

# DETERMINING THE EFFICACY OF TRANS-ARTERIAL CHEMO-EMBOLIZATION FOR HEPATOCELLULAR CARCINOMA ON FOLLOW-UP QUADRIPHASIC COMPUTED TOMOGRAPHY

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## ABSTRACT

**BACKGROUND:** Trans-arterial chemoembolization (TACE) is the first line treatment in limited unresectable multinodular lesions, with no vascular invasion, no extrahepatic spread and with well- preserved liver functions. Post TACE reduction in tumour burden can be assessed by modified RECIST (mRECIST) criteria on follow up Triphasic CT in which tumour enhancement is evaluated within 3 months after TACE. **OBJECTIVE:** The aim of this study was to evaluate the efficacy of trans-arterial chemo embolization therapy in cirrhotic patients with HCC on follow up quadriphasic computed tomography. **MATERIAL AND METHOD:** This study is a retrospective study that was conducted from March 2016 to January 2019 at Radiology unit Kuwait Teaching Hospital. 181 consecutive cirrhotic patients with HCC, treated with trans-arterial chemoembolization and evaluated with follow-up quadriphasic CT at a Radiology unit of Kuwait Teaching Hospital. All patients had least one image examination (quadriphasic contrast-enhanced CT) after treatment and were included into the study. **RESULTS:** Between March 2016 and January 2019, 181 consecutive patients diagnosed with hepatocellular carcinoma presented for TACE. Response assessment in the largest lesion on the basis of mRECIST criteria revealed complete response(CR) in 78, partial response(PR) in 96, stable disease(SD) in 1 and progressive disease(PD) in 6 patients. **CONCLUSION:** High quality screening, proper management and provision of therapy improves survival from HCC. Early and accurate assessment of tumour response to therapy is mandatory.

**Key words:** Hepatocellular carcinoma, TACE, quadriphasic CT, mRECIST criteria.

## Introduction

Hepatocellular carcinoma (HCC) is associated with chronic liver disease<sup>1</sup> with highest incidence in Asia and Sub-Saharan Africa. This is due to chronic hepatitis B infection is endemic in these regions.<sup>2</sup>

In Western countries the Barcelona Clinic Liver Cancer (BLCL) staging system is commonly used for management of HCC. Trans-arterial chemoembolization (TACE) is the first line treatment for intermediate stage HCC.<sup>3</sup> Candidates for TACE are asymptomatic patients with limited unresectable multinodular lesions, with no vascular invasion, no extrahepatic spread

and with well-preserved liver functions. According to treatment stage migration concept those patients in whom recommended treatments are not suitable or have failed, can also benefit from TACE.<sup>4</sup>

Two TACE techniques are used which are conventional TACE (cTACE) and TACE with drug-eluting beads (DEB- TACE). In conventional TACE cytotoxic drug is emulsified in oily radio-opaque Lipoidal agent. It is followed by intra-arterial embolic agent such as gelatin sponge, polyvinyl alcohol particles or microspheres injected intra-arterially.<sup>5</sup> Tumour microcirculation is

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embolised resulting in combined ischemia in tumour and cytotoxic effect.<sup>6</sup>

Post TACE reduction in tumour burden can be assessed by modified RECIST (mRECIST) criteria in which tumour enhancement is evaluated within 3 months after TACE.<sup>7-8</sup> On CT necrotic area of tumour retains iodized oil and enhanced foci represents viable tumour which appear hyper-attenuating or iso-attenuating on hepatic arterial phase and hypo-attenuating on unenhanced and porto venous phases.<sup>9</sup> The mRECIST defines four categories as: complete response (CR) (100% disappearance of enhancing tissue in target lesions), partial response (PR) (>30% decrease in the sum of diameters of viable target lesions-enhancement in arterial phase, taking as reference baseline sum of the diameters of enhancing tissue in target lesions); progressive disease (PD) (>20% increase in sum of diameters of viable target lesion taking as reference the baseline sum of diameter of viable target lesion recorded since the start of treatment and stable disease (SD) (neither PD nor PR).<sup>10</sup>

The aim of this study was to evaluate the efficacy of trans-arterial chemo embolization therapy in cirrhotic patients with HCC on follow up quadriphasic computed tomography.

