeding. Patients who are considered poor surgical candidates with Child B or C hepatic cirrhosis might have emergency embolization as a life-saving measure. Failure TAE is not depends on only technique but also depends on underlying disease and general condition prior embolization.

Introduction

Hepatocellular carcinoma (HCC) is a disease with a high prevalence rate in South East Asia due to the high incidence of hepatitis associated cirrhosis. The clinical presentation can be varied. Patients may present with jaundice, weight loss, and abdominal mass or abdominal pain. Others may be asymptomatic and picked up incidentally on routine screening for carriers of the hepatitis virus. Also, it is not uncommon to have spontaneous rupture of a tumor as the initial presentation. In the Far East, the rupture rate is as high as 10%, while in Hong Kong the rupture rate is around 9.7%.[1-4] without any treatment, the outcome is poor and survival rate is only 10%. Ruptured HCC is the major life-threatening complication. Traditionally, surgeons operate on those patients who present with ruptured HCC and the treatment is varied, consisting of packing, hepatic artery ligation and hepatectomy. However, surgery is often associated with a high mortality rate; the latter has been reported to be as high as 70%.[2-4] Therefore, a relatively less invasive procedure should be considered for patients with rupture of HCC and transcatheter hepatic arterial embolization (TAE) is gaining popularity in this area. The purpose of our retrospective study was to determine technical and outcome of patients who underwent TAE that we achieved in 3 years in Department of Radiology, Siriraj hospital.

Material and Method

Patients' selection

Medical records of patients with ruptured HCC who had undergone TAE during March 2003 - December 2006, were retrospectively reviewed and the outcome was analyzed. Informed consent for embo-lization was obtained from all conscious patients. This retrospective study was approved by the Ethics Committee of our hospital.

The diagnosis of ruptured HCC was based on two major criterias:

(1) clinical presentation of acute abdominal pain, distension, hypotension or shock.

(2) radiological findings of a liver tumor with evidence of bleeding - either frank hemoperitoneum or a subcapsular hematoma.

All of the patients who underwent TAE also was confirmed with ultrasound, non-contrast-enhanced CT, dual-phase CT or abdominal paracentesis, or combinations of any of these modalities before transcatheter arterial embolization.

Sex, age, clinical presentation, laboratory data and Child-Pugh classification were recorded in each patient.

Informed consent for embolization was also obtained.

Modality for work up ruptured hepatocellular carcinoma :-

- Abdominal paracentesis: blood-stained ascites or unclotted blood.

- Ultrasonography (US): High echoic area localized around tumor

- Computed tomography (CT) scan: Useful in detecting HCC rupture by showing tumor, by defining the extent of the hematoma, and by showing serial density changes with the age of the hematoma. The hyperdensity of acute hematoma is best visualized on noncontrast CT.

Optimal CT protocol for this condition triphasic phase:-

- Precontrast phase allows for assessment of hematoma. Arterial phase demonstrates enhancement of the mass. Portal venous phase allows for assessment of the portal veins.

CT Features of ruptured hepatocellular carcinoma:

(1) Discontinuity of the hepatic surface
(2) Active extravasations of contrast
(3) Subcapsular hematoma
(4) Presence of a sentinel clot
(5) Extra hepatic hematoma with high attenuation
(6) Marked ascites or hemoperitoneum
(7) Subtle rim enhancement (enucleation sign)
(8) Densely enhancing peripheral rim with marginal break.

Angiography: hyper vascular with tumor staining mass, extravasations of contrast medium and aneurysm.

Time from onset to angiography, amount of blood for resuscitation before angiography, baseline hemoglobin were recorded.

Intervention data were analyzed as follow;

Angiographic finding; Extravasations, hyper vascular with tumor staining and vascular abnormality such as aneurysm.

Arterial embolization; RHA, LHA and both or accessory RHA or others size of tumor and tumor location.

The agents used for embolization were basically gelfoam, stainless steel coils or polyvinyl alcohol sponge (Ivalon); the choice was primarily depending on the size of the artery being embolized and the radiologists' preference. In general, gelfoam was the preferred option, as the arteries could be recanalized providing an opportunity of further chemoembolization.

