

Radiological Response in Saudi Patients Undergoing Transarterial Chemoembolization for Hepatocellular Carcinoma

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ABSTRACT

Background: Hepatocellular carcinoma (HCC) is the second commonest cancer affecting males and the eighth most common one affecting females in Saudi Arabia. Transarterial chemoembolization (TACE) is currently considered the first line therapy for multifocal HCC in selected patients. **Objective:** To evaluate HCC response to TACE based on triphasic computerized tomography (CT) of the liver obtained 6 weeks after the procedure. **Materials and Methods:** A retrospective chart review of 15 patients who underwent TACE in King Khalid University Hospital for unresectable HCC. Patients were staged according to the Child-Pugh, Okuda, and CLIP scoring systems. The first triphasic CT of the liver after TACE was evaluated for Lipiodol uptake and interval change in tumor burden. **Results:** The mean age was 63 years (40-82), 10 were males (66.7%), and five were females. About 11 patients had cirrhosis (73.3%). Eight patients (53.3%) were Child-Pugh class A while seven (46.7%) were Child-Pugh class B. One patient died and two were lost to follow up. Four patients had a complete response to TACE (26.7%), two had a partial response (13.3%), five showed no change (33.3%) and none showed progression of disease. Tumoral Lipiodol uptake in five patients was >75% (33.3%), in two 75-50% (13.3%) while in four patients it was <50% (26.7%). **Conclusion:** Our results show that TACE is an effective method of reducing the tumor burden in selected patients with unresectable HCC.

Key Words: Hepatocellular carcinoma, transarterial chemoembolization

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Hepatocellular carcinoma (HCC) is the commonest primary malignancy of the liver.^[1] World wide it ranks the fifth most common cancer and the third most common cause of cancer related death. HCC is a significant cause of mortality and morbidity in Saudi Arabia, constituting 6.1% of all newly diagnosed cancers and 87.6% of all liver cancers. According to the most recent publication of the National Cancer Registry of Saudi Arabia, HCC is the second commonest cancer affecting males and the eighth commonest cancer in females.^[2]

Patients' management with HCC varies from liver transplantation to palliation. Transarterial chemoembolization (TACE) is a technique that has emerged as a modality of treating patients with unresectable multifocal HCC without vascular invasion or metastasis.

In this study, we describe our initial experience with 15 patients who underwent TACE for HCC with a special emphasis on tumor response based on the initial triphasic CT of the liver.

MATERIALS AND METHODS

The charts of all patients who had TACE for HCC from

November 2003 to November 2005 were reviewed. These patients were diagnosed with HCC either at King Khalid University Hospital, Riyadh, Saudi Arabia or referred with the diagnosis from other hospitals. The diagnosis was based on the recommendations of the European Association for the Study of Liver in which the diagnosis of HCC in cirrhotic patients would be made if the patient had a lesion more than 2 cm in size with arterial hypervascularization on two imaging techniques (ultra sound, spiral CT, MRI, and angiography) or had a lesion more than 2 cm in size with arterial hypervascularization and an AFP level more than 400 ng/mL.^[3]

Only patients with Child-Pugh class A or B with no evidence of extrahepatic spread or portal vein thrombosis were considered for TACE. Patients were classified according to the Okuda^[4] and Cancer of the Liver Italian Program (CLIP)^[5] staging systems.

All patients had triphasic CT of the liver to evaluate tumor burden, arterial anatomy, and portal vein (PV) patency prior to the procedure. TACE procedure was performed within 6 weeks from initial diagnostic CT scan. Each patient had full explanation of the procedure and signed a consent form.

