



## INCIDENCE AND PREDICTIVE ACCURACY OF POST EMBOLIZATION SYNDROME FOR SURVIVAL IN HEPATOCELLULAR CARCINOMA PATIENTS AFTER TRANSARTERIAL CHEMOEMBOLIZATION

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### Abstract

**Objective:** To assess the prevalence and predictive accuracy of post embolization syndrome on long-term survival outcomes in HCC patients after undergoing TACE.

**Methodology:** A total of 150 patients with hepatocellular carcinoma confirmed by biopsy or imaging who underwent TACE were retrospectively analysed Radiology Department of PKLI, Lahore from January 2024 to January 2025. Post embolization syndrome was diagnosed as fever that maybe accompanied by right upper quadrant abdominal pain within 2 weeks of the procedure. Patients were followed up 1, 3 and 4 months after TACE and imaging with MRI or CT was performed and laboratory parameters were recorded.

**Results:** ACE was successful the first time in 147 (98%) patients and 3 (2%) required additional procedure for chemoembolization. 51 (34%) had post embolization syndrome. The incidence of post embolization syndrome was significantly related to mortality in the Cox regression analysis (hazard ratio: 1.9, 95 CI: 1.5-3.6, p=0.009). Multi-vascular invasion (HR: 5.0, 95% CI: 2.6-8.8, p<0.001), Child Pugh score B (HR: 2.3, 95% CI: 0.8-3.6, p=0.037) and Child Pugh score C (HR: 6.8, 95% CI: 2.9-15.4, p <0.001) were also significant predictors of mortality. Multivariable logistic analysis showed that bilobar tumor (odds ratio: 2.11, 95% CI: 0.98-4.20, p=0.052) and beads TACE (OR: 0.38, 95% CI: 0.22-1.02, p=0.050) were independently associated with post embolization syndrome.

**Conclusion:** Post embolization syndrome is significantly predictor of poor prognosis and mortality in HCC patients who underwent TACE.

**Keywords:** Hepatocellular carcinoma, Mortality, Post embolization syndrome

### Introduction

Hepatocellular carcinoma is a common cancer type affecting more than 0.7 million people each year and is a leading cause of death.<sup>1</sup>The overall long-term prognosis and survival rates of HCC are poor

with remission in only 12% patients.<sup>2</sup>A limited number of HCC patients are candidates for treatments for liver transplant and resection. Liver directed therapies including transarterial chemoembolization are also used in patients awaiting transplant.

TACE is used in combination with other treatments and has a reported overall survival of 26-47% after 3 years of treatment which is significantly higher than in untreated patients.<sup>3</sup> Several meta-analysis, guidelines and American Association for Study of Liver Diseases recommend TACE as primary treatment for unresectable HCC.<sup>4, 5</sup>Advanced liver disease and vascular invasion are the major risk factors impacting the prognosis and outcomes of TACE. Post embolization syndrome is one of the major complications after TACE, but there is little data to analyze its effect on long-term outcome.<sup>6</sup>

The objective of this study was to assess the prevalence and predictive accuracy of post embolization syndrome on long-term survival outcomes in HCC patients after undergoing TACE.

## Methodology

A retrospective study was conducted in the Radiology Department of PKLI, Lahore from January 2024 to January 2025. A total of 150 patients with hepatocellular carcinoma confirmed by biopsy or imaging who underwent TACE were included in the study. Patients with metastatic disease and those who underwent chemotherapy, liver ablation, liver resection or transplantation were excluded. All patients agreed to be apart of the study by written consent. The ethical approval board of the hospital approved the study.

Patients' information was collected including demographics, clinical features, hepatic function tests, tumor characteristics and staging. Treatment information including selective or non-selective embolization technique for TACE, chemotherapy agents, conventional TACE or drug eluting TACE and number of procedures was recorded. Dindo Clavien classification was used to note incidence and severity of post-TACE complications. Post embolization syndrome was diagnosed as fever that maybe accompanied by right upper quadrant abdominal pain within 2 weeks of the procedure. Patients were followed up 1, 3 and 4 months after TACE and imaging with MRI or CT was performed and laboratory parameters were recorded.

All data was analyzed by STATA version 12. Chi-squared test was performed to compare categorical data and t-test and Mann Whitney U test was performed to compare continuous data. Overall survival was the primary endpoint measured from performance of TACE to death by Kaplan Meier method and compared by log-rank test. Relationship between post embolization syndrome and overall survival was evaluated by Cox regression analysis while adjusting for confounding factors. A probability value of less than 0.05 was considered significant.

## Results

A total of 150 patients with a mean age of 63 years were selected for analysis. Almost all the patients (96%) were men. Majority of the patients (82%) had a high comorbidity index with 144 (96%) cirrhotic patients and 105 (70%) had portal hypertension (Table I).105 (70%) subjects had multiple tumors and 15 patients (10%) had macroscopic vascular invasion. 45 patients (30%) had intermediate and 15 (10%) had advanced tumors (Table II).

TACE was successful the first time in 147 (98%) patients and 3 (2%) required additional procedure for chemoembolization.135 (90%) underwent TACE through selective technique and only 36 (24%) underwent traditional TACE. 60 (40%) had more than one TACE with median number of procedures 1-5. Half of the patients experienced complications within 1 month follow up after TACE while 9 (6%) severe complications including death. 51 (34%) had post embolization syndrome (Table III).