## Materials and Methods

This study is a retrospective study that was conducted over period of 3 years i.e. from March 2016 to January 2019 at Radiology unit Kuwait Teaching Hospital. 181 consecutive cirrhotic patients with HCC, treated with trans-arterial chemoembolization therapy and evaluated with follow-up imaging at a Radiology unit of Kuwait Teaching Hospital. All patients had least one image examination (quadriphasic contrast-enhanced CT) after treatment and were included into the study. Approval was taken from the hospital's ethical committee before conducting the study. Diagnosis of HCC was based on radiological finding and alpha-fetoprotein level. Biopsy was performed in atypical HCC.

**Inclusion criteria** for transarterial chemoembolization of HCC was as follows: no extrahepatic tumor spread; HCC size less 50% of hepatic volume; absence of

thrombosis of main portal vein; transaminases levels < 300 U/L, serum bilirubin levels < 0.3 mg/L; serum creatinine < 0.18 mg/L; white blood cell count > 2.5 × 10<sup>3</sup>/μL; platelets count > 35 × 10<sup>3</sup>/μL; no ascites, CHILD-PUGH score A-B.

**Exclusion criteria** for transarterial chemoembolization of HCC are as follows: extrahepatic spread of tumor; ascites that cannot be controlled by diuretics; hepatic encephalopathy; gastrointestinal bleeding (active or recent i.e. less than 4 week); obstructive jaundice; severely debilitated patients; infection or sepsis; positive pregnancy; heart failure with ejection fraction less than 50%; severe pulmonary dysfunction; serum creatinine levels > 0.2 mg/L; serum bilirubin level > 0.3 mg/L; Hemoglobin level < 8 g/dL; WBC count < 2.5 × 10<sup>3</sup>/μL; platelet count < 35 × 10<sup>5</sup>/μL.

**TACE procedure:** After informed consent the Seldinger technique was followed for hepatic artery catheterization. Using digital subtraction angiography, the 6F catheter was inserted from the right femoral artery and guided to the hepatic artery or its branches for angiography. Tumor-feeding arteries were then super selectively engaged with microcatheter (Pro-great) based on understanding of the tumor blood supply, revealed via hepatic arteriography. Doxorubicin was injected in the lesion and feeding artery embolised with small size PVA particles.

Patient was admitted for 24 hours for post procedure care and was discharged in stable condition as per department protocol.

**Assessment of response:** Contrast-enhancement quadriphasic CT was performed 1 month after Trans catheter arterial chemoembolization, and the results were evaluated according to the modified Response Evaluation Criterion Solid Tumors (mRECIST) to assess tumor response.<sup>11</sup> Based on the results, patients were divided into the following 4 categories: complete response (CR), which was described as the disappearance of intratumoral arterial enhancement in all target lesions; partial response (PR), defined as a reduction of at least 30% in the sum of the

diameter of the (arterial phase) target lesions compared with the baseline diameter of the target lesions; stable disease (SD), including any case that did not meet the criteria for PR or progressive disease (PD); PD, defined as an increase of at least 20% in the sum of the diameter of residual (enhanced) target lesions compared with the minimum sum of the diameter of target lesions at the beginning of treatment. The rate of overall response (OR) was calculated as the rate of CR plus PR. Statistical analysis was performed using statistical software (SPSS version 20).

## Results

Between March 2016 and January 2019, 181 consecutive patients diagnosed with hepatocellular carcinoma presented for TACE. 176 patients were diagnosed as HCC by clinical findings, pre TACE quadruphasic CT scan and raised alpha feto protein levels. 6 atypical lesions were confirmed by biopsy to be HCC and then subjected to TACE. The demographic details of study population are (Tab. 1).

Response assessment in the largest lesion on the basis of mRECIST criteria revealed complete response (CR) in 78, partial response (PR) in 96, stable disease (SD) in 1 and progressive disease (PD) in 6 patients. 33 patients with partial response were subjected to second TACE, of which 19 showed CR, 13 showed PR and 1 had SD. 2 patients were subjected to third TACE which showed CR. Of the second largest lesion subjected to TACE 31 showed CR, 14 had PR, 4 had SD, and 2 PD. 1 patient had combined RFA and TACE for HCC management. 5 patients had percutaneous ethanol ablation (PEA) done for small lesions while 21 patients had PEA to the lesion with residual disease after TACE. New lesion were observed in 34 patients. On follow up CT 2 patients had pulmonary metastasis, 1 had lymph nodal metastasis and 1 had adrenal metastasis. Overall response revealed CR in 83 patients, PR in 71, SD in 1 and PD in 22 patients.