Immediately following embolization, hepatic arteriogram was repeated to ascertain the success of hemostasis.

The catheter for selection; 5 Fr Cobra, 5 Fr Yashiro catheter, Simm1 catheter, 5 Fr Shepherd Hook catheters and coaxial micro catheter were used.

Patients were monitored closely for any signs of rebleeding and complications, which included liver failure, fever, abdominal pain and wound problems. If patients had clinical sign of rebleeding, doctor will referred for surgery or repeat angiography with embolization.

Data analysis

Angiographic diagnosis and embolization technical success rate were analyzed by one interventional radiologist (experience > 15 yrs). Technical success means the result of embolization immediately after the intervention. 30-day mortality rate mean rate of number of patients who died within 30 day.

For the survival time period, we had follow-up the patients until death or until the end of the study observation time. (31 March 2007)

The final outcomes were analyzed as follow;

- Technical success, 0-3 day clinical success, 30days mortality rate, complication and survival time.
- Technical success (bleeding target devascularization) was assessed the result immediately after embolization, if immediate follow up arteriography showed devascularization of target vascular lesion or disappearance of extravasations, success was considered.
- They were divided in two types: partial and complete success.
- The complete success was defined as disappearance of extravasations or significant devascularized target vascular lesion.
- The partial success was defined as remaining minimal extravasations.

- 0-3 day clinical success was observation period to detect therapy-related failures.

- If patient had died or rebleeding, 0-3 day clinical unsuccess was considered.

- Rebleeding was described as unstable vital sign or no response to PRC or IV fluid or shock during resuscitation.

- Hematologic parameters (Hb) were serially followed up. Follow up imaging was reevaluated when clinical was indicated.

- In all patients, hemorrhage ceased almost immediately after embolization, as confirmed by the occlusion of feeding arteries of tumors, normalization of blood pressure and stabilization of hemoglobin levels.

- 30 days mortality rate was calculated for evaluate after treatment within 30 days and review most common cause.

- Complications were analyzed such as low grade fever, right upper quadrant or epigastric pain, liver failure or other.

- Correlation between portal vein thromboses with liver failure was calculated.

- The overall mean survival rate and mean survival of each Child-Pugh were calculated.

- Moreover, we also compared the survival of patients with respect to different possible prognostic indicators by using the survival Kaplan-Meier survival curves. Statistical significance was defined as $p \leq 0.05$.

Statistical analysis

SPSS statistical software version 11.5. Descriptive statistic analysis: report with frequency and percentage. Kaplan Meier curve for survival time in respect to prognostic factor.

Results

From March 2003 - December 2006, there were 54 patients who underwent TACE.16 cases were excluded due to not available film and medical record. 38 patients with spontaneous ruptured HCC were retrospectively reviewed. Altogether, there were 35 men and 3 women in our study aged 17-89 years with a mean age of 53.11 years. (Table 1).

Clinical presentation :The most patients presented with sudden onset of abdominal pain (44.7%) and distension (42.2%). (Table 1) Most of patient was sent to angiography within 24 hrs from initial symptom.

On admission, most of patients had hemoglobin < 8 g/dl and received blood transfusion in 2 units before angiography. 2 patients had Child A liver cirrhosis, 13 Child B and 23 Child C disease. (Table 1 (continued))

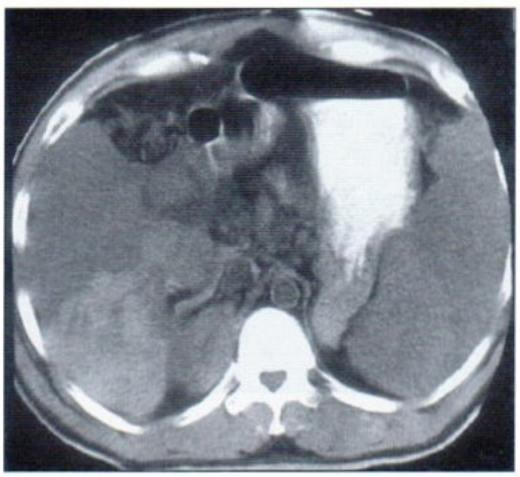
Location of tumor: The most common location of tumor was right lobe of liver (52.6%) (fig.1-2). Left lobe and bilobes were 5.3 and 42.1%, respectively. The right hepatic artery was selected in 25 patients (65.8%). The left hepatic, both of them and accessory right hepatic arteries were selected in 4, 3 and 6 patients, respectively. (Table 1 (continued))

