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Original Article

Therapeutic Value of Portal Vein Stenting before Chemoembolization for Treating Hepatocellular Carcinoma with Portal Vein Thrombosis

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ABSTRACT

Background: Portal vein stenting [PVS] combined with transarterial chemoembolization [TACE] is a potential treatment strategy to improve outcomes in hepatocellular carcinoma [HCC] with portal vein tumor thrombosis [PVTT].

Aim of the work: This work evaluated the feasibility, safety, and therapeutic value of PVS followed by TACE for treating patients with HCC and PVTT.

Patients and methods: This prospective observational study involved patients with clinically diagnosed HCC and PVTT who underwent PVS followed by TACE. Patients were categorized into two groups based on the interval between PVS and TACE. Procedural metrics, clinical outcomes, stent patency, tumor progression, and survival rates were assessed.

Results: This study involved 54 patients. The mean stent patency duration was 18.36 ± 2.53 months. At the end of the study, stent occlusion was observed in 40 [67.8%] patients, tumor progression in 33 [55.9%] patients, and 40 [67.8%] patients died. The 1-year survival probability was 53.7% [95% CI: 41.9%–68.8%], declining to 33.3% [95% CI: 22.9%–48.6%] at 2 years, with a median survival of 381 days [95% CI: 316–661 days]. Stent patency probabilities were 42.6% [95% CI: 31.3%–58.1%] at 1 year and 25.9% [95% CI: 16.5%–40.7%] at 2 years, with a median patency duration of 243 days [95% CI: 115–556 days]. Child-Pugh classification, the number of TACE procedures, and group were significant predictors of better survival outcomes. For stent patency, HBV status, the number of TACE procedures, and group were significant predictors.

Conclusion: PVS followed by TACE is a feasible and effective therapeutic approach for HCC patients with PVTT. PVS facilitates sequential TACE. Stent patency and survival are influenced by liver function [Child-Pugh classification], number of TACE sessions, and group assignment.

Keywords: Hepatocellular carcinoma; Portal vein stenting; Tumor thrombosis; Stent patency; Survival.

INTRODUCTION

Hepatocellular carcinoma [HCC] is among the most prevalent malignant tumors globally. It has become the leading cause of cancer-related deaths among men in rural areas and the second leading cause in urban regions [1, 2]. HCC has a marked tendency to invade the portal venous system, forming portal vein tumor thrombus [PVTT]. PVTT occurs in 44% of HCC cases according to autopsy studies and 31–34% in clinical evaluations [3]. It leads to partial or complete portal vein occlusion and facilitates extensive intrahepatic or extrahepatic metastasis [4]. PVTT in the main portal trunk increases portal vein pressure, which can cause gastrointestinal bleeding, ascites, and the dissemination or recurrence of intrahepatic tumors. Without treatment, the prognosis for patients with HCC and PVTT is dismal, with a median survival of only 2.7–4.0 months compared to 24.4 months in patients without PVTT [5].

Effective treatments for these patients remain elusive and highly debated. The majority of HCC cases with PVTT are not resectable or amenable to curative therapies. Palliative options include TACE, portal vein chemotherapy, percutaneous ethanol injection, and ablation. Among these, TACE is considered safe and effective for HCC with PVTT when adequate collateral circulation exists. However, PVTT significantly diminishes the efficacy of TACE and adversely affects therapeutic outcomes [6]. Additionally, TACE can inadvertently embolize blood supply to normal liver tissue, increasing the risk of liver failure. Concurrently, the rise in portal vein pressure caused by PVTT elevates the risk of esophageal and gastric bleeding, potentially leading to death [7].

Restoring portal vein patency and reperfusion the portal vein may improve TACE outcomes, which can be achieved using portal vein stenting [PVS] [8]. The combination of PVS and TACE has shown promise in treating HCC with PVTT. However, data on this combined therapeutic approach remain limited [9].

THE AIM OF THE WORK

This work was designed to evaluate the feasibility, safety, and therapeutic value of PVS followed by TACE for treating patients with HCC and PVTT.

PATIENTS AND METHODS

This observational, prospective study included 54 patients admitted to the National Liver Institute, Menoufia University, and the Medical Scientific Research Center between April 2023 and June 2024 for TACE of HCC with portal PVTT.

