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OUTCOMES OF TRANSARTERIAL CHEMOEMBOLIZATION IN HCC PATIENTS WITH SEGMENTAL PORTAL VEIN TUMOR THROMBOSIS

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Abstract

Background:
Hepatocellular carcinoma (HCC) complicated by portal vein tumor thrombosis (PVTT) carries a poor prognosis, with limited therapeutic options and reduced survival. Transarterial chemoembolization (TACE) is commonly used in patients with unresectable HCC; however, outcomes among those with segmental PVTT remain less clearly defined in many regions, including Pakistan. This study evaluates the therapeutic response, survival outcomes, and safety profile of TACE in HCC patients presenting with segmental PVTT.

Methods:
This prospective observational study included 80 patients with radiologically confirmed HCC and segmental PVTT who underwent TACE. Eligible patients had Child-Pugh A or B liver function and ECOG performance status ≤2. TACE was performed using Lipiodol-doxorubicin emulsion followed by Gelfoam embolization. Tumor response at 4–6 weeks post-procedure was assessed using mRECIST criteria. Survival outcomes were analyzed using Kaplan–Meier curves, and complications were recorded. A p-value <0.05 was considered statistically significant.

Results:
The cohort had a mean age of 58.7 ± 9.2 years, with males comprising 82.5%. Hepatitis C infection was the predominant etiology (71.3%). The objective response rate (CR + PR) was 58.8%, with complete response in 17.5% and partial response in 41.3% of patients. Median overall survival (OS) was 13.6 months, and median progression-free survival (PFS) was 8.9 months. Patients with Child-Pugh A had significantly better OS than those with Child-Pugh B (15.4 vs. 11.1 months; $p = 0.021$). Responders (CR + PR) demonstrated superior OS compared to non-responders (17.8 vs. 10.2 months; $p < 0.001$). Post-embolization syndrome occurred in 58.7% of patients, while major complications were infrequent, including hepatic failure (5%) and liver abscess (2.5%). No peri-procedural mortality was observed.

Conclusion:
TACE provides a favorable therapeutic response and acceptable safety profile in HCC patients with segmental PVTT, offering meaningful survival benefits, especially among those with better baseline liver function. Objective responders and Child-Pugh A patients demonstrated significantly improved outcomes, reaffirming the value of careful patient selection.

Keywords: Hepatocellular carcinoma, portal vein tumor thrombosis, TACE, mRECIST, survival outcomes, liver cancer

Introduction

Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver and is associated with a high mortality rate, making it a significant public health issue worldwide [1, 2]. The disease often develops against a background of chronic liver disease, particularly cirrhosis, complicating treatment options [1, 3]. As the disease progresses, the presence of portal vein tumor thrombosis (PVTT) is a concerning prognostic factor that significantly affects treatment outcomes and survival rates [4, 5]. PVTT in HCC indicates advanced disease, frequently associated with multifocal lesions and worsened liver function due to impaired portal blood flow [6, 3].

Transarterial chemoembolization (TACE) has emerged as a standard locoregional therapy for patients with unresectable HCC, especially those with PVTT [7, 8]. TACE involves selectively infusing chemotherapeutic agents combined with embolic agents into the hepatic artery, targeting tumor vascularization while minimizing systemic exposure [8]. The therapeutic approach of combining TACE with systemic therapies, such as immunotherapy and targeted agents, is being explored to enhance treatment efficacy and improve patient outcomes [9, 10]. Despite its promise, TACE, particularly in the context of PVTT, presents unique challenges, including a higher risk of post-embolization syndrome and liver function deterioration [8, 11].

Recent studies have highlighted variations in outcomes based on the degree of PVTT, as classified using systems such as Cheng's classification, which categorizes involvement as types I-IV based on the anatomical involvement of the portal vein [4]. The clinical implications of these classifications are substantial, as they influence prognosis and treatment decisions. For patients with advanced PVTT (types III and IV), outcomes remain particularly poor, necessitating a more aggressive treatment approach [5].

In the context of the Pakistani population, where the prevalence of HCC continues to rise due to factors such as hepatitis B and C infections and the high incidence of cirrhosis related to non-alcoholic fatty liver disease, effective management is critical [12, 11]. TACE is widely employed in Pakistan; however, its outcomes in patients with PVTT are less well documented than in more developed healthcare systems. Understanding these outcomes is essential to refining treatment protocols, improving patient stratification, and ultimately enhancing survival rates for HCC patients within this demographic.