Tumor size: The size of the HCC was determined on ultrasound or CT and ranged from 4.0 to 23.0 cm in maximum diameter. All embolizations were performed via the femoral approach. The 5 Fr catheters were used in 28 patients (73.7%). The other such as Yashiro, Simm[1], Shepherd and micro catheter were also used.

Angiographic findings:The most angiographic findings seen in our study was hyper vascular with tumor staining in 22 patients (56.4%). Extravasations and aneurysm were demonstrated in 14 and 2 patients, respectively. (Table 2 and fig.3-8).

Table 1 Patient demographic data and bleeding parameters

Parameter	Number of Patients (Percentage)
Sex	
Male : Female	35 (92.1) : 3 (7.9)
Age group (y) Mean age = 53 years	
≤ 20: 21-60 : 61-80 : > 80	1 (2.6) : 27 (71.1):9(23.7): 1 (2.6)
Presentation	
Abdominal pain	17 (44.7)
Abdominal distention	16 (42.2)
Abdominal pain with shock	4 (10.5)
Abdominal distention with Hct drop	1 (2.6)
Time from onset to angiography (day)	
< 1 : 1-3: 3-6: ≥ 7	16 (42.1) : 11 (28.9): 5 (13.2): 6 (15.8)
Hb (g/dl)	
< 8 : 8-10: ≥ 10	17 (44.7) : 12 (31.6): 9 (23.7)
Blood transfusion (units)	
0 : 1-2: 3-4: >4	6 (15.8) : 27(71): 4(10.6): 1 (2.6)
Child-Pugh classification	
A : B: C	2 (5.3) : 13 (34.2): 23 (60.5)
Location	
RL : LL : Both lobes	20 (52.6) : 2 (5.3): 16 (42.1)
Arterial embolization	
RHA : LHA: Both: Accessory RHA	25 (65.8) : 4 (10.5): 3 (7.9): 6 (15.8)



1.

2.

Fig.1 and 2 Noncontrast and contrast-enhanced CT show enhancing ill-defined mass at segment 5 of right lobe liver. Large amount of ascites was noted.

There were hepatoportal shunt in 8 pts and hepatohepatic shunt in 1 pt. There were main portal vein thromboses in 14 pts (36.8%), right portal vein thrombosis in 16 pts (42.1%) and left portal vein thrombosis in 13 pts (34.2%). (Table 2).

Gelfoam pledget about 1-2 mm. were used in

3.