We included patient with clinically diagnosed HCC and PVTT, tumor thrombi invading the portal vein while sparing at least one primary branch, Child-Pugh Class A/B liver function, no distant metastasis, and normal coagulation function [prothrombin concentration ≥60%]. However, participants with the following conditions were excluded from the study: coagulation disorders that could not be corrected, widespread metastases, massive ascites, encephalopathy or biliary obstruction, and cardiac or renal insufficiency.

Patients were divided into two groups. In Group A, the time interval between PVS and TACE was 2 weeks. In Group B, the time interval between PVS and TACE was >2 weeks. All eligible patients signed an informed consent after full explanation of the study aim, producers and assurance of all patient rights. In addition, the study protocol was reviewed and approved by medical research and the National Liver Institute, Menoufia University Ethics Committee [REC].

Each patient underwent clinical and laboratory evaluations, including medical history, physical examination, complete blood count [CBC], liver function tests [LFTs], prothrombin time [PT] and concentration, tumor markers, and renal function tests [RFTs]. Radiological imaging was reviewed for treatment planning. The PVS procedure involved assessing the stenosis location/extent, pre-/post-stenting pressure gradients [PGs], and stent parameters. Stent patency was monitored via routine computed tomography [CT] or symptom-driven evaluations, with clinical outcomes and post-stent treatments recorded.

Patient Preparation: Participants were instructed to fast overnight and were admitted to the hospital on the morning of the procedure. Patients on medications confirmed their regimens with a physician, taking routine medications, if permitted, with minimal water. Any pre-existing conditions, such as asthma, diabetes, or allergies to iodine, shellfish, drugs, or latex, were disclosed. Peripheral venous access was established for intravenous [IV] hydration using normal saline [150–300 mL/h] before administering premedications, including antiemetics and steroids. Prophylactic antibiotics, such as cefazolin [1g] and metronidazole [500mg], were administered; for patients allergic to penicillin, cefazolin was substituted with Bactrim DS [160mg trimethoprim/800 mg sulfamethoxazole]. In patients with bilioenteric anastomosis or biliary stents, moxifloxacin [400mg] was given, starting three days before and continuing for 17 days after the procedure. Prophylactic antiemetics included ondansetron [16mg], dexamethasone [10mg], and diphenhydramine [50mg]. The procedures were performed using Philips Allura Xper FD20 and Toshiba Infinix-Vc-1 fluoroscopy systems.

Trans-Femoral Trans-Arterial Chemoembolization: Patients were positioned supine under mild sedation on the angiography table, enabling C-arm rotation to visualize the liver in the CT field. Transfemoral arterial access was established via the right common femoral artery using an 18-G needle and the modified Seldinger technique at a 45° angle below the femoral head center. A 6-Fr arterial sheath was inserted, followed by catheterization of the aorta with a C25-Fr cobra or Bern catheter. Abdominal aortography [3–40 mL contrast, 10–20 mL/s] was performed to assess arterial anatomy. Selective angiograms of the superior mesenteric artery [30 mL contrast, 4–5 mL/s] and celiac artery [8–12 mL contrast, 4 mL/s] were conducted to evaluate hepatic vasculature and portal vein patency. Chemoembolic agents [Doxorubicin hydrochloride 50 mg] were delivered after confirming catheter positioning. Post-procedure, femoral sheath removal was followed by compression hemostasis and application of a pressure bandage. Patients rested with extended lower limbs for six hours, and access-site complications were monitored before discharge **[Figure 1]**

Portal Vein Stent [PVS] was performed by two interventional radiologists. Local anesthesia with lidocaine and pethidine was administered. Transhepatic puncture of the intrahepatic portal vein was conducted under sonographic and fluoroscopic guidance using a 21-gauge needle. The needle was replaced with a 4-French coaxial dilator, and a 6- to 8-French sheath was inserted over a 0.035-inch guidewire. Direct portography using a 5-French cobra catheter confirmed stenosis, collateral formation, and thrombus presence, with portal vein pressures and PGs recorded. Aspiration thrombectomy was performed for thrombus at the bifurcation. Stenotic segments were dilated with a balloon catheter, and self-expanding metallic stents [Wallstent, Zilver, or Express LD] were deployed. Post-stenting portography verified positioning and restored intrahepatic flow, with repeated PG measurements. Embolization of the transhepatic parenchymal track with stainless steel coils and N-butyl cyanoacrylate glue prevented bleeding. Anticoagulant therapy was not routinely administered. Vital signs, including blood pressure [BP], pulse, oxygen saturation [SpO_2], and electrocardiograms [ECG], were monitored throughout the procedure. **[Figure 2].** In stent thrombosis cases, 5000 IU

of heparin were infused rapidly inside the PVS without any patients experienced side effects.

