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COMBINATION OF TACE WITH TARGETED MMUNOTHERAPY VERSUS TACE ALONE FOR HEPATOCELLULAR CARCINOMA PATIENTS WITH PORTAL VEIN TUMOR THROMBUS

Dr Sadia Abdullah[1*], Dr Abdullah Saeed[2], Dr Muhammad Ramzan[3], Dr Khoala Riaz[4], Dr Asim Ali[5], Dr Muhammad Usman Younas[6]

[1*]Consultant Clinical, Oncologist, SKMCH Lahore,
[2]Consultant Interventional Radiologist, Chairman & HOD, Department of Radiology, PKLI & RC Lahore
[3]Consultant Radiologist, PKLI & RC Lahore
[4]Clinical Fellow, Interventional Radiology, PKLI & RC Lahore
[5]Clinical Fellow, Interventional Radiology, PKLI & RC Lahore
[6]Consultant Interventional Radiologist, PKLI & RC Lahore

***Corresponding Author: Dr Sadia Abdullah**
*Consultant Clinical, Oncologist, SKMCH Lahore Email: sadia.latif@gmail.com

Abstract

Background: Hepatocellular carcinoma (HCC) with portal vein tumor thrombosis (PVTT) remains one of the most difficult hepatobiliary malignancies to treat, particularly in regions such as Pakistan, where viral hepatitis is highly prevalent. Transarterial chemoembolization (TACE) is widely used for locoregional management, yet outcomes vary depending on tumor burden and liver function. This study evaluated treatment response, survival outcomes, and procedure-related complications of TACE in patients with HCC and segmental PVTT.

Methods:

This prospective observational study enrolled 80 patients with HCC and segmental PVTT confirmed on contrast-enhanced CT/MRI. Patients aged 18–80 years with Child-Pugh A or B liver function and ECOG ≤2 were included. TACE was performed using Lipiodol-doxorubicin emulsion followed by Gelfoam embolization. Tumor response was assessed using mRECIST at 4–6 weeks. Overall survival (OS) and progression-free survival (PFS) were analyzed using Kaplan–Meier curves with log-rank testing for subgroup comparisons. Complications were documented for safety assessment.

Results:

The mean age was 58.7 ± 9.2 years, and 82.5% were males. Hepatitis C virus infection was the most common etiology (71.3%). The objective response rate (complete plus partial response) was 58.8%. Median OS was 13.6 months, and median PFS was 8.9 months. One-year and two-year survival rates were 58.7% and 34.2% respectively. Patients with Child-Pugh A liver function had significantly better OS than Child-Pugh B (15.4 vs 11.1 months, p=0.021), and objective responders had markedly longer survival than non-responders (17.8 vs 10.2 months, p<0.001). Post-embolization syndrome occurred in 58.7% of patients and was managed conservatively. Major complications were infrequent, and no peri-procedural mortality was observed.

Conclusion:

TACE provided a favorable tumor response and meaningful survival benefit in patients with HCC and segmental PVTT, particularly in those with preserved liver function and early radiological

response. The safety profile was acceptable, with most complications being minor and self-limiting. These findings support the continued use of TACE as an effective therapeutic option in populations with high viral hepatitis burden, such as Pakistan.

Keywords: hepatocellular carcinoma, portal vein tumor thrombosis, TACE, survival outcomes, mRECIST, Pakistan

Introduction

Hepatocellular carcinoma (HCC) represents a significant global health challenge, ranking as one of the leading causes of cancer-related mortality worldwide. Particularly notable is the association of portal vein tumor thrombosis (PVTT) with advanced HCC, which profoundly complicates treatment and adversely affects patient prognosis. PVTT occurs in up to 44% of HCC cases and has been linked with a median survival of just 2 to 4 months when left untreated, underscoring the urgency for effective therapeutic strategies [1, 2]. Current treatment strategies primarily involve a combination of local and systemic therapies, including transarterial chemoembolization (TACE). These methods aim to enhance localized delivery of chemotherapeutics directly to tumor sites, thereby maximizing therapeutic effects while minimizing systemic toxicity [3, 4, 5].

