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Original Article

Impact of Trans-Arterial Chemo-Embolization on Tumor Response in Hepatocellular Carcinoma Patients: A Retrospective Study

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ABSTRACT

Trans-arterial Chemo-embolization is a treatment done for hepatic metastatic tumors caused by Chronic Liver Disease to reduce the tumor load on the liver. **Objective:** To assess the treatment response of TACE (Trans-Arterial Chemo-Embolization) in patients with HCC (Hepatocellular Carcinoma) based on the m-RECIST criteria. **Methods:** The retrospective study was conducted for a duration of one year; from December 2021 to December 2022. The Data were collected from Allied Hospital Faisalabad. TACE was done on a total of 80 patients with Hepatocellular Carcinoma ages between 31 to 80 years and the response was evaluated by m-RECIST criteria on a CT Triphasic scan. The chi-square test was used to find the association between gender and tumor response. **Results:** A total of 80 TACE-treated patients of Hepatocellular Carcinoma, (n=56) 70% were males and (n=24) 30% were females. Tumor response was evaluated as CR in (n=45) 56% of patients, (n=26) 32% showed PR, (n=6) 8% had SD, while (n=3) 4% had PD. Most of the patients showed significant tumor necrosis, 70-90% tumor necrosis was seen in 52% of the patients. An association between gender (male participants; n=56) and tumor response to TACE (71 responded out of which 56 were males) was found to be significant. **Conclusions:** TACE is a better treatment option for unresectable and larger HCC if proper care, management, and continuation of disease assessment are done after the treatment, as it results in tumor burden reduction and improved chances of qualifying for liver transplant in suitable cases.

INTRODUCTION

The most frequent primary cancer of the liver is Hepatocellular Carcinoma (HCC). The fifth most prevalent cancer in men and the seventh most frequent cancer in women in the world. Hepatitis B virus (HBV) and Hepatitis C virus (HCV) play a major part in the formation of HCC [1]. Patients who have been infected with the hepatitis C virus (HCV) are at risk of acquiring morbid consequences [2]. HCC is linked to Chronic Liver Disease (CLD) and is the leading cause of death in Asia and Sub-Saharan Africa [3]. If identified with relapsed illness, Liver carcinoma has a five-year survival probability of 5% due to the advanced stage at diagnosis. Multiple symptoms are typical in Hepatic Carcinoma patients including pain, tiredness, weight loss, and obstructive conditions such as ascites and jaundice. As existing therapy choices are ineffective, proactive symptom management is critical in maintaining physical function and quality of life [4]. TACE is a non-surgical and least invasive method of injection of chemo-embolic agents into the hepatic artery under local anesthesia through the Seldinger Technique for HCC growth reduction. For the treatment of scattered tumors, catheterization of the common hepatic artery may be

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necessary, however, for the smaller tumors precise methods of catheterization are done through the subdivisions of the hepatic artery. Its main objective is to reduce the tumor burden on the liver by causing tumour necrosis and reducing its size [5]. In the healthy liver, the ratio of blood flow to the hepatic artery and portal vein is 3:1. The cirrhotic liver nevertheless receives blood from both routes given that this ratio alters in hepatic cirrhosis. Elevation of the effects of embolic agents occurs when lipiodol (Ethiodized oil) is inoculated with anti-neoplastic preparations in the hepatic artery [6]. In 1981 World Health Organization presented criteria for the evaluation of the tumor response initially known as RECIST criteria. It included four types; Complete Response, Partial Response, Stable Disease, and Progressive Disease. The currently used version for HCC management is m-RECIST (modified Response Evaluation Criteria for Solid Tumors) and RECIST 1.1 presented by WHO [7]. It is frequently practised by researchers throughout the world, moreover, assessment of response to therapy is a crucial component in tumor treatment [8]. As a quantitative indicator of tumor load, RECIST 1.1 includes the total measurements from all targeted lesions and their single-dimensional diameters [9]. Complete Response: Total eradication of the targeted lesions along with non-targeted lesions and lymph nodules within short alignment <10 mm, and tumor marker level returning to normal [10]. Partial Response: Using the baseline total diameter as a benchmark, a minimum of 30 % reduction in the sum of the diameters of the targeted lesions, retaining a tumor marker level above the normal range or recurrence of one or more nontargeted lesions [10]. Stable Disease: Using the least total diameters as a base, neither adequate reduction of the tumor to qualify for PR nor enough growth to meet the criteria for PD [10]. Progressive Disease: The total diameters of the targeted lesions must rise by 20%, using the smallest sum of the study as a reference value, The advancement of remaining untreated lesions or one or more new lesions is also deliberated as a progressive disease [10]. Computed Tomography (CT) plays a vital role in the evaluation of disease response produced by treated (post-TACE) or untreated (pre-TACE) HCC. The widely used technique for pre- and post-TACE assessment is the CT Liver Triphasic Scan [11]. Hepatic Carcinoma is a prevailing and most common type of cancer in South Asia, it has high rates of mortality in Pakistan if left untreated. The study aims to investigate the association between treatment response and gender, as well as the age and etiology of HCC. The study aims to assess the treatment response of TACE (Trans-Arterial Chemo-Embolization) in patients with HCC (Hepatocellular Carcinoma) based on the m-RECIST criteria.