Demographic Details		No. of Patients
Age(years)	20-30	1
	30-40	2
	40-50	29
	50-60	77
	60-70	63
	>70	9
Gender	male	127
	female	54
Etiology	HBS	51
	HCV	127
	others	3
Alpha feto protein(ng/ml)	<25	12
	>25	156
Bilirubin (mg/dL)	<2	179
	2-3	2
Albumin (G/dl)	>3.5	178
	2.8-3.5	2
	<2.8	1
INR	<1.70	157
	1.71-2.20	23
	>2.20	1
Ascites	None	181
	Mild	0
	moderate	0
Hepatic encephalopathy	None	181
	Grade 1-2	0
	Grade 3-4	0
Child Pugh score	A	179
	B	2
BLCL stage	A	117
	B	49
	C	15
No. of lesions	1	117
	2	36
	3	17
	>3	11

Table 1: Demographic details study population

	Frequency	Percent	Valid Percent	Cumulative Percent
complete response	78	43.1	43.1	43.1
partial response	96	53.0	53.0	96.1
Valid Stable	1	.6	.6	96.7
progressive disease	6	3.3	3.3	100.0
Total	181	100.0	100.0	

target lesion response

	Frequency	Percent	Valid Percent	Cumulative Percent
CR	31	17.1	60.8	60.8
PR	14	7.7	27.5	88.2
Valid stable	4	2.2	7.8	96.1
progressive	2	1.1	3.9	100.0
Total	51	28.2	100.0	
Missing System	130	71.8		
Total	181	100.0		

second lesion response

	Frequency	Percent	Valid Percent	Cumulative Percent
CR	19	10.5	57.6	57.6
PR	13	7.2	39.4	97.0
Valid SDa	1	.6	3.0	100.0
Total	33	18.2	100.0	
Missing System	148	81.8		
Total	181	100.0		

response after second tace

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid CR	2	1.1	100.0	100.0
Missing System	179	98.9		
Total	181	100.0		

response after 3rd tace

	Frequency	Percent	Valid Percent	Cumulative Percent
CR	83	45.9	46.9	46.9
PR	71	39.2	40.1	87.0
Valid SD	1	.6	.6	87.6
PD	22	12.2	12.4	100.0
Total	177	97.8	100.0	
Missing System	4	2.2		
Total	181	100.0		