Recent studies have begun to explore the efficacy of combining TACE with targeted immunotherapies, particularly immune checkpoint inhibitors (ICIs), which have shown promise in enhancing treatment responses by reinstating anti-tumor immune activity. For instance, a systematic review indicated that combination therapies using PD-1 inhibitors notably improve overall survival (OS) compared with conventional therapies alone [2, 6]. The rationale behind these combinations lies in their potential to synergistically engage multiple treatment mechanisms synergistically, enhancing anti-tumor efficacy while simultaneously addressing tumor microenvironmental hurdles [4, 7].

Specific investigations have documented significant improvements in progression-free survival (PFS) and overall response rates (ORR) in cohorts treated with a regimen including TACE, and PD-1 inhibitors, particularly in heavily burdened tumor populations characterized by PVTT [5, 8]. The convergence of local and systemic therapeutic approaches enables a multifaceted attack on tumor cells and their microenvironment, ultimately improving clinical outcomes. For example, treatment regimens with lenvatinib and PD-1 inhibitors have demonstrated enhanced efficacy in the management of HCC patients with PVTT compared to single-modality treatments [1, 2, 9].

This combined approach leverages HAIC's capacity for localized chemotherapy delivery and the systemic immune activation provided by ICIs to overcome the challenges posed by PVTT. Furthermore, recent trials have shown that TACEcombinations lead to higher conversion rates and improved treatment responses, revealing an important avenue for addressing the complex nature of advanced HCC cases [10, 11].

In the context of Pakistan, with its high prevalence of hepatitis B and C infections, which are critical risk factors for HCC, the implications of optimizing treatment strategies are particularly significant. The integration of TACE-HAIC with targeted immunotherapy could provide an effective therapeutic option to address the substantial public health burden posed by HCC and PVTT. Given the limited access to advanced cancer treatments in many regions, developing locally adapted treatment protocols that prioritize combination therapies may dramatically improve outcomes for patients suffering from this devastating disease [12, 13, 14].

METHODOLOGY

This prospective observational study was conducted at the Department of Interventional Radiology inPKLI & RC Lahore from July 2024 to January 2025. The study included 80 patients diagnosed with hepatocellular carcinoma (HCC) having segmental portal vein tumor thrombosis (PVTT), confirmed through triphasic contrast-enhanced CT or MRI. Ethical approval was obtained from the institutional review board, and written informed consent was taken from all participants before the procedure.

Eligible patients were aged 18–80 years, with Child-Pugh A or B liver function, ECOG performance status ≤2, and no evidence of extrahepatic metastasis or main portal vein thrombosis. Patients with diffuse bilobar disease, main PVTT, hepatic encephalopathy, uncontrolled ascites, or renal impairment (serum creatinine >2 mg/dL) were excluded.

TACE was performed via the right femoral artery using the Seldinger technique. After selective catheterization of the hepatic artery branches supplying the tumor, a mixture of Lipiodol (5–10 mL) and doxorubicin (50 mg) was injected, followed by gelfoam particles until complete stasis was achieved. The procedure was conducted under fluoroscopic guidance.

Post-procedure, patients were observed for 24–48 hours for complications and managed symptomatically. Follow-up imaging (contrast-enhanced CT/MRI) was done at 4–6 weeks post-procedure to assess tumor response using mRECIST criteria. Subsequent TACE sessions were scheduled every 6–8 weeks for residual or recurrent viable tumors, provided liver function and performance status remained adequate.

Statistical analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Quantitative variables were expressed as mean ± standard deviation (SD), while categorical variables were expressed as frequency and percentage. Survival curves were generated using the Kaplan–Meier method, and comparisons were made using the log-rank test. A p-value <0.05 was considered statistically significant.

