

OUTCOMES OF TACE IN PATIENTS WITH HEPATOCELLULAR CARCINOMA LARGER THAN 10 CM

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(Received, 24th October 2024, Revised 25th December 2024, Published 30th December 2024)

Abstract: Hepatocellular carcinoma (HCC) is a prevalent and aggressive liver malignancy, often presenting at advanced stages where surgical resection is not feasible. Transcatheter arterial chemoembolization (TACE) is a minimally invasive treatment modality that has shown promise in managing unresectable HCC, yet its effectiveness for large tumors (>10 cm) remains underexplored. **Objective:** To evaluate the outcomes of transcatheter arterial chemoembolization in patients with large unresectable hepatocellular carcinoma. **Methods:** A retrospective, case-control study was conducted in the Department of Interventional Radiology, PKLI, Lahore from September 2022 to September 2024. A total of 45 patients with hepatocellular carcinoma larger than 10 cm, eligible for TACE but refused aggressive treatment were selected as a control group of the study. A total of 50 age, tumor characteristics, and liver function-matched HCC patients who had undergone TACE were selected as the case group of the study. In the 2-3 months follow-up after TACE, tumor response by recorded by ultrasound or AFP assay. **Results:** The survival rate in cases (10 months, 95% CI: 5.1-14.3 months) was significantly higher than the control group (2 months, 95% CI: 1.05-3.22 months) ($p < 0.0001$). The 1-year survival was 42% and 8% in cases and controls, respectively. The 2-year survival was 23% and 8%, respectively. Univariable analysis shows INR 1.2 or less, total bilirubin less than 1.6 mg/dL, liver reserve, and TACE were significantly associated with survival. Multi-variable analysis showed that INR of 1.2 or less and TACE remained significant for longer survival. **Conclusion:** TACE is a successful and safe treatment option for unresectable HCC tumors larger than 10 cm.

Keywords: Hepatocellular Carcinoma, Hcc, Tace, Transcatheter Arterial Chemoembolization

Introduction

Hepatocellular carcinoma is a common form of cancer in Asia which accounts for 80% of its total incidence (1). Since routine screening is not common in developing countries like Pakistan, patients are often diagnosed with HCCs >10 cm which can be treated with surgical resection. However, resection is very complex in large tumors due to intrahepatic dissemination, poor liver reserve, and lympho-vascular invasion (2). Transcatheter arterial chemoembolization (TACE) is a minimally invasive, first-line treatment for the resection of large tumors i.e. larger than 10 cm (3). However, it can cause excessive liver damage so risk management for liver decompensation and the effectiveness of tumor treatment must be analyzed before choosing TACE (4). Large tumor size is independently associated with poor outcomes in HCC patients which increases the risk of complications after TACE. A recent study reported that TACE performed in patients with large HCC tumors had yielded a high mortality rate.5 However, the results on this subject are scarce. This study was conducted to evaluate the outcomes of transcatheter arterial chemoembolization in patients with large unresectable hepatocellular carcinoma.

Methodology

A retrospective, case-control study was conducted in the Department of Interventional Radiology, PKLI, Lahore from September 2022 to September 2024. A total of 45 patients with hepatocellular carcinoma larger than 10 cm, eligible for TACE but refused aggressive treatment were

selected as a control group of the study. A total of 50 age, tumor characteristics, and liver function-matched HCC patients who had undergone TACE were selected as the case group of the study. All patients provided their informed consent to become a part of the study. The ethical committee of the hospital approved the study. HCC was diagnosed by biopsy or AFP assay along with radiological examination by CT, ultrasound, or coeliac angiography. The performance of case patients was evaluated by a performance status test. TACE was performed by selective catheterization of hepatic arteries and super-selection of arteries connected to the tumor. A mixture of IV Adriamycin (20-30 mg) and lipiodol (5-10 ml) was administered. 2-3 mm gelform strips were used for embolization of feeding arteries. In the 2-3 months follow-up after TACE, tumor response by recorded by ultrasound or AFP assay. In case of recurrence, TACE was repeated if patients were eligible. Patients were advised to visit every 3-6 months for follow-up. All data was analyzed by SPSS version 24. Cases and control patients were compared by student's t-test and Wilcoxon rank test where necessary. Kaplan Meier curve was made for survival analysis which was compared by log rank test. Multivariable analysis was performed by including statistically significant variables from univariate analysis. A p-value less than 0.05 achieved statistical significance.

Results

Both groups were comparable in terms of demographics and baseline laboratory parameters as shown in Table I. 31

(62%) in the cases group and 33 (73.4%) in the control group were HBV positive. 3 (6%) in the cases group and 6 (13.4%) in the control group had a PST of 3 and the remaining patients mostly had 2-3 PST (p=0.398).

The patients in the cases group underwent 102 courses of TACE with an average of 2 courses. Four patients (8%) could not survive the procedure due to complications among which 2 patients died after two months due to liver decompensation and 2 patients died 1 month after the procedure due to acute renal failure. The survival rate in cases (10 months, 95% CI: 5.1-14.3 months) was

significantly higher than the control group (2 months, 95% CI: 1.05-3.22 months) (p<0.0001). The 1-year survival was 42% and 8% in cases and controls, respectively. The 2-year survival was 23% and 8%, respectively.

Univariable analysis shows INR 1.2 or less, total bilirubin less than 1.6 mg/dL, liver reserve, and TACE were significantly associated with survival (Table II). Tumor characteristics, CLIP score, and vascular invasion were not related to survival. Multi-variable analysis showed that INR of 1.2 or less and TACE remained significant for longer survival (Table III).