overall response

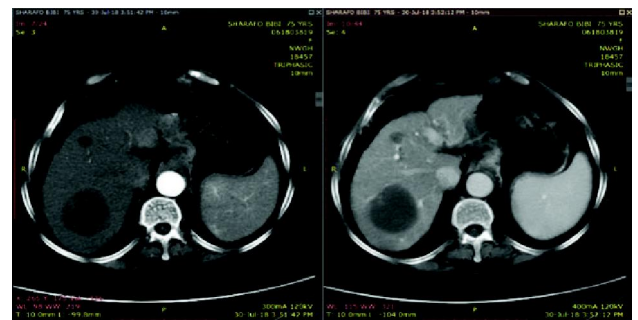
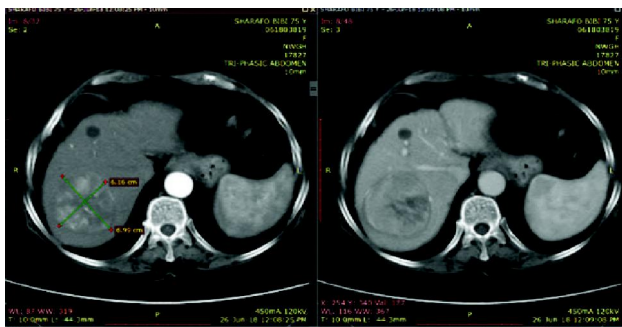
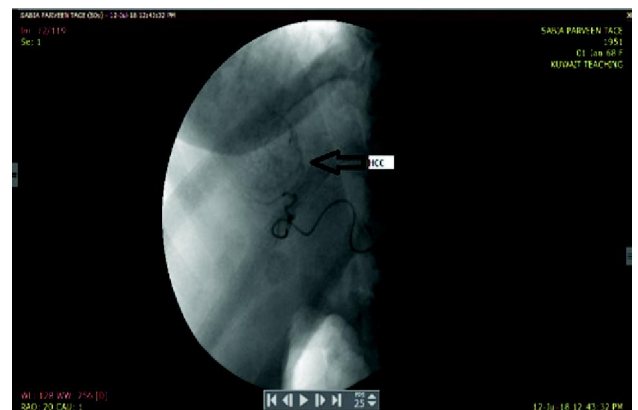
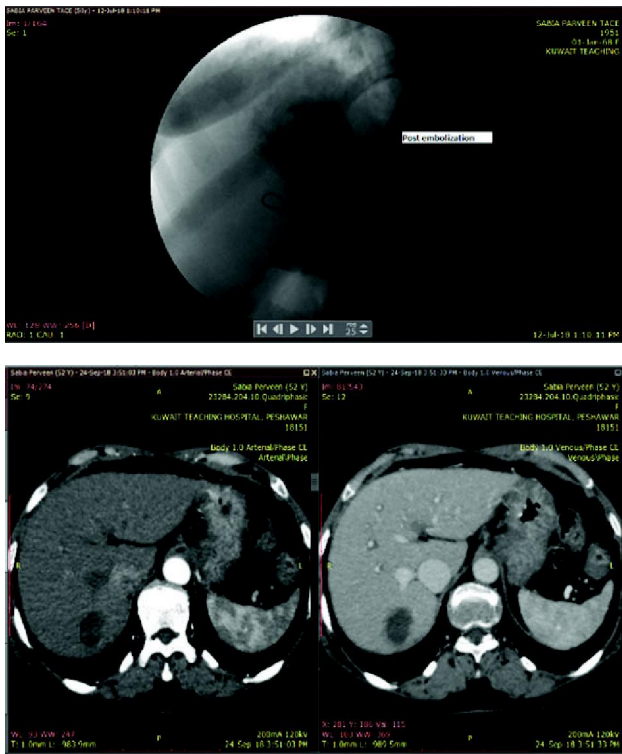


Figure 1: Complete response of HCC in right lobe of liver on follow up Quadraphasic CT after TACE





**Figure 2:** HCC in right lobe liver was subjected to TACE. Follow up Quadriphasic CT shows complete response.

## Discussion

In cirrhotic patients resection of HCC is associated with significant morbidity and mortality.<sup>12</sup> TACE is used for unresectable HCC that cannot be treated with percutaneous ablation.<sup>13</sup> Bridge study has revealed TACE to treat approximately 50% of patients from stage 0 to stage D HCC in daily practice.<sup>14</sup> It has been reported by Lien et al<sup>15</sup> that morbidity, mortality and survival after TACE for HCC eligible for Radiofrequency ablation (RFA) are comparable to response from RFA in literature. In our study 78 target lesions showed complete response on first TACE and 31 second lesion showed complete response. 12% of lesions were 2.1-3.0cm, 25% measured 3.1-4.0cm and 43.6% measured 4.1-5.0cm which showed complete response to first TACE. These findings are comparable to study by Miraglia et al.<sup>16</sup> Lesion that showed partial response to first TACE were large in size, majority >10 cm. 51 out of 96 patients that showed partial response to first TACE for the first lesion failed to continue treatment after first TACE. Overall 22 patients showed progressive

disease. 34 patients showed new lesions on follow up quadriphasic CT. 4 patients had developed metastasis on follow up CT. In some patients TACE was performed for palliative intent. 5 patients had large HCC with perforation.

No major complication was observed in all patients. This explains patient selection accuracy. Majority of patients selected had Child- Pugh score A or B. Super selective embolization using segmental and sub segmental treatment limits injury to surrounding non-tumoral liver parenchyma.<sup>17</sup>

Limitation to our study included failure of follow up of many patients after first TACE. Another limitation to our study was inability to determine number of TACE applied until complete response. This again was consequence of our first limitation.

## Conclusion

High quality screening, proper management and timely provision of therapy improves survival from HCC. Early and accurate assessment of tumour response to therapy is mandatory. The mRECIST criteria should be incorporated in our daily practice to assess response to TACE as it helps in evaluating not only tumour dimensions but also lesion viability. This helps in decision making for adequate therapy until complete response to treatment of lesion is achieved.

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