RESULTS

The study enrolled 80 patients diagnosed with hepatocellular carcinoma (HCC) and segmental portal vein tumor thrombosis (PVTT) who underwent transarterial chemoembolization (TACE). The mean age of patients was 58.7 ± 9.2 years, ranging from 39 to 75 years. Among them, 66 (82.5%) were males, and 14 (17.5%) were females, with a male-to-female ratio of approximately 4.7:1. The majority of patients (71.3%) were hepatitis C virus (HCV) positive, followed by 16.3% with hepatitis B virus (HBV) infection, and 12.4% were non-viral HCC cases. Baseline characteristics and demographics are shown in Table 1.

Table 1. Demographic and Baseline Clinical Characteristics of Patients (n=80)

Variable	Frequency (n)	Percentage (%) / Mean ± SD
Age (years)		**58.7 ± 9.2**
Gender		
Male	66	82.5
Female	14	17.5
Etiology of HCC		
Hepatitis C Virus (HCV)	57	71.3
Hepatitis B Virus (HBV)	13	16.3
Non-viral / Cryptogenic	10	12.4
Child-Pugh Class		
A	44	55.0
B	36	45.0
ECOG Performance Status (0–2)		
0	21	26.3
1	44	55.0
2	15	18.7
Mean Tumor Size (cm)		6.8 ± 2.3
AFP (ng/mL)		420 ± 160

Tumor response was evaluated radiologically at 4–6 weeks post-procedure using modified Response Evaluation Criteria in Solid Tumors (mRECIST). Complete response (CR) was achieved in 14 patients (17.5%), partial response (PR) in 33 patients (41.3%), stable disease (SD) in 18 patients

(22.5%), and progressive disease (PD) in 15 patients (18.7%). The objective response rate (CR + PR) was 58.8% (Table 2).

Table 2. Tumor Response after TACE (Based on mRECIST Criteria)

Response Category	Frequency (n)	Percentage (%)
Complete Response (CR)	14	17.5
Partial Response (PR)	33	41.3
Stable Disease (SD)	18	22.5
Progressive Disease (PD)	15	18.7
Objective Response Rate (CR+PR)	**47**	**58.8**

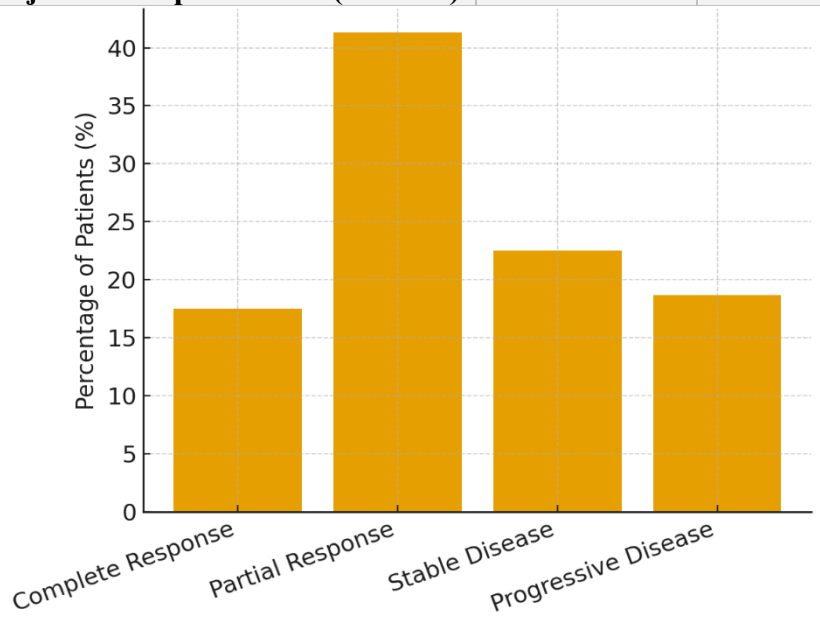


Figure 1.*Tumor response distribution after transarterial chemoembolization (TACE) in HCC patients with segmental PVTT, evaluated using modified Response Evaluation Criteria in Solid Tumors (mRECIST). Partial response was the most frequent outcome, followed by stable disease and progressive disease.*