METHODS

A retrospective cohort study was conducted in Allied Hospital for a duration of a year; December 2021 to December 2022. 80 HCC patients (males and females) treated by TACE for follow-up CT triphasic were selected via a purposive sampling technique. However, patients with Portal Vein Thrombosis and Extrahepatic spread of Tumors were excluded from the study. The Seldinger technique was used to catheterize the hepatic artery after receiving informed consent. The 6F catheter was inserted from the right femoral artery and directed to the hepatic artery or one of its branches for angiography using digital subtraction angiography. Based on the knowledge of the tumor blood supply, as shown by hepatic arteriography, tumor-feeding arteries were specifically engaged with a microcatheter (Progreat). Then Doxorubicin was injected into the tumor-feeding arteries along with PVA particles. A 64-slice helical CT machine was used to evaluate the follow-up patients. The data were collected on a pre-designed Performa having the following CT findings; Gender, Age, Etiology of HCC, Percentage Tumor Necrosis, BCLC staging system, and Disease Response were taken according to m-RECIST criteria as CR, PR, SD, and PD. Data were analyzed by SPSS version 22. The chi-square test was used to find the association between gender and tumor response. Privacy and confidentiality of data were maintained. Identifying information was removed or anonymized to protect privacy. Data were securely stored and accessed only by authorized personnel. An MOU was established with institutions providing data access. Clear data retention and destruction policies were established to ensure that data were not kept longer than necessary and was disposed of securely. Ethical oversight through an ethics committee of Faisal Hospital (FIHS), Faisalabad, Pakistan approved for ethical standards.

RESULTS

Eighty consecutive patients of HCC having liver cirrhosis were taken for the study and were treated by TACE. The targeted lesions were evaluated based on the Child-Pugh scoring system and the response of the treatment was evaluated by the m-RECIST criteria through the follow-up CT-Triphasic scan on a multi-slice CT scanner 3 to 4 weeks after the chemo embolic agents were injected into the hepatic supply of the tumor. Figure 1 shows the gender distribution of HCC patients treated with TACE out of which 56 (70%) were males and 24 (30%) were females. The figure also shows the prevalence of Hepatic carcinoma is higher in men as compared to women.

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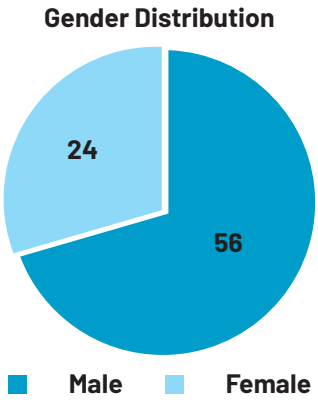

Figure 1: Gender distribution of HCC patients treated with TACE

Patients were taken according to their age ranging between 31 to 80 years. Table 1 shows age distribution patterns in the sample. According to the analysis, the most common age group having HCC was between 51 to 60 years with a percentage of (50%), the second one shows between 61-70 years (18%), third was between 71-80 years (14%), fourth was between 41-50 years (16%) and the fifth one was among 31-40 years with (2%).

Table 1: Age distribution patterns in 80 patients

Age Group	Frequency (%)
31-40 years	2 (2)
41-50 years	13 (16)
51-60 years	40 (50)
61-70 years	14 (18)
71-80 years	11 (14)

The etiology of HCC can be seen in Figure 2 as HCV-related HCC was (n=70) 88%, HBV-related HCC was (n=7) 8%, and other factors related were (n=3) 4%.

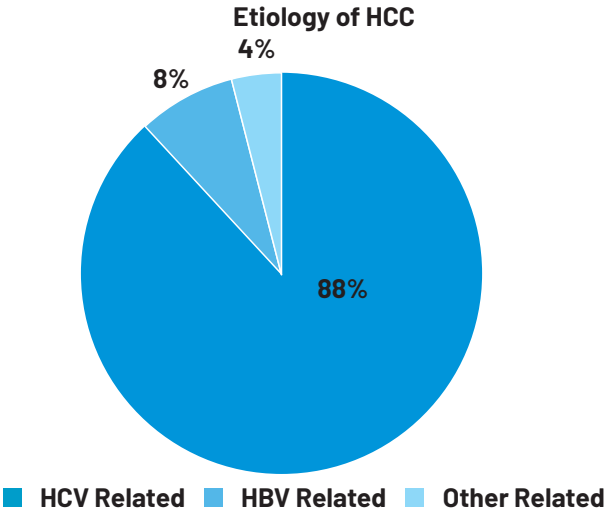

Figure 2: Etiology of Hepatocellular Carcinoma in 80 patients

Table 2 shows the percentage of tumor necrosis of the targeted lesions that underwent embolization. Out of 80 treated HCCs, 66% (n=53) showed 80-90% tumor necrosis, 14% (n=11) showed 70-80% necrosis and 20% (n=16) of the treated lesions showed 10-20% tumor necrosis. It also showed the BCLC (Barcelona Clinic Liver Cancer) staging system. Stage A had 14% (n=11) of people, stage B had 66% (n=53), and stage C had 20% (n=16) of the total sample size.