Follow-Up: Patients underwent biweekly laboratory tests and duplex ultrasonography, with monthly imaging [CT or MRI] to evaluate stent patency. Documented outcomes included pre-/post-stenting PGs, technical and clinical success, complications, and portal venous flow. Technical success was defined as stent deployment with <30% residual stenosis and improved flow, while clinical success reflected enhanced liver function and alleviated portal hypertension symptoms. Complications were categorized as major or minor based on severity and intervention requirements.

Statistical Analysis of data: Continuous variables were expressed as mean ± SD and compared using Student's t-test. Categorical variables were analyzed using Chi-squared or Fisher's Exact Tests. Survival and stent patency were evaluated using Kaplan-Meier [K-M] analysis, and comparisons employed the log-rank test. Cox regression identified survival predictors and tumor progression risk factors. Paired t-tests compared portal vein pressures before and after stenting. A p-value <0.05 was considered statistically significant. All analyses were performed using R Software [v4.4.0, R Foundation for Statistical Computing, Vienna, Austria].

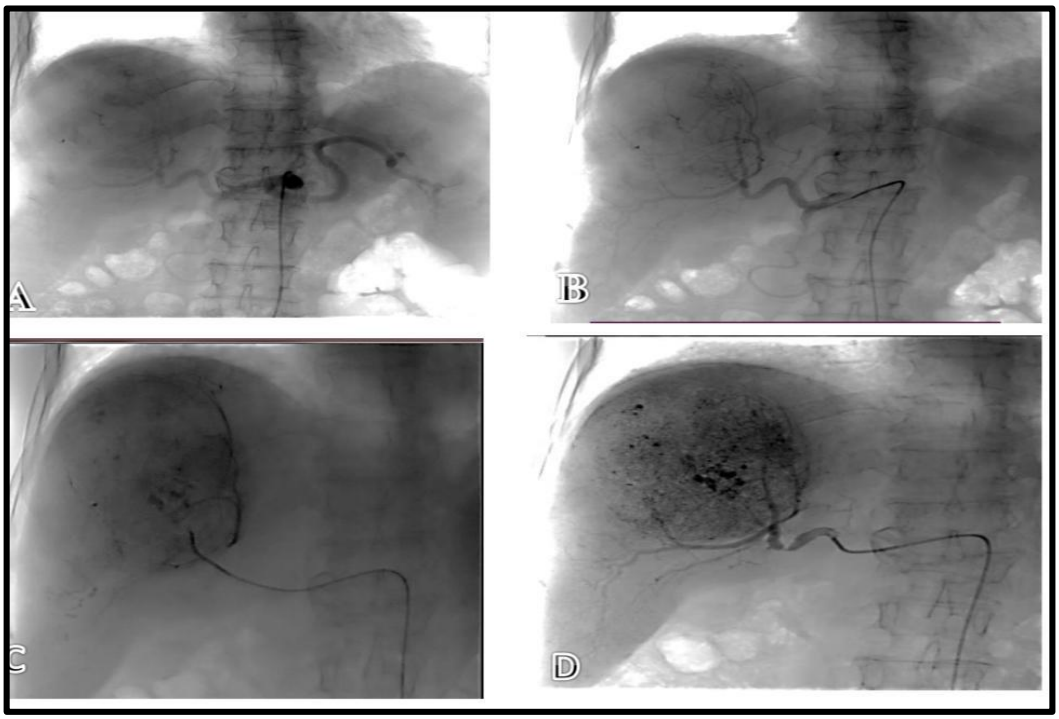


Figure [1]: Trans-arterial chemo-embolization steps for HCC**.** A- catheterization of the celiac trunk. B - catheterization of the hepatic artery. C - selective catheterization of the feeding artery. D - embolization of the tumor.