In conclusion, as the burden of HCC with PVTT grows globally, including in Pakistan, an in-depth exploration of TACE outcomes to evaluate its effectiveness and associated risks becomes imperative. This research aims to contribute valuable insights into optimizing treatment strategies for this vulnerable patient population.

Methodology

This prospective observational study was conducted at the Department of Radiology in PKLI & RC Lahore from February 2024 to February 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**

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)

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). (Table 4)

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

Discussion

In our study involving 80 patients diagnosed with hepatocellular carcinoma (HCC) and segmental portal vein tumor thrombosis (PVTT), we observed demographic and clinical characteristics akin to those reported in the literature. Our cohort had a mean age of 58.7 years, predominantly male (82.5%), with a notable prevalence of hepatitis C virus (HCV) infections (71.3%). These patterns corroborate findings by Patıdar et al. (2021), who also noted similar demographics and etiology, highlighting the larger burden of HCV in HCC cases in similar geographic settings Patıdar et al. [13]. The male-to-female Ratio in our study of approximately 4.7:1 aligns with patterns seen in global and regional studies, suggesting gender predisposition remains a consistent observation in HCC presentations [14, 15, 16].

The evaluation of tumor response following transarterial chemoembolization (TACE) revealed a complete response (CR) in 17.5% of patients and a partial response (PR) in 41.3%, yielding an objective response rate (ORR) of 58.8%. Such findings resemble those reported by [17], who indicated

ORRs between 57% and 70% in patients with advanced HCC and PVTT treated with TACE [17]. Likewise, [18] observed that effective responses were notably influenced by the extent of hepatic involvement and overall liver function, emphasizing the critical role of assessing individual patient profiles in predicting outcomes post-TACE [18]. Our results reinforce the notion that TACE remains a viable option, particularly for patients with segmental PVTT rather than more extensive involvement.

Survival outcomes in our study are noteworthy, with a median overall survival (OS) of 13.6 months. Factors contributing to better OS included Child-Pugh Class A versus Class B (15.4 vs. 11.1 months, $p = 0.021$) and objective response rates (CR + PR), which correlated significantly with survival (17.8 vs. 10.2 months, $p < 0.001$). These findings align with those of [19,] who demonstrated that Child-Pugh scores serve as pivotal indicators of both OS and progression-free survival (PFS) in patients with PVTT [19]. Additional studies suggest that stratification based on Child-Pugh classifications is essential, with a clear correlation between liver function and treatment efficacy across various therapeutic modalities [20].

Post-embolization syndrome was experienced by 58.7% of our cohort, which correlates with literature values indicating up to 70% incidence rates in similar patient groups undergoing TACE [21]. While major complications occurred in a smaller cohort (5% hepatic failure and 2.5% liver abscess), these rates are within the range reported in recent meta-analyses, consolidating the safety profile of TACE treatments [22, 23]. The absence of peri-procedural mortality in our study is consistent with the findings of 19, who observed that mortality is associated with sufficient liver function at the time of TACE and careful patient selection [19, 24].

Our study's findings contextualize the Pakistani population within the broader spectrum of global evidence, emphasizing local characteristics, including high rates of viral hepatitis leading to HCC and associated comorbidities affecting treatment efficacy. The growing body of evidence suggests a need for tailored treatment protocols addressing the local prevalence of HCV and HBV as underlying causes of HCC. Integrative approaches involving multidisciplinary management and potential combinations with targeted therapies may provide additional benefits, particularly for patients with advanced-stage HCC and PVTT [25, 26].

In conclusion, our findings provide valuable insights into the treatment of HCC with segmental PVTT using TACE, highlighting the importance of careful patient selection, liver function monitoring, and individualized responses to optimize outcomes. Our results support the need for ongoing research and exploration of treatment combinations to further enhance survival in this patient population.

Conclusion

TACE demonstrated encouraging antitumor activity and survival benefits in patients with HCC and segmental PVTT, with an objective response rate of nearly 60% and a median survival exceeding one year. Better outcomes were strongly associated with preserved liver function and favorable early radiologic response. Complications were manageable and no peri-procedural mortality occurred, underscoring the safety of TACE in appropriately selected patients. These findings support the continued use of TACE as an effective and viable treatment option for segmental PVTT in resource-limited settings, while highlighting the need for further research integrating combination therapies to enhance long-term survival.

