

# Early Experience of Transarterial Therapy in Ruptured Hepatocellular Carcinoma

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## ABSTRACT

### Introduction:

Hepatocellular carcinoma (HCC) is the 3rd leading cause of cancer-related mortality. Ruptured HCC carries a high mortality if untreated. Peripherally located HCC has a higher risk of rupture. However, most of the ruptured HCCs on presentation are in an advanced stage and, hence are unresectable. Henceforth treatment options available are conservative and transcatheter embolization.

### Methods:

Retrospectively, 8 patients with ruptured HCC who underwent trans arterial embolization were studied for hemostasis and 30-day mortality. Clinical history and laboratory data were obtained from the medical records of the patients, and radiological images were extracted from picture archiving and communication systems and studied.

### Results:

The age ranged between 31 to 78 years and 7 were male. In patients presenting with sudden onset pain abdomen, ruptured HCC was suspected if there was a hemoperitoneum with or without extravasation of contrast adjacent to peripherally located HCC on CT angiography. Angiography revealed tumour blush with sentinel vessels in all. Two showed active contrast extravasation. Seven patients with relatively preserved liver function (Child A and B) attained both radiological and clinical hemostasis. One patient with Child C status died due to MODS on day 3 of embolisation. Three patients survived more than a year with additional liver-directed therapies. Two patients were lost to follow-up after discharge and two after six months.

### Conclusions:

Transarterial embolization for ruptured HCC is an effective method of hemostasis and helps in achieving better survival by the additional benefit of tumor control and poor functional status of the liver predicts lower survival.

**Keywords:** Child; Hemoperitoneum; Liver Neoplasms; Medical Records; Radiology Information Systems

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## INTRODUCTION

Hepatocellular carcinoma (HCC) causes 600,000 deaths worldwide per year and is the 3rd leading cause of cancer-related mortality. HCC most commonly occurs in cirrhotic liver and hepatitis (B and C) endemic areas. Ruptured HCC carries high mortality (25-75%) due to hemorrhagic shock and liver failure in the acute phase. Peripherally located tumors have a higher risk of rupture. The mortality is significantly higher in the Asian population as compared to the West. Very early HCC are managed by hepatectomy with curative benefits. However, most of the ruptured HCC on presentation are in the advanced stage and, hence are unresectable. Henceforth treatment options available are conservative and transcatheter embolisation.<sup>1,2,3</sup>

## METHODS

Ethical clearance for retrospective study was taken from the ethical board of the hospital. Retrospectively, hemostatic and survival outcomes were studied in cases of ruptured HCC who underwent transarterial embolization in Medanta, The Medicity, India from Nov 2014 to Oct 2016. All cases were diagnosed on CT angiography. Patients who had HCC beyond Barcelona-Clinic Liver Cancer (BCLC) stage 0 underwent transarterial embolization if surgical intervention was unfeasible. After baseline investigations, the right common femoral artery was accessed with a 5F sheath. Using either a Cobra 1 or Simmons 1 diagnostic catheter, a superior mesenteric angiogram was taken, followed by a celiac angiogram. Tumor feeders were super selectively catheterized using a microcatheter (Microferret, Cookmedical, Bloomington, USA) and microwire (Cirrus, Cookmedical, Bloomington, United States of America). Bland Embolisation using gel foam or Poly Vinyl Alcohol (PVA) particles (350-500 microns) was done for ruptured HCC with hemoperitoneum. Conventional transarterial chemoembolization using a doxorubicin-lipiodol mixture was done for contained subcapsular ruptured HCC. Stasis in the feeder was identified as endpoint for embolisation. Post-embolization hemodynamic parameters, hemoglobin and liver function tests

were closely monitored in the intensive care unit.