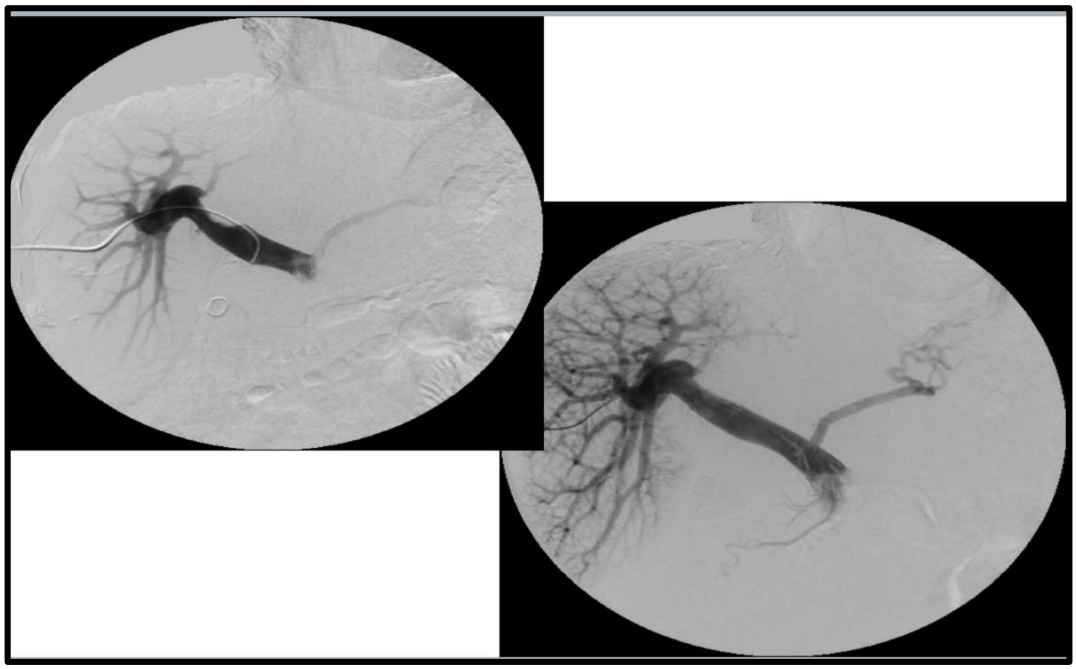


Figure [2]: Conventional angiography before and after portal vein stent

RESULTS

The mean age of the studied patients was57.05 ± 10.58. The majority of participants were male 43 [72.9%%]. Hepatitis B virus [HBV%] was present in 7 [11.9%%] of the cases, while hepatitis C virus [HCV%] was the most common infection, affecting 46 [78.0%]. Regarding gastrointestinal symptoms, 2 [3.4%] had constipation and 6 [10.2%] experienced diarrhea. Abdominal pain was reported by 14 [23.7%] of participants and ascites in 24 [40.7%]. The mean creatinine was 1.52 ± 0.77, urea was 77.02 ± 1.01, total bilirubin was 1.59 ± 0.52, mean ALT was 141 ± 29.75 and AST was 165.64 ± 21.18. Albumin had a mean of 3.37 ± 0.40, and platelet count [PC] was 75.31 ± 11.6. Electrolyte levels showed a mean sodium [Na] of 125.03 ± 2.02 and potassium [K] of 3.47 ± 0.50. Hemoglobin [Hb] had a mean of 11.98 ± 1.01, and total leukocyte count [TLC] was 14.51 ± 5.69. 33 [55.9%] patients were classified as Child-Pugh Class B. Regarding the characteristics of portal vein tumor thrombosis, 10 [16.9%] had lesions in the left portal vein branch [LPVB], 14 [23.7%] in the right portal vein branch [RPVB], 10 [16.9%] in the main portal vein [MPV] with LPVB, and 25 [42.4%] in the MPV with RPVB. 24 [40.7%] had ascites [Table 1]. Stenting approach was left in 29 [49.2%], right in 16 [27.1%], and splenic in 14 [23.7%]. Stent extension was meso-portal in 25 [42.4%], porto-portal in 24 [40.7%], and spleno-portal in 10 [16.9%]. The mean stent diameter was 10.54 ± 1.22 mm, and the mean length was 10 ± 0 mm. Regarding the complications of the stenting technique, portal dissection occurred in 2 [3.4%] patients, while 57 [96.6%] did not experience it. Bleeding was observed in 8 [13.6%] patients, and 7 [11.9%] experienced thrombosis, with 51 [86.4%] unaffected in both cases. The mean stent patency duration was 18.36 ± 2.53 months. The mean time to TACE was 5.16 ± 3.29 weeks, and the mean dose administered was 30.0 ± 6.93. Regarding the repetition of TACE, 10 [18.5%] patients underwent one repetition, 13 [24.1%] had two repetitions, 10 [18.5%] had three repetitions, 1 [1.8%] had four repetitions, and 1 [1.8%] had five repetitions. Regarding the results at the end of the study, stent occlusion was observed in 40 [67.8%] patients. Tumor progression occurred in 33 [55.9%] patients. 40 [67.8%] patients died, with 14 [23.7%] surviving [Table 2].