The average follow-up duration was 10 months with an overall survival rate of 70% at the end of the study. Univariate analysis revealed that patients without post embolization syndrome had better overall survival at 1 year (78%) and 15 months (54%) follow-up ( $p=0.025$ ). The incidence of post embolization syndrome was significantly related to mortality in the Cox regression analysis (hazard ratio: 1.9, 95 CI: 1.5-3.6,  $p=0.009$ ) (Table IV). Multi-vascular invasion (HR: 5.0, 95% CI: 2.6-8.8,

p<0.001), Child Pugh score B (HR: 2.3, 95% CI: 0.8-3.6, p=0.037) and Child Pugh score C (HR: 6.8, 95% CI: 2.9-15.4, p <0.001) were also significant predictors of mortality. Additional TACE procedures had a protective effect (HR: 0.7, 95% CI: 0.5-1.1, p=0.006). Multivariable logistic analysis showed that bilobar tumor (odds ratio: 2.11, 95% CI: 0.98-4.20, p=0.052) and beads TACE (OR: 0.38, 95% CI: 0.22-1.02, p=0.050) were independently associated with post embolization syndrome.

**Table I: Patients' demographic information**

Variables	N (%)
Mean age	63 ± 7.1
Younger than 65	102 (68%)
Older than 65	48 (32%)
Sex	
Male	144 (96%)
Female	6 (4%)
Mean BMI	28 ± 4.7
Less than 30	96 (64%)
30 or higher	54 (36%)
ECOG	
0-1	111 (74%)
2-4	39 (26%)
Charlson's comorbidity index	
0-2	27 (18%)
3 or higher	123 (82%)
Cirrhosis	144 (96%)
Portal hypertension	105 (70%)
Child Pugh score	
A	84 (56%)
B	54 (36%)
C	15 (10%)
Median MELD score	9 (7-24)

**Table II: Tumor characteristics**

Features	N (%)
Tumor type	
Primary	141 (94%)
Recurrent	9 (6%)
Number of tumors	
Single	45 (30%)
Multiple	105 (70%)
Location	
Unilobar	84 (56%)
Bilobar	66 (44%)
BCLC staging	
Early	60 (40%)
Intermediate	45 (30%)
Advanced	15 (10%)
Terminal	30 (20%)

**Table III: Intra and post TACE data**

Variables	N (%)
Successful procedure	147 (98%)
Technique	
Selective	135 (90%)
Non-selective	15 (10%)
TACE type	
Traditional	36 (24%)
Beads	114 (76%)
Chemotherapy type	
Single agent	114 (76%)
Multiple agent	36 (24%)
Complications	
GI bleeding	6 (4%)
Severe hyperbilirubinemia	3 (2%)
Respiratory failure	3 (2%)
Death	1 (0.7%)
Post embolization syndrome	51 (34%)
Nausea or vomiting	15 (10%)
Mild hyperbilirubinemia	9 (6%)
Ascites	6 (4%)
Hepatic encephalopathy	6 (4%)
Other	18 (12%)

**Table IV: Predictors of Survival by Multivariate Cox Regression Model**

	Hazard ratio	95% CI	P
ECOG score 2-4	3.2	0.9-9.0	0.139
Multiple tumors	1.1	0.8-1.7	0.581
Macrovascular invasion	5.0	2.6-8.8	<0.001
Child Pugh score B	2.3	0.8-3.6	0.037
Child Pugh score C	6.8	2.9-15.4	<0.001
Post embolization syndrome	1.9	1.5-3.6	0.009
Multiple TACE	0.7	0.5-1.1	0.006

## Discussion

This study was conducted to evaluate the incidence and predictive accuracy of post embolization syndrome for survival in HCC patients who underwent TACE. The results showed that the incidence of post embolization syndrome was significantly related to mortality in the Cox regression analysis (hazard ratio: 1.9, 95 CI: 1.5-3.6, p=0.009). Additionally, bilobar disease and conventional TACE were independently associated with post embolization syndrome. These findings are similar to previous studies.<sup>7, 8, 9</sup>

The incidence of post embolization syndrome was 34% in our study as compared to 15-90% as reported in literature.<sup>10, 11</sup> It is also indicated that it decreases the likelihood of survival with twice more risk of mortality than patients without PES. A similar study was conducted by Bai et al which reported that PES and long-term survival were not related after TACE.<sup>12</sup> A South Korean study tested the impact of incidence of PES in patients undergoing TACE with lipiodol infusion.<sup>13</sup> The findings showed a high prevalence of PES but this is in contrast to present study as majority of patients were treated with beads TACE.

A higher Child's Pugh score (B, C) and incidence of multi vascular invasion were independent predictive factors of poor prognosis in the multivariate analysis in current study. Prior research has

shown various risk factors including neutrophil to lymphocyte ratio which is an inflammatory marker as in our study.<sup>14, 15</sup>

Our study has some limitations. There maybe a selection bias that would have contributed to the findings due to retrospective study design. Secondly, majority of our population was male, hence the findings are generally applicable to all public especially females.

## Conclusion

Post embolization syndrome is significantly predictor of poor prognosis and mortality in HCC patients who underwent TACE.

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