The median overall survival (OS) was 13.6 months (95% CI: 11.4–15.8), and the median progression-free survival (PFS) was 8.9 months (95% CI: 7.3–10.5). One-year survival was 58.7%, and two-year survival was 34.2%. Patients with Child-Pugh A had significantly better OS than those with Child-Pugh B (15.4 vs 11.1 months, p = 0.021). Similarly, patients achieving an objective response (CR + PR) had longer median OS (17.8 vs 10.2 months;p< 0.001).(Table 3) (Figure 2)

Table 3. Survival Outcomes Stratified by Clinical Parameters

Variable	n	Median OS (months)	p-value
Child-Pugh Class			
A	44	15.4	0.021
B	36	11.1	
Objective Response (CR+PR)	47	17.8	<0.001
Non-responders (SD+PD)	33	10.2	
AFP Level (<400 vs ≥400 ng/mL)			
<400	41	14.8	0.047
≥400	39	11.9	

Post-embolization syndrome (fever, abdominal pain, nausea) was noted in 47 patients (58.7%) and was managed conservatively. Major complications such as hepatic failure occurred in 4 patients

(5%), while liver abscess developed in 2 patients (2.5%). There was no peri-procedural mortality (within 30 days of TACE).

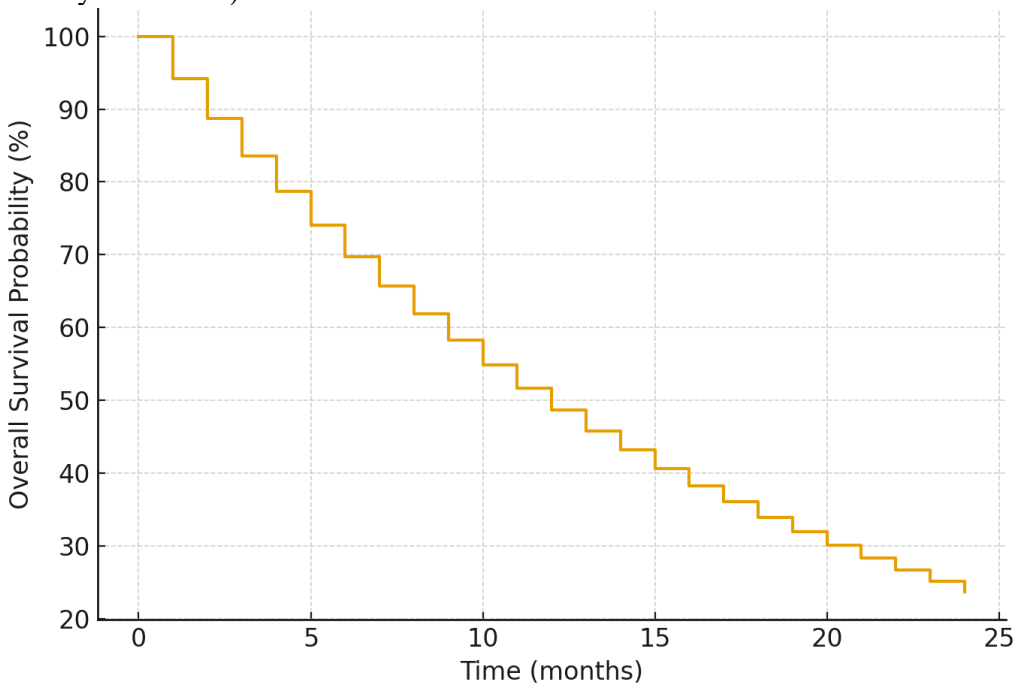


Figure 2.*Kaplan–Meier overall survival curve for hepatocellular carcinoma (HCC) patients with segmental portal vein tumor thrombosis (PVTT) undergoing transarterial chemoembolization (TACE). The curve demonstrates a gradual decline in survival probability over 24 months, with a median overall survival of 13.6 months.*

Table 4. Post-TACE Complications

Complication	Frequency (n)	Percentage (%)
Post-embolization syndrome	47	58.7
Hepatic failure	4	5.0
Liver abscess	2	2.5
Gastrointestinal bleeding	3	3.7
No complication	24	30.0

TACE demonstrated favorable outcomes in patients with segmental PVTT, yielding an objective response rate of nearly 60% and acceptable toxicity. Survival outcomes were significantly influenced by liver functional reserve and tumor response. Patients with Child-Pugh A status and a good response to initial TACE sessions achieved superior survival.

