

**INTRATUMORAL LIPIODOL ACCUMULATION PATTERN AND TUMOR RESPONSE  
IN TRANSCATHETER ARTERIAL CHEMOEMBOLIZATION (TACE) FOR THE  
TREATMENT OF UNRESECTABLE HEPATOCELLULAR CARCINOMA (HCC)  
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**ABSTRACT**

Hepatocellular carcinoma (HCC) is a commonly occurring hepatic malignancy. Transarterial chemoembolization (TACE) has proved to be an effective method of palliative therapy for unresectable multifocal HCC without vascular invasion or metastasis. The study design is a retrospective record of all patients that underwent Transarterial chemoembolization (TACE) procedure for advanced stage hepatocellular carcinoma (HCC) over a period of one year in a single center in Saudi Arabia. There are four types of lipiodol deposition, according to classification defined as follows: type 1, diffuse homogeneous opacification of the tumor focus and around it; type 2, homogeneous opacification of the majority of the mass; type 3, weak heterogeneous opacification; type 4, very weak or no opacification of the tumor focus. 9 (26.47%), 5 (14.7%), 10 (29.41%) and 10 (29.41%) patients showed types I, II, III, and IV lipiodol deposition, respectively. Univariate analysis demonstrated that local tumor response and intra-tumoral lipiodol covering is a significant predictor of tumoral response at (P<0.05).

**KEYWORDS:** Hepatocellular carcinoma (HCC), Lipiodol, TACE (Transarterial chemoembolisation).**INTRODUCTION**

Hepatocellular carcinoma (HCC) is a commonly occurring hepatic malignancy. It is one of a major causes of death and morbidity in Saudi Arabia, accounting for 6.1% of all newly diagnosed malignancy and 87.6% of all cancers of the liver.<sup>[1, 2]</sup> Management of patients with HCC differs from liver transplantation, ablation or palliation depending on the disease stage. Transarterial chemoembolization (TACE) has proved to be an effective method of palliative therapy for unresectable multifocal HCC without vascular invasion or metastasis.<sup>[3-6]</sup> Quite a considerable amount of research has been done on the effectiveness of this technique in comparative analysis with supportive therapy, also there are many papers and research articles published and most of it are related to the efficiency, technique, and survival percentage of this therapy.<sup>[7-16]</sup>

**AIMS AND OBJECTIVES**

This is a study done in Saudi Arabia with 34 patients who underwent TACE for HCC with a specific objective to correlate the pattern of lipiodol uptake with tumor response.

**METHODS AND MATERIALS**

**Study method and population:** The study design is a retrospective record of all patients that underwent Transarterial chemoembolization (TACE) procedure for advanced stage hepatocellular carcinoma (HCC) in between Jun 2017 to June 2018.

**Objectives of the study:** The primary goal for conducting this study is to analyze the tumor response after TACE using mRECIST criteria and correlate it with the intra-tumoral lipiodol accumulation.

**TACE procedure:** The diagnosis of hepatocellular carcinoma is made according to specialized body imaging consultants with the help of the European Association for the Study of Liver recommendations in which the diagnosis of HCC in cirrhotic patients would be established if tumor size 10 - 20 mm in diameter with hypervascular lesion confirmed in multiphase CT or MRI and wash-out in portal venous and/or equilibrium phases or tumor larger than 20 mm with hypervascular lesion confirmed in multiphase CT or MRI.

TACE was done on patients with advanced stage of HCC including patients having Child's A or B type cirrhosis without extrahepatic spread or portal vein thrombosis.

TACE therapy was done by transfemoral access. An arteriogram along the celiac axis was obtained at first. Selective cannulation was then done to the hepatic artery supplying the tumor mass. The catheter was advanced as near as possible to the tumor. The drug emulsion used for chemotherapeutic purpose consisted of drug Doxorubicin 50 mg, 6-8 ml of non-ionic iodinated contrast media diluted in saline and 8 ml of iodized oil (Lipiodol). The emulsion drug was prepared by repeated agitation of the mixture using two connected glass syringes attached by a three-way stopcock connector.

This prepared chemotherapeutic emulsion was then injected into the cannulated hepatic artery that feeds the tumor. The amount of drug emulsion to be injected was decided varyingly, during the procedure. The injection of the emulsion was stopped when the whole of intra-tumor space was covered with lipiodol, or reflux of emulsion was seen to the adjacent normal hepatic arteries. Every arterial branch supplying the tumor mass was individually catheterized, and the drug was delivered. However, the amount of drug varies with every case according to the condition. Immediately after the administration of the drug, embolization was done with gelatin sponge pledgets.