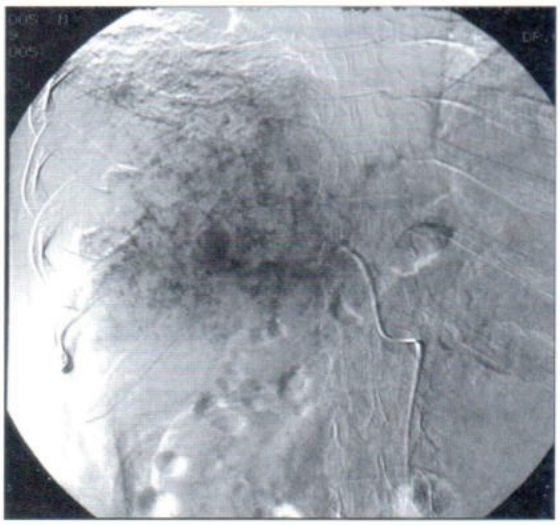


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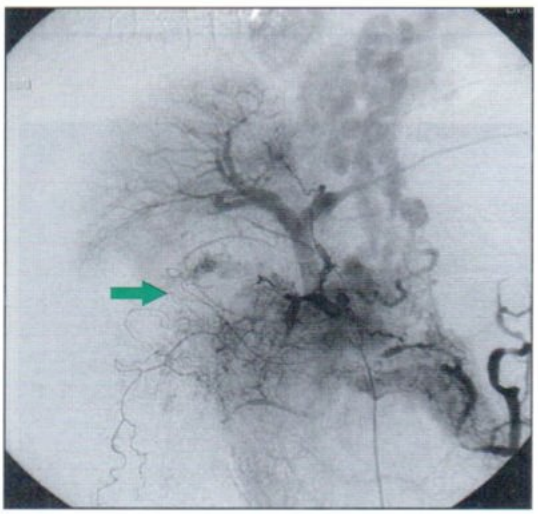
Fig. 3 Angiogram showed extravasations of contrast medium at inferior aspect of right lobe liver. Medial displacement of liver is noted which could be due to large amount of ascites or hemoperitoneum.

Fig. 4 Angiogram showed hypervascular mass with tumor staining scattered in the entire right lobe liver.



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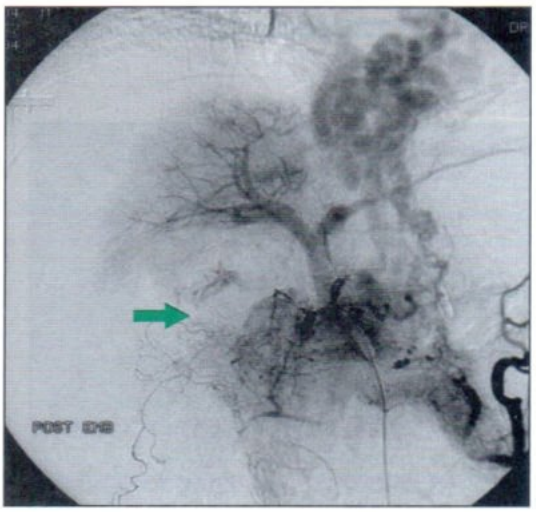

6.

Fig. 5 Preembolization showed extravasations of contrast medium at segment 5. Paraesophageal varices are also noted.

Fig. 6 Postembolization showed remaining of minimal extravasations of contrast medium. On 6 hours later, he developed hypotension and no response to blood replacement. The patient died within 24 hours later.

7.

8.

Fig.7 and 8 Hepatic angiogram showed diffuse hypervascular masses with main and right portal vein thrombosis. After TAE, liver enzyme rising was demonstrated. 11 days later, he died due to liver failure

every cases. Additional Lipiodol in four cases were performed. (Table 3)

After TAE, bleeding was arrested in all 38 patients, which was confirmed by the post TAE arteriogram

Clinical outcome:The technical success rate of embolization was achieved in all 38 patients (100%). Complete technical success rate of embolization was 34 patients (89.5%) Partial technical success rate that mean partial decreased vascularity of the target vascular lesion or minimal contrast material extravasations was in 4 patients (10.5%). (Table 4).

Early 3-day Failure. 76.3% (29 of 38 patients) who underwent technically successful embolization had no clinical evidence of reruptured tumor within 3 days. While early failure rate was 23.7% (9 of 38 patients) and 30 days mortality rate is 63.2% (24 of 38 patients). (Table 4)

From days 1-3 after embolization, two patients had re-ruptured tumor and one of cases died on day 2 and another case was followed by explore laparotomy and discharge later, while three cases of partial success angiogram died within 24 hrs, three cases experienced liver failure and died within 3 days and one case died within 3 days due to pneumonia and renal failure. (Table 4)

Apart from liver failure in seven patients (29%), which was the major cause of death during admission, three patients had partial success of angiography, six patients died from underlying medical condition, two patients developed re-ruptured without resuscitation or other treatment, and six patients died at home and outside hospital. (Table 5).