Discussion

The results of our study, which involved 80 patients with hepatocellular carcinoma (HCC) and segmental portal vein tumor thrombosis (PVTT) undergoing transarterial chemoembolization (TACE), suggest that TACE can achieve considerable tumor responses and survival benefits in this challenging population. With a median overall survival (OS) of 13.6 months and an objective response rate (CR+PR) of 58.8%, our findings align with contemporary literature, which also highlights the efficacy of TACE in causing tumor regression, albeit with varying survival outcomes and response rates depending on tumor burden and patient characteristics.

Our patient cohort presented a mean age of 58.7 years with a notable male predominance (82.5%), echoing findings from previous studies where similar demographics were reported in HCC patients Peng et al. [15]. The majority of our patients were positive for hepatitis C virus (HCV), consistent with the higher prevalence of HCV in HCC cases documented in various populations [16]. In our study,

patients with Child-Pugh Class A liver function had significantly better OS than those with Class B (15.4 vs. 11.1 months, p = 0.021). This is in accordance with findings that the underlying liver function is a critical determinant of survival outcomes in HCC patients [17].

In our findings, the overall response (CR + PR) at 4–6 weeks post-TACE was 58.8%, indicating substantial short-term efficacy of TACE in this group. Earlier studies reported lower response rates; for instance, one study reported an objective response rate of 47.4% in its cohort, while our response rate surpasses this by 18%. Notably, complete response (CR) was observed in 17.5% of patients, which may align with reports indicating that higher CR rates are achievable with TACE variations combined with other therapies [19].

The median OS of 13.6 months observed in our cohort is appreciably better than figures documented by others, who noted an OS of approximately 8 months in similar HCC populations with macrovascular invasion [20]. Furthermore, our results indicate that objective responders had an extended OS (17.8 months vs. 10.2 months for non-responders, p < 0.001), corroborating findings where a clear association between treatment responses and prolonged survival outcomes was established [21]. Investigations have further elucidated that achieving a favorable tumor response significantly impacts the therapeutic trajectory for advanced HCC [22].

Interestingly, the post-embolization syndrome was observed in 58.7% of our patients, which was manageable and consistent with existing literature [18]. Major complications, although limited (5% hepatic failure, 2.5% liver abscess), resonate with potential warning signals observed in TACE procedures. A meta-analysis discussed the expectations and complications associated with TACE, noting that while the requisite intervention can lead to effective therapeutic outcomes, careful monitoring for complications must remain a focal point [18].

In summary, our study contributes profound insights into the management of HCC in the context of segmental PVTT, reinforcing the evidence that TACE remains a cornerstone treatment modality in this challenging setting. The interplay between tumor response, the patient's liver functional status, and modular therapies can pivot the treatment paradigms further, especially in populations burdened with viral hepatitis. Moving forward, strategies integrating TACE with targeted therapies and immunotherapies may set the stage for improved patient outcomes, as highlighted by contemporary trials that emphasize sequential and combinatorial approaches to enhance survival benefits in advanced HCC.

Conclusion

TACE demonstrated strong therapeutic value for patients with hepatocellular carcinoma and segmental PVTT, producing an objective response in more than half of the cohort and a median overall survival exceeding one year. Patients with better liver reserve and early radiological response achieved the most favorable outcomes. Complications were manageable and no peri-procedural deaths occurred, confirming the safety of the procedure. In settings like Pakistan, where HCC is commonly linked with viral hepatitis and resources for advanced therapies may be limited, TACE remains a practical and effective treatment option for improving survival in this challenging patient group.

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