Table 2: Tumor necrosis of the targeted lesions that underwent embolization and BCLC staging

Tumor Necrosis	
Necrosis	**Frequency (%)**
80-90%	53 (66)
70-80%	11 (14)
10-20%	16 (20)
BCLC Staging	
BCLC Stage	**Frequency (%)**
Stage A	11 (14)
Stage B	53 (66)
Stage C	16 (20)

Table 3 shows the disease response as CR (Complete Response), PR (Partial Response), SD (Stable Disease), and PD (Progressive Disease) evaluated on a Follow-up CT scan. Out of those eighty patients that received one or more sessions of TACE, (n=45) 56% of patients showed CR, (n=26) 32% showed PR, (n=6) 8% had SD, while (n=3) 4% of the candidates presented with PD. However, for the statistical results, CR and PR were considered as Respondents (total 88%, n=71), and PD and SD were taken as non-respondents (total 12%, n=9). Of the total 71 Respondents, 56 were males and 15 were females, and of the total 9 non-respondents, all were females.

Table 3: Disease Response Based on m-RECIST Criteria

Response	Frequency (%)
CR	45 (56)
PR	26 (32)
SD	6 (8)
PD	3 (4)
Respondents vs non-respondents	
Respondents (CR+PR)	71 (88)
Non-respondents (SD+PD)	9 (12)

The chi-square test showed that there was an association between gender (male participants; n=56) and tumor response to TACE (71 responded out of which 56 were males), and the association was found to be statistically significant with a p-value of 0.005 which is less than 0.05.

DISCUSSION

It is clear from worldwide research that hepatic carcinoma was widely spreading across Asian and Sub-Saharan countries, mainly becoming the most fatal disease in these regions. In the given study, the TACE treatment was done for patients with unresectable tumors that can neither be treated by Radiofrequency Ablation nor conventional therapy. A study by Kwan *et al.*, in 2012 showed that 81% were males and 19% were females in the study [12]. The

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gender distribution was well correlated with the gender distribution of the given study, with the majority of males (70%). A study by Kwan *et al.*, in 2012 showed that the most common cause of HCC was HCV-related (61%) as compared to HBV-related (23%) [12]. According to the study by Dioguardi *et al.*, in 2019, the most common cause of liver carcinoma was HCV (n=23), HBV (n=10), alcohol-associated (n=4), and others (n=13) [13]. The results of both of the studies were well marginalized with the given study as the most common cause of HCC was HCV-related (n=70). A study by Yang *et al.*, in 2008 probed tumor necrosis of 37.5% in 78 HCC patients by TACE [14]. A study conducted by Golfieri, *et al.*, in 2011 revealed that total necrosis was observed in 64.7% of 122 after one TACE session, and complete tumour-necrosis was shown by 53.8% in super selective TACE [15]. The results of both studies were well correlated with the given study as 80 to 90% necrosis was observed in 66% (n=53) of the patients. A study conducted by Prajapati *et al.*, in 2014 made two groups of patients. The BCLC staging in both groups revealed there were 21 cases of Stage A, 62 cases of Stage B, and 11 cases of Stage C [16]. The results of the study well correlated with the given study; stage A has 11 cases, stage B has 53, and stage C has 16 cases of the total sample size. According to the study by Dioguardi *et al.*, in 2019, out of the total patients that were treated with chemo-embolization, 56% showed CR, 8% showed PR, 33% showed SD, and 2% showed PD [13]. A study by Miraglia *et al.*, in 2007 revealed that CR to TACE treatment was seen in 94 patients (58%) out of 162 patients who underwent TACE [17]. A study by Sato *et al.*, in 2013 revealed that 185 showed CR, 74 showed PR, 65 showed SD, and only 1 showed SD [18]. The results of the current study were well correlated with all of the studies showing almost similar responses; 56% (n=45) of patients showed CR, 32% (n=26) showed PR, 8% (n=6) had SD, and 4% (n=3) of the candidates presented with PD [19, 20].

CONCLUSIONS

According to the current study, TACE is an effective treatment for HCC patients, particularly in male individuals, as indicated by a significant association between gender and tumor response. The response was assessed using the m-RECIST criteria based on follow-up CT-Triphasic scans; 56% showed CR, 32% showed PR, 8% had SD, and 4% had PD. HCV-related HCC was the most prevalent etiological factor, accounting for 88% of cases. The finding underscores the potential for TACE as a valuable treatment strategy for unresectable HCC, as it resulted in tumor burden reduction and improved the chances of qualifying for liver transplant in suitable cases.

Authors Contribution

Conceptualization: AMK
Methodology: AK
Formal analysis: ZG
Writing-review and editing: AMK, AK, ZG

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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