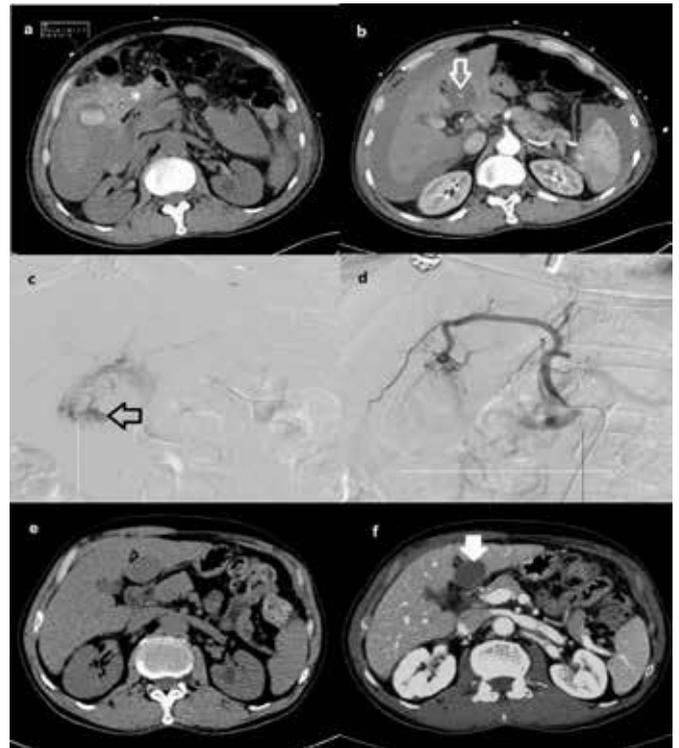
## RESULTS

During the study period, 8 patients underwent transarterial embolization for ruptured HCC. Seven were male. The age of the study population ranged between 31 to 78 years. Seven cases were native liver chronic liver disease (CLD) with hepatocellular carcinoma and one was post-liver transplant with HCC recurrence. The etiology of CLD was as follows: Hepatitis C related- 4 patients, Hepatitis B related- 1 patient, Nonalcoholic steatohepatitis- 2 patients and alcohol related- 1 patient. Out of eight cases, one was Child C, three were Child B and four Child A status. Five cases had a Model For End-Stage Liver Disease (MELD) score of less than 10 two had MELD between 10 and 15, and one had MELD score more than 15. All patients presented with sudden onset pain abdomen. Five patients with hemoperitoneum had anaemia at presentation with significantly low hemoglobin (Less than 6 gm/dL), whereas three patients with subcapsular rupture had hemoglobin more than 9 gm/dL. Tumor size ranged between 4.4 and 16 cm in the largest dimension. In 2 cases, tumor occupied the entire right lobe, in 4 it was peripherally located and in 2 exophytic in location. Segmental portal vein tumor thrombosis (PVTT) was present in 1 case.

Three patients were successfully embolized with gel foam, and 2 with PVA particles. In 3 patients who had limited subcapsular rupture, conventional TACE (cTACE) was done. Stasis and near stasis of the feeding arteries were achieved in all cases. In all the patients, there was no further drop in hemoglobin levels. Seven patients in whom hemostasis was achieved were hemodynamically stable post-procedure and were subsequently discharged from the hospital. However, one case with Child C status with bilirubin of 38, died due to shock and multi-organ dysfunction syndrome (MODS). Two patients survived more than a year and later underwent radiofrequency ablation of the primary tumor. One patient who underwent subsequent selective internal radiotherapy survived more than a year. Two patients were lost to follow-up after discharge and 2 after 6 months. (Table 1)

***Table 1: Clinical and radiological characteristics of patients with ruptured hepatocellular carcinoma treated with transarterial embolisation***

	Number (n=8)
Etiology	
HBV	1
HCV	4
ALD	1
NASH	2
Child's Score	
A	4
B	3
C	1
MELD	
<10	5
10-15	2
>15	1
BCLC	
0	-
A	-
B	5
C	2
D	1
Size	
<5 cm	4
5-10cm	2
>10 cm	2
Location	
Bulging	2
Peripheral	4
Large	2
Portal vein Tumor thrombus	
MPV	-
Lobar	-
Segmental	1
Embolization	
Bland- Gelfoam	3
Bland- PVA	2
cTACE	3



***Figure 1: Bland embolisation for ruptured HCC with hemoperitoneum a). NCCT showing hemoperitoneum (asterisk) b). CTA showing contrast extravasation ( white arrow) c). Angiogram showing sentinel vessel and contrast extravasation ( black arrow) d). Post embolisation angiogram showing no contrast extravasation and stasis in feeder vessel e). Six months Post TAE follow-up NCCT and f). CECT showing tumor necrosis (solid white arrow)***



***Figure 2: Conventional TACE for ruptured HCC with contained subcapsular hematoma a). Hyperdense subcapsular hematoma (asterisk) b).***