1. **References:**

1. Patıdar Y., Mukund A., & Sarin S..Transarterial chemoembolization in unresectable hepatocellular carcinoma with portal vein tumor thrombosis: a tertiary care center experience. Indian Journal of Radiology and Imaging 2021;31(02):270-276. https://doi.org/10.1055/s-0041-1734367
2. Falette-Puisieux M., Nault J., Bouattour M., Lequoy M., Amaddeo G., Decaens T.et al. Beyond atezolizumab plus bevacizumab in patients with advanced hepatocellular carcinoma: overall

efficacy and safety of tyrosine kinase inhibitors in a real-world setting. Therapeutic Advances in Medical Oncology 2023;15. https://doi.org/10.1177/17588359231189425

3. Hasegawa K., Takemura N., Yamashita T., Watadani T., Kaibori M., Kubo S.et al.. Clinical practice guidelines for hepatocellular carcinoma: the Japan Society of Hepatology 2021 version (5th JSH-HCC guidelines). Hepatology Research 2023;53(5):383-390. https://doi.org/10.1111/hepr.13892
4. Li L., Huang X., Cheng N., Weng X., Jiao Y., Liu J.et al.. Efficacy and safety of endovascular brachytherapy combined with transarterial chemoembolization for the treatment of hepatocellular carcinoma patients with type III-IV portal vein tumor thrombosis. 2021. https://doi.org/10.21203/rs.3.rs-952408/v1
5. Zhou T., Chen S., Wang H., Weng S., Zhou G., Zhang Y.et al.. Safety and efficacy of drug-eluting bead transarterial chemoembolization with callispheres® microspheres for hepatocellular carcinoma with portal vein tumor thrombus: a preliminary study. Journal of Cancer 2021;12(15):4522-4529. https://doi.org/10.7150/jca.54650
6. El-Araby A., Al-Alfy M., Habila M., & Shaheen M. Epidermal growth factor as a biomarker for early detection of hepatocellular carcinoma. Al-Azhar International Medical Journal 2022;0(0):0-0. https://doi.org/10.21608/aimj.2022.142492.1966
7. Chang Y., Jeong S., Jang J., & Kim Y.. Recent updates ontransarterialchemoembolization in hepatocellular carcinoma. International Journal of Molecular Sciences 2020;21(21):8165. https://doi.org/10.3390/ijms21218165
8. Kashfi S., Murdakhayev E., Rehmani R., & Sharma S.. Post-embolization syndrome complicated by hypertensive emergency and severely elevated transaminases. Cureus 2021. https://doi.org/10.7759/cureus.15446
9. Zou X., Xu Q., You R., & Yin G. Correlation and efficacy of tace combined with lenvatinib plus PD-1 inhibitor in the treatment of hepatocellular carcinoma with portal vein tumor thrombus based on immunological features. Cancer Medicine 2023;12(10):11315-11333. https://doi.org/10.1002/cam4.5841
10. Cheng A., Qin S., Ikeda M., Galle P., Ducreux M., Kim T.et al. Updated efficacy and safety data from imbrave150: atezolizumab plus bevacizumab vs. sorafenib for unresectable hepatocellular carcinoma. Journal of Hepatology 2022;76(4):862-873. https://doi.org/10.1016/j.jhep.2021.11.030
11. Asano K., Kageyama K., Yamamoto A., Jogo A., Nakano M., Murai K.et al.. Predictors of immediate deterioration of the Child-Pugh classification from A to B after transcatheter arterial chemo-embolization for treatment-naive hepatocellular carcinoma. Cancer Medicine 2024;13(21). https://doi.org/10.1002/cam4.70367
12. Ghrewati M., Mahmoud A., Beliani T., Keegan S., & Kumar M. Tumor thrombus of hepatocellular carcinoma: a direct extension from the liver to the right atrium. Cureus 2024. https://doi.org/10.7759/cureus.55158
13. Patıdar Y., Mukund A., & Sarin S..Transarterial chemoembolization in unresectable hepatocellular carcinoma with portal vein tumor thrombosis: a tertiary care center experience. Indian Journal of Radiology and Imaging 2021;31(02):270-276. https://doi.org/10.1055/s-0041-1734367
14. Huang Y., Zhang Z., Liao W., Hu K., & Wang Z.. Combination of sorafenib, camrelizumab, transcatheter arterial chemoembolization, and stereotactic body radiation therapy as a novel downstaging strategy in advanced hepatocellular carcinoma with portal vein tumor thrombus: a case series study. Frontiers in Oncology 2021;11. https://doi.org/10.3389/fonc.2021.650394
15. Ding X., Sun W., Chen J., Li W., Shen Y., Guo X.et al.. Percutaneous radiofrequency ablation combined with transarterial chemoembolization plus sorafenib for large hepatocellular carcinoma invading the portal venous system: a prospective randomized study. Frontiers in Oncology 2020;10. https://doi.org/10.3389/fonc.2020.578633