After the completion of the therapy, a three-phase CT within three-month intervals to analyze the disease response, if the follow up showed persistent or recurrent disease or formation of new lesions TACE was performed again at an interval of 12-13 weeks from the previous session, but tied to the condition that the Child's cirrhosis status was A or B. If all the biochemical and clinical analysis of the patient went normal, the CT was done on annual intervals.

**Data collection:** After TACE application, follow up triphasic CT within 6 weeks and at three-months intervals until 12 months post procedure was reviewed. The most important outcome of all the obtained data was the local area tumor response, as examined based on triphasic CT, the tumor response was grouped and sub-grouped using mRECIST criteria for solid tumors.

**Data Analysis:** The first result analyzed from the collected data was the dynamic response of the local tumor to TACE which varied and was classified into four classes, these classes are defined as, (1) Complete Response, (2) Partial Response (3) Stable Disease and (4) Progressive Disease.

Contrast enhanced axial CT of the liver shows hepatocellular carcinoma in segment 5. DSA after selective catheterization of segmental hepatic artery branch shows tumor blush. Post chemoembolization image shows lipiodol fixation within the tumor. Axial

CT scan on 1 month follow up shows intra-tumoral lipiodol deposition.

Four types of lipiodol deposition on plain axial CT scan: A: Type 1- diffuse homogeneous opacification of the tumor focus; B: Type 2 - mostly homogeneous opacification; C: Type 3 - weak heterogeneous opacification; D: Type 4 - very weak or no opacification of the tumor focus

## RESULTS AND DISCUSSION

The population of the study was 34 patients represented by 25 males (77.3%) and 9 females (22.7%). The mean age was 63 years (45-79), 17 patients had chronic hepatitis C (52.9%), 11 had chronic hepatitis B (32.3%) and 5 had neither virus (14.7%). these 34 patients underwent a total of 42 sessions of TACE (28 single session patients, 3 double session patients, 0 triple session patients, and 2 four-session patients).

In Child-pugh classification, the patients were classified as A – 23 patients (67.65%) and B – 11 (32.35%).

**Characteristics of the patients who underwent transarterial chemoembolization**

Age	Sex	Child's Score	Etiology of cirrhosis
61	M	A	HBV
62	M	A	NASH
79	F	A	HCV
62	M	A	Unknown
57	F	A	HBV
74	F	A	HCV
68	M	A	HCV
59	M	A	NASH
45	M	A	Unknown
52	M	B	Unknown
68	F	B	HBV
64	M	B	HCV
61	F	A	HCV
68	F	A	HBV
69	M	B	HCV
64	M	A	HBV
61	M	A	HCV
61	M	B	HCV
64	M	A	HBV
58	M	A	HCV
59	M	B	HCV
62	F	A	HBV
71	M	B	HCV
56	M	B	HBV
64	M	A	HCV
68	M	B	HCV
64	F	A	HBV
69	M	A	HCV
66	F	B	HBV
63	M	A	HCV
68	M	A	HCV
70	M	B	HBV
68	M	A	HCV

The average tumor size measured to be 5.8 cm, and the smallest and largest tumors measured 2 cm and 15 cm, respectively. A single HCC was seen in 15 patients (44.1%), and multiple HCC were seen in 19 subjects (55.9%).

All the treated patients were followed up post-TACE therapy for at least 6 months. These treated subjects were followed up for a mean time period of 3.8 ± 9.2 months. The response of the local tumor to TACE is analyzed through mRECIST criteria for HCC. 8 (23.52%), 15 (44.11%), 8 (23.52%), 3 (8.82%) patients had complete response, partial response, stable disease, progressive disease (PD).

There are four types of lipiodol deposition, according to classification defined as follows: type 1, diffuse homogeneous opacification of the tumor focus and around it; type 2, homogeneous opacification of the majority of the mass; type 3, weak heterogeneous opacification; type 4, very weak or no opacification of the tumor focus. 9 (26.47%), 5 (14.7%), 10 (29.41%) and 10 (29.41%) patients showed types I, II, III, and IV lipiodol deposition, respectively. Univariate analysis demonstrated that local tumor response and intra-tumoral lipiodol covering is a significant predictor of tumoral response at (P<0.05).