All patients were admitted to the hospital one day prior to the procedure. PV patency was confirmed with Doppler prior to procedure. Based on arterial anatomy, revealed by the CT, the tumor-feeding artery (whether it arises from celiac or superior mesenteric artery) was then catheterized with subsequent injection of an emulsion of 10 mL of Lipiodol Ultrafluid with 5 mL of Omnipaque 300 mixed with Doxorubicin. Doxorubicin dose given was 75 mg/m² if bilirubin was <15.5 mmol/L, 50 mg/m² if bilirubin was 25.5-51.3 mmol/L and 25 mg/m² if bilirubin >51.3 mmol/L as per the Barcelona protocol.^[6] Then the feeding artery was embolized with poly vinyl alcohol. Its size and amount varies with the size of the feeding vessel till stagnation of blood flow was achieved. Patients are kept in the hospital for observation for 5 days. After 6 weeks, triphasic CT of the liver was obtained to assess treatment response. This was based on Lipiodol uptake and the interval change in tumor burden. Lipiodol uptake was classified as >75%, 50-75% or <50%, while assessment of tumor burden was assessed on the World Health Organization (WHO) criteria,^[7] in which complete response means no evidence of neoplastic disease; partial response means reduction in total tumor load of more than 50%; no change means reduction of less than 50% or increase of less than 25%; and progressive disease, increase of equal or more than 25%.

RESULTS

A Total of 15 patients underwent TACE. The mean age was 63 years (40-82). About 10 patients were males (66.7%) and five were females [Table 1]. Eight patients had chronic hepatitis C (53.3%), two had chronic hepatitis B (13.3%), four had both HCV and HBV concomitantly (26.7%), and one had neither virus. Eleven patients (73.3%) had cirrhosis. Eight patients were Child-Pugh class A (53.3%), seven were child B (46.7%) and none were class C as per protocol. Three patients had histology proven HCC (18.75%). Five patients were Okuda

stage I (33.3%), nine were stage II (60%), and one was stage III (6.7%). On the CLIP staging system, two were stage 0 (13.3%), seven were stage 1 (46.7%), four were stage 2 (26.7%) and two were stage 3 (13.3%) [Table 2].

Four patients had a complete response to TACE (26.7%), two had a partial response (13.3%), six showed no change (40%) and none showed progression of disease. Five patients had tumoral lipiodol uptake of >75% (33.3%), two showed an uptake of 75-50% (13.3%) and five showed an uptake of <50% (33.3%).

Complications of TACE included fever in eight patients (53.3%), abdominal pain in four (26.7%), vomiting in three (20%). Two patients developed ascites (13.3%) and one patient had systemic side effects including alopecia and febrile neutropenia and received supportive treatment with complete recovery. One patient developed pneumonia, which was treated with antibiotics and seven patients (46.7%) had an increase in the transaminase level more than double the upper limit of normal. Post TACE data were not available on two patients.

One patient died post TACE secondary to bleeding from a ruptured HCC. This patient was doing well until the third day after TACE when the patient noticed rapid abdominal distention followed shortly by hypotension. The patient had obvious bluish discoloration in both flanks. Urgent CT scan of the abdomen and ascitic tap confirmed the diagnosis of a ruptured HCC with intraperitoneal bleeding. The patient was aggressively resuscitated and was taken for urgent angiography and hepatic artery embolization. In spite of successful embolization, unfortunately the patient died of shock.

DISCUSSION

TACE has achieved immense popularity recently and has

Table 1: Characteristics of the patients who underwent transarterial chemoembolization

Sex	Age	Cirrhosis	Virus	Child-Pugh	Histology
F	58	Yes	HCV + HBV	B	No
M	82	No	-	A	Yes
M	65	Yes	HCV	B	No
F	62	Yes	HCV+ HBV	A	No
M	64	Yes	HCV	A	No
M	46	Yes	HBV	A	No
M	69	No	HBV	A	Yes
M	70	No	HCV	A	Yes
M	73	No	HCV + HBV	A	No
M	40	Yes	HCV	B	No
F	60	Yes	HCV	B	No
F	64	Yes	HCV	B	No
F	67	Yes	HCV	B	No
M	53	Yes	HCV + HBV	B	No
M	74	Yes	HCV	A	No