Overall mean survival time and mean survival for each child classification. The overall mean survival time of those after TAE was 61.92 days. Mean

Table 2 Angiographic findings

Findings	Number (n=38)	Percentage
Extravasations	14	36.8
Hyper vascular with tumor staining	22	56.4
Pseudo aneurysm	2	5.1
Main portal vein thrombosis	14	36.8
Right portal vein thrombosis	16	42.1
Left portal vein thrombosis	13	34.2
Hepatoportal shunt	8	21
Hepatohepatic shunt	1	2.6

Table 3 Embolic agents

Embolic agents	Number (n=38)	Percentage
Gel foam : Gel foam+Lipiodol: Glue	34 : 4 : 0	89.5 : 10.5 : 0

Table 4 Clinical outcome

Outcome	Yes Number of Patients (Percentage)	No Number of Patients (Percentage)
Technical success (n=38)	38 (100) - complete = 34(89.5), - partial = 4 (10.5)	0 (0)
0-3 days clinical success	29 (76.3)	9 (23.7)
30 days clinical success	14 (36.8%)	24 (63.2%)

Table 5 0-3 days failure rate (n=9) (23.7%)

Cause	Number	Percentage
Liver failure	3	33.33%
Re-rupture	2	22.22%
Partial success of angiographic finding with suspected rebleeding (survival <24 hrs)	3	33.33%
Multifactor	1	11.11%

**8 cases death within 3 days

*1 case - rebleed with follow by explore lap and discharge later

Table 6 Survival in each Child-Pugh classification

Child pugh	Survival period (months)					Mean
	0-1	1-3	3-6	6-12	>12	survival(days)
A: B : C	0: 7 :17	1: 2 : 6	0: 3 : 0	0: 1 : 0	1: 0 : 0	521.5: 66.9: 19

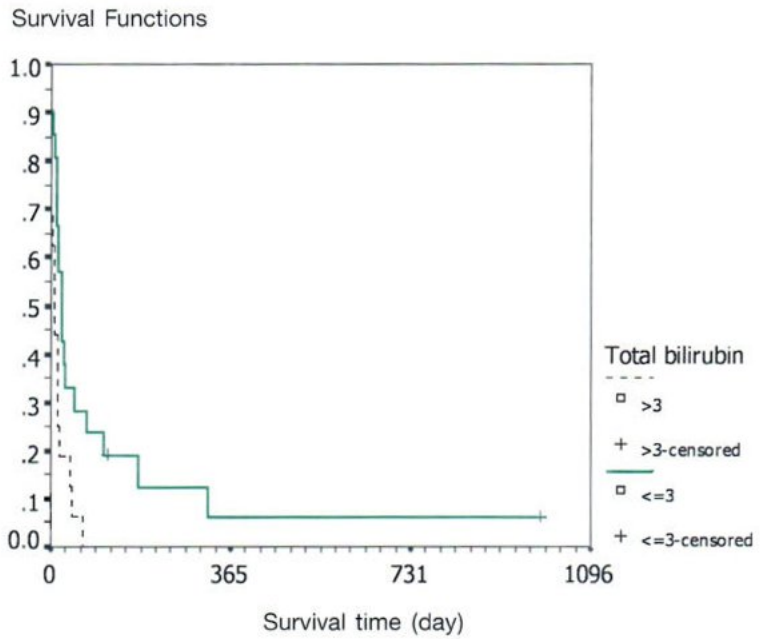

Fig. 9 Cumulative survival curves of patients having serum total bilirubin level above or below 3 mg/dl.

survival period of child A was 521.5 days, Child B was 66.9 days and Child C was 19 days. (Table 6)

Complications: The most common complication after procedure was fever in seven patients and liver failure in seven pts. Other complication, five patients complained of right upper quadrant or epigastric pain, six patients did not have any postembolization symptoms, one patient experienced hematoma at right groin and one patient experienced chill on perioperation.

The significant prognostic factor was the level of bilirubin. Those with a bilirubin level more than 3 mg/dl had a mean survival of 21 days, whereas those patients with a level less than 3 mg/dl had a mean survival of 115days (P=0.05). (fig.9)

The other prognostic factors; age > 60 or tumor size did not alter the outcome in terms of life expectancy. (fig.9)

Conclusion

TAE should be considered in the management of patients with ruptured HCC It is effective in arresting tumor bleeding. Patients who are considered poor surgical candidates with Child's B or C hepatic cirrhosis might have emergency embolization as a life-saving measure. However, the proce-

dure should be done selectively as not all the patients will benefit from this intervention. Failure TAE is not depends on only technique but also depend on underlying disease and general condition prior embolization.

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