16. Tang Q., Huang W., Liang J., & Xue J. Efficacy and safety of transarterial chemoembolization in elderly patients of advanced hepatocellular carcinoma with portal vein tumor thrombus: a retrospective study. Frontiers in Oncology 2021;11. https://doi.org/10.3389/fonc.2021.646410
17. Zhou T., Chen S., Wang H., Weng S., Zhou G., Zhang Y.et al.. Safety and efficacy of drug-eluting bead transarterial chemoembolization with callispheres® microspheres for hepatocellular carcinoma with portal vein tumor thrombus: a preliminary study. Journal of Cancer 2021;12(15):4522-4529. https://doi.org/10.7150/jca.54650
18. Chen P., Chiu S., Tsai M., Chang K., Chang W., Lin H.et al.. Combination therapy of sorafenib and drug-eluting bead transarterial chemoembolization for advanced hepatocellular carcinoma with and without hepatic arteriovenous shunt. Journal of the Chinese Medical Association 2022;85(4):491-499. https://doi.org/10.1097/jcma.0000000000000696
19. Chen K. and Gao J. Factors influencing the short-term and long-term survival of hepatocellular carcinoma patients with portal vein tumor thrombosis who underwent chemoembolization. World Journal of Gastroenterology 2021;27(13):1330-1340. https://doi.org/10.3748/wjg.v27.i13.1330
20. Zhao Y., Shu-wei W., Xue Y., Dang Z., Nan Z., Wang D., et al.Transarterial chemoembolization combined with lenvatinib plus tislelizumab for unresectable hepatocellular carcinoma: a multicenter cohort study. Frontiers in Immunology 2024;15. https://doi.org/10.3389/fimmu.2024.1449663
21. Cai M., Liang L., Zhang J., Chen N., Huang W., Guo Y., et al. Lenvatinib plus drug-eluting bead transarterial chemoembolization with/without hepatic arterial infusion chemotherapy for hepatocellular carcinoma larger than 7 cm with major portal vein tumor thrombosis: a multicenter retrospective cohort study. International Journal of Surgery 2024;110(12):7860-7870. https://doi.org/10.1097/js9.0000000000001819
22. Liu B., Gao S., Zhu X., Guo J., Kou F., Liu S.et al.. Combination therapy of chemoembolization and hepatic arterial infusion chemotherapy in hepatocellular carcinoma with portal vein tumor thrombosis compared with chemoembolization alone: a propensity score-matched analysis. Biomed Research International 2021;2021(1). https://doi.org/10.1155/2021/6670367
23. Ji X., Zhang A., Duan X., & Wang Q.. Stereotactic body radiotherapy versus lenvatinib for hepatocellular carcinoma with portal vein tumor thrombosis: a propensity score analysis. 2023. https://doi.org/10.21203/rs.3.rs-2974472/v1
24. Cai M., Huang W., Huang J., Shi W., Guo Y., Liang L., et al.Transarterial chemoembolization combined with lenvatinib plus PD-1 inhibitor for advanced hepatocellular carcinoma: a retrospective cohort study. Frontiers in Immunology 2022;13. https://doi.org/10.3389/fimmu.2022.848387
25. Ye Z., Li Z., Song M., Yang Z., Zhang W., Zhang J.et al.. Drug-eluting bead transarterial chemoembolization as neoadjuvant therapy pre-liver transplantation for advanced-stage hepatocellular carcinoma. World Journal of Gastrointestinal Oncology 2024;16(6):2476-2486. https://doi.org/10.4251/wjgo.v16.i6.2476
26. Cao Y., Sun T., Guo X., Ouyang T., Kan X., Chen L.et al.. Sorafenib versus apatinib, both combined with transarterial chemoembolization for hepatocellular carcinoma with portal vein tumor thrombosis: a comparative retrospective study. Frontiers in Oncology 2021;11. https://doi.org/10.3389/fonc.2021.673378