Table 2: Patients tumor stage before transarterial chemoembolization (TACE) and lipiodol uptake after TACE

CLIP score	Largest mass	No. of masses	After 2 months	Lipiodol uptake (%)
2	6×5	3	No change	75-50
1	6.5×5.5	2	Lost follow up	
2	7×5	3	No change	<50
1	4×4	>3	No change	<50
0	4×4	1	Complete response	>75
1	4×5	2	Complete response	>75
1	0.7×2	2	Partial response	>75
1	1.5×1.5	2	Complete response	>75
2	18×12	1	No change	<50
1	5.5×3.5	1	Complete response	>75
2	3.5×2.5	>3	Partial response	75-50
1	12×11	2	no change	<50
3	8×10	1	Died	
3	10×9	1	Lost follow up	
0	9×8	1	No change	<50

CLIP - Cancer of the Liver Italian Program

become the first line non-curative therapy for patients with unresectable multifocal HCC.^[8] Initially six randomized controlled trials (RCT) showed a significant effect on tumor size but did not achieve a survival benefit when comparing TACE to conservative management.^[3] Later on, two well-done RCT's and one meta-analysis showed a significant survival benefit for patients receiving TACE as opposed to conservative management. In the Barcelona group paper,^[6] the 2 year survival was 62% in the TACE arm, 50% in the embolization arm and 27% in the untreated arm. In similar RCT from Korea,^[9] the survival was 57% at 1 year, 31% at 2 years, and 26% at 3 years in the TACE arm as compared to 32% at 1 year, 11% at 2 years, and 3% at 3 years in the control group. Similarly in a meta-analysis performed by Llovet and colleagues,^[10] TACE reduced the two year mortality from 41% in the control group vs. 27% in the TACE group. A possible explanation for the favorable results of the last two trials is the selectivity of patients with less advanced liver disease and smaller tumors compared to previous trials. In addition, in the last two trials patients received multiple sessions of TACE regardless of the initial response.

The survival benefit associated with TACE is thought to be mediated via an increase in the amount of chemotherapeutic agent delivered to the tumor mass with less systemic toxicity.^[11] As a treatment modality, it is gaining popularity for several reasons some of which are prolonged waiting lists for liver transplantation with the low number of donors especially in this part of the world and the increased number of HCC detected on surveillance.

Our study is the first to describe results of TACE in the Middle East where HCC is a very important and relatively common disease. Our results showed that this procedure is effective in reducing the tumor burden in the majority of patients with

relatively low complication rate. These results are comparable to previously published trials in Europe and Asia.^[6,9]

Complication rates in our study were also very comparable to other studies. The one patient who died had a large tumor that was very close to the capsule of the liver. Although not clearly documented by others, we have abandoned this form of intervention in patients with tumors close to the capsule. The patient who developed severe cytotoxic side effects was a patient who developed HCC 3 years after receiving kidney transplantation. He was on Cyclosporine and Mycophenolate mofetil. After about 3 weeks of supportive therapy with blood product transfusions and granulocyte stimulation factors, he had a complete recovery.

As anticipated, the patients who achieved a complete response were CLIP stage 1 or less (26.7%) and the majorities were Child-Pugh class A apart from one who was class B. In fact one of the patients who achieved a complete response is awaiting orthotopic liver transplantation. On the other hand, the majority of patients who showed no response had masses that were considerably large. Although not clearly documented by others, we have limited the size of tumors to be treated in the future to a maximum of 10 cm. In our experience tumors larger than 10 cm have a very small chance of having a significant response. This conforms to the recommendations of the Saudi Gastroenterology Association.^[12] As proven in previous studies, the favorable outcome obtained in these patients was due to the optimum selection of patients for TACE.

CONCLUSION

A favorable outcome was achieved in properly selected patients treated with TACE in Saudi Arabia.

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