Table 1: Patients' baseline features

Variables	Cases group (n=50)	Control group (n=45)	P value
Mean age	60.2 ± 13.3	58.5 ± 14	0.610
Gender			0.622
Male	42 (84%)	44 (97.8%)	
Female	8 (16%)	1 (2.2%)	
Multinodular tumors	19 (38%)	20 (44.5%)	1
Mean tumor size	14.1 ± 4.3	13.6 ± 4.5	0.594
Median alpha-fetoprotein	578 (4-320,019)	570 (4-260,000)	0.9
Albumin	4.0 ± 0.5	4.0 ± 0.7	0.823
Creatinine	1.0 ± 0.33	0.98 ± 0.34	0.911
Total bilirubin	1.27 ± 0.74	1.42 ± 0.60	0.232
ALT	121 ± 149.2	132 ± 127.6	0.480
INR	1.10 ± 0.2	1.21 ± 0.3	0.199
Vascular invasion	16 (32%)	25 (55.6%)	0.172
Child-Pugh			
A	38 (76%)	35 (77.8%)	1
B	12 (24%)	10 (12.2%)	
Performance status test			
0	3 (6%)	2 (4.5%)	0.929
1	39 (78%)	36 (80%)	
2	5 (10%)	6 (13.4%)	
3	3 (6%)	6 (13.4%)	
Number of CLIP score			
2	21 (42%)	16 (35.6%)	0.398
3	16 (32%)	11 (24.5%)	
4	11 (22%)	12 (26.8%)	
5	2 (4%)	6 (13.4%)	
Hepatitis B	31 (62%)	33 (73.4%)	0.634
Anti-HCV	8 (16%)	8 (17.8%)	1

Table 2: Univariate analysis

Variables	95% CI	P value
Age		
60 years or younger	3.38 (0-7.09)	0.49
Older than 60 years	4.42 (1.47-7.25)	
Gender		
Male	3.97 (2.5-5.86)	0.70
Female	3.24 (0-17.81)	
Albumin		
3.5 g/dl or less	3.58 (2.17-4.63)	0.52
Higher than 3.5 g/dl	5.06 (0.73-9.62)	
ALT		
100 U/L or less	4.05 (2.94-5.11)	0.33
Higher than 100 U/L	6.54 (0-13.15)	
INR		
1.2 or less	5.12 (2.86-7.28)	0.0031
Higher than 1.2	1.85 (1.23-2.46)	
Creatinine		

[Citation Ali, A., Riaz, K. (2024). Outcomes of TACE in patients with hepatocellular carcinoma larger than 10 cm. *Biol. Clin. Sci. Res. J.*, 2024: 1435. doi: <https://doi.org/10.54112/bcsrj.v2024i1.14351>]

1.2 mg/dl or less	4.28 (2.14-6.63)	0.64
Higher than 1.2 mg/dl	3.04 (0-6.56)	
Child-Pugh		
A	5.13 (2.87-7.24)	0.38
B	3.58 (3.34-3.49)	
Single tumor	5.67 (2.41-9.06)	0.30
Multi-nodular tumors	3.38 (2.68-4.25)	
Tumor size		
15 cm or less	5.14 (1.98-8.07)	0.39
Larger than 15 cm	2.65 (1.26-3.73)	
Vascular invasion	2.48 (0.97-4.23)	0.53
AFP		
400 ng/mg or less	5.09 (2.46-7.67)	0.55
Higher than 400 ng/mg	3.55 (2.13-4.98)	
CLIP score		
2-3	5.08 (2.34-7.91)	0.36
4-5	3.36 (2.23-4.75)	
TACE treatment	1.9 (0.9-3.26)	<0.0001

Table 3: Multi-variable analysis

Variables	Regression coefficient	OR	P value
TACE	0.309	3.229 (1.748-6.010)	<0.001
INR 1.2 or less	0.463	2.765 (1.133-6.798)	0.032

Discussion

This study was conducted to evaluate the outcomes of TACE in patients with large HCC tumors. The results showed a significant difference between survival rates of TACE patients (10 months) as compared to 2 months in controls. Only 4 patients (8%) died due to TACE complications. Similar results were reported by studies conducted on patients with large tumors treated with TACE (6, 7, 8).

Previous studies reported that tumor size, staging and number, albumin levels, and vascular invasion in HCC patients were related to survival (9, 10). However, our univariable and multi-variable analysis showed no significant relationship between the aforementioned factors and survival. Instead, liver reserve including INR total bilirubin level, and TACE were significantly related to good prognosis and survival.

Tumor characteristics and CLIP score vascular invasion were not significant factors for survival. However, a previous study found CLIP score was an excellent indicator of patient survival (11). In our study, the sample size was limited to evaluate tumor stage as a predictive factor. Our results prove the effectiveness of TACE in treating large unresectable HCC tumors as it was an independent predictor of long-term survival in univariable and multivariable analyses. A recent meta-analysis confirmed our findings and reported that TACE is a successful alternative treatment to surgical resection for HCC patients (12).

Our study has some limitations. The sample size was limited due to which several factors did not achieve statistical significance.

Conclusion

TACE is a successful and safe treatment option for unresectable HCC tumors larger than 10 cm.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department Concerned. (IRBEC-TCHMM-0922323/23)

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared absence of conflict of interest.

Author Contribution

ASIM ALI (Fellow Interventional Radiology)

Coordination of collaborative efforts.

Study Design, Review of Literature.

KHOALA RIAZ (FELLOW Interventional Radiology)

Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript.

Conception of Study, Final approval of manuscript.

Manuscript revisions, critical input.

Coordination of collaborative efforts.

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