*Angiogram showing contrast extravasation (black arrow ) c). Post cTACE angiogram showing lipiodol deposit and stasis in tumor feeder d). POST cTACE NCCT showing lipiodol deposit in HCC*

## DISCUSSION

HCC is the fifth most common tumor in the world and the third leading cause of cancer-related deaths. HCC most commonly occurs in alcohol and chronic viral hepatitis-related cirrhosis. Tumor rupture occurs in 3-15% of cases of HCC due to its hypervascular nature and neoangiogenesis and has a grave prognosis if untreated. The presenting age of rupture varies between 44 and 68 years, with male to female ratio of 3:1.<sup>5,6</sup>

Although the risk factors are not well known, vascular erosion, venous thrombosis by tumor, and rapid tumor growth with necrosis present a higher risk of rupture. Surface tumor rupture leads to hemoperitoneum presenting as sudden onset pain abdomen and shock. On the other hand, intraparenchymal tumor rupture is confined without causing hemoperitoneum or shock. All cases in our study presented with sudden onset pain abdomen.<sup>2,5</sup>

CT findings of ruptured tumor include a peripherally located tumor in contact with a liver capsule with a bulging outline, discontinuity of hepatic surface, contrast extravasation, haematoma at the site of rupture, hemoperitoneum and separation of tumor content from a peripheral enhancing rim causing the “enucleation sign”. In our series, all cases had tumor reaching up to the liver surface, 5 with moderate hemoperitoneum and 3 with contained hemoperitoneum. Contrast extravasation was seen in 3 cases.<sup>7,8,9,10,11</sup>

The initial step in the management of ruptured HCC is to attain hemodynamic stability and hemostasis. Very early and early HCC (BCLC stage 0 and A) with rupture are treated by hepatectomy with curative benefits. Other modalities such as packing or ligation of the hepatic artery are inferior to transarterial embolisation (TAE) for achieving hemostasis. Conservative management has the worst outcome. At presentation, most of the ruptured HCC are beyond BCLC stage A and, hence are unresectable.<sup>5,7</sup>

In transarterial embolisation, the hepatic artery or its branches supplying the tumor is selectively cannulated via common femoral artery approach. Angiography is done using a low osmolar non-ionic contrast medium. Ruptured HCC may show sentinel vessel (disproportionately dilated and tortuous vessel), hypovascular area, delayed dot (dot-like stain in delayed phase) and contrast extravasation. All cases in our study showed sentinel vessels, 3 showed delayed dots and 2 showed contrast extravasation.<sup>10,11</sup>

After angiography, embolization is done using gel foam or PVA particles in bland embolisation. During conventional transarterial chemoembolisation (cTACE), chemotherapy lipiodol aliquot is used and topped up with gel foam or PVA particle. In 3 of our cases with contained ruptured HCC, cTACE was done using lipiodol doxorubicin aliquot with top-up gel foam embolisation. Of the 5 cases with hemoperitoneum, bland tumor embolization was done with gel foam in 3 cases and PVA particles in 2 cases. Near stasis in the main vessel (“Winter tree” appearance on angiography) is the endpoint for embolisation.<sup>12</sup> All cases in our series showed post-embolisation near stasis.

In ruptured HCC with preserved liver function (Child A and B), TAE or TACE showed a high success rate for immediate hemostasis and 30-day survival. The survival after TAE is lower in advanced cirrhosis. In our series, seven patients with Child A and B status survived more than 30 days, whereas one patient who had Child C cirrhosis succumbed to MODS even after successful embolization. Even for ruptured resectable HCC, transarterial embolisation to achieve hemostasis before hepatectomy has shown to be beneficial. Three patients with subsequent locoregional therapies (RFA and SIRT) showed long-term survival of more than 1 year.<sup>5,6,7,13,14,15,16,17,18</sup>

TACE done for ruptured HCC with patent PV and contained subcapsular hematoma and super-selective TAE done for ruptured HCC with portal vein tumor thrombosis (PVTT) or hemoperitoneum, showed good hemostasis and 30 days survival in our cases with good functional status (Child A and B; MELD<15; BCLC 0, A and B). Additional survival

benefit was observed in cases with subsequent locoregional therapies in due course.

## CONCLUSION

Transarterial embolisation for ruptured HCC is an effective method of hemostasis and helps in achieving better survival through the additional benefit of tumor control and the poor functional status of the liver predicts lower survival.

## CONFLICT OF INTEREST

None

## SOURCES OF FUNDING

None

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