Pattern of Lipiodol Accumulation (number of cases)	Patience response			
	Progression of disease	stable	partial response	complete response
Homogeneous Good Accumulation (9)	0	0	1	8
Less Homogeneous Good Accumulation (5)	0	0	5	0
Partial Accumulation (10)	0	3	9	0
Weak Accumulation (10)	3	5	0	0
Total (34 cases)	3	8	15	8

**CONCLUSION**

TACE technique is a safe and efficient palliative procedure for advanced cases of hepatocellular carcinoma (HCC). Despite the presence of large-sized tumors in our study population, TACE demonstrated efficient and convincing good response and the results were synonymous to those reported by other authors and

researchers. Intra-tumoral lipiodol deposition was a significant predictor of tumoral response.

**REFERENCES**

1. Parkin DM, Bray F, Ferlay J, Pisani P. Estimating the world cancer burden. *Globocan Int J Cancer*, 2001; 94: 153-6.

2. Kingdom of Saudi Arabia ministry of health. National Cancer Registry, 2017-2018.
3. Yumoto Y, Jinno K, Tokuyama K, Araki Y, Ishimitsu T, Maeda H, et al. Hepatocellular carcinoma detected by iodized oil. *Radiology*, 1985; 154: 19-24.
6. Ohishi H, Uchida H, Yoshimura H, Ohue S, Ueda J, Katsuragi M, et al. Hepatocellular carcinoma detected by iodized oil: Use of anticancer agents. *Radiology*, 1985; 154: 25-9.
4. Takayasu K, Shima Y, Muramatsu Y, Moriyama N, Yamada T, Makuuchi M, et al. Hepatocellular carcinoma: Treatment with intraarterial iodized oil with and without chemotherapeutic agents. *Radiology*, 1987; 163: 345-51.
5. Llovet JM, Real MI, Montana X, Planas R, Coll S, Aponte J, et al. Arterial embolization or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: A randomised controlled trial. *Lancet*, 2002; 359: 1734-9.
6. Caturelli E, Siena DA, Fusilli S, Villani MR, Schiavone G, Nardella M, et al. Transcatheter arterial chemoembolization for hepatocellular carcinoma in patients with cirrhosis: Evaluation of damage to nontumorous liver tissue-long-term prospective study. *Radiology*, 2000; 215: 123-8.
7. Takayasu K, Arii S, Ikai I, Omata M, Okita K, Ichida T, et al. Prospective cohort study of transarterial chemoembolization for unresectable hepatocellular carcinoma in 8510 patients. *Gastroenterology*, 2006; 131: 461-9.
8. Ji SK, Cho YK, Ahn YS, Kim MY, Park YO, Kim JK, et al. Multivariate analysis of the predictors of survival for patients with hepatocellular carcinoma undergoing transarterial chemoembolization: Focusing on super selective chemoembolization. *Korean J Radiol*, 2008; 9: 534-40.
9. Savastano S, Miotto D, Casarrubea G, Teso S, Chiesura-Corona M, Feltrin GP. Transcatheter arterial chemoembolization for hepatocellular carcinoma in patients with Child's grade A or B cirrhosis: A multivariate analysis of prognostic factors. *J Clin Gastroenterol*, 1999; 28: 334-40.
10. Miyayama S, Yamashiro M, Okuda M, Yoshie Y, Sugimori N, Igarashi S, et al. Chemoembolisation for the treatment of large Hepatocellular carcinoma. *J Vasc Interv Radiol*, 2010; 21: 1226-34.
11. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics. *CA Cancer J Clin*, 2005; 55: 74-108.
12. Paul SB, Chalamalasetty SB, Vishnubhatla S, Madan K, Gamanagatti SR, Batra Y, et al. Clinical Profile, Etiology and Therapeutic Outcome in 324 Hepatocellular Carcinoma Patients at a Tertiary Care Center in India. *Oncology*, 2009; 77: 162-71.
13. Kumar R, Saraswat MK, Sharma BC, Sakhuja P, Sarin SK. Characteristics of hepatocellular carcinoma in India: A retrospective analysis of 191 cases. *Q J Med*, 2008; 101: 479-85.
14. Bruix J, Sherman M, Llovet JM, Beaugrand M, Lencioni R, Burroughs AK, et al. EASL Panel of Experts on HCC. EASL panel of experts on HCC: Clinical management of hepatocellular carcinoma. Conclusions of the Barcelona EASL conference. European Association for the study of liver. *J Hepatol*, 2001; 35: 421-30.
15. Cillo U, Vitale A, Grigoletto F, Farinati F, Brolese A, Zanusi G, et al. Prospective validation of the Barcelona Clinic Liver Cancer staging system. *J Hepatol*, 2006; 44: 723-31.
16. Llovet JM, Burroughs A, Bruix J. Hepatocellular carcinoma. *Lancet*, 2003; 362: 1907-17.