Before stenting, the mean portal vein pressure was 30.10 ± 4.83 mmHg, which significantly decreased to 18.42 ± 2.56 mmHg after stenting [P < 0.001]. The 1-year survival probability for patients was 53.7% [95% CI: 41.9% - 68.8%], while the 2-year survival probability was 33.3% [95% CI: 22.9% - 48.6%]. The median survival time for patients was 381 [95% CI: 316 - 661%] days. The 1-year probability of stent patency is 42.6% [95% CI: 31.3% - 58.1%], while the 2-year probability decreases to 25.9% [95% CI: 16.5% - 40.7%]. The median stent patency time was 243 days [95% CI: 115-556 days] [Table 3].

In the univariate analysis, Child-Pugh classification, the number of Transarterial Chemoembolization [TACE] procedures, and group classification were significant predictors of improved survival outcomes, while age, sex, and hepatitis status [HBV or HCV] showed no significant association with survival. For stent patency, HBV status, the number of TACE procedures, and group classification significantly predicted prolonged stent functionality, whereas age, sex, HCV status, and Child-Pugh classification did not have significant associations. Regarding tumor progression, both Child-Pugh classification and group classification were significant predictors, with patients in Child-Pugh class B and Group 2 exhibiting lower odds of tumor progression compared to their counterparts. However, in the multivariate analysis, only the number of TACE procedures and group classification remained significant predictors for better survival and extended stent patency. No variables were found to be significant predictors of tumor progression after adjusting for other factors [Table 4].

Table [1]: Demographic and clinical characteristics of the study population

		N=59
Age [years]		57.05 ± 10.58
Sex	**Male**	43 [72.9%]
	Female	16 [27.1%]
Hepatitis	**HBV**	7 [11.9%]
	HCV	46 [78.0%]
Gastrointestinal symptoms	**Constipation**	2 [3.4%]
	Diarrhea	6 [10.2%]
Abdominal pain		14 [23.7%]
Ascites		24 [40.7%]
Laboratory tests	**Creatinine**	1.52 ± 0.77
	Urea	77.02 ± 1.01
	Total bilirubin	1.59 ± 0.52
	ALT	141 ± 29.75
	AST	165.64 ± 21.18
	Albumin	3.37 ± 0.40
	PC	75.31 ± 11.6
	NA	125.03 ± 2.02
	K	3.47 ± 0.50
	Hb	11.98 ± 1.01
	TLC	14.51 ± 5.69
Child-Pugh classification	**Class A**	26 [44.1%]
	Class B	33 [55.9%]
Location of PVTT	**LPVB**	10 [16.9%]
	RPVB	14 [23.7%]
	MPV + LPVB	10 [16.9%]
	MPV + RPVB	25 [42.4%]

Data is presented as mean ± or frequency [%]. ALT: Alanine Aminotransferase. AST: Aspartate Aminotransferase. GIT: Gastrointestinal Tract. Hb: Hemoglobin. HCV: Hepatitis C Virus. HBV: Hepatitis B Virus. K: Potassium. LPVB: Left Portal Vein Branch. MPV: Mean Platelet Volume. NA: Sodium. PC: Platelet Count. RPVB: Right Portal Vein Branch. TLC: Total Leukocyte Count. Urea: Blood Urea Nitrogen.

Table [2]: Stenting characteristics, TACE dose and timing, and clinical outcomes

	N=59	
Stenting Approach	**Left**	29 [49.2%]
	Right	16 [27.1%]
	Splenic	14 [23.7%]
Diameter of stent [mm]		10.54 ± 1.22
Length of stent		10 ± 0
Stenting Complications	**Portal dissection**	2 [3.4%]
	Bleeding	8 [13.6%]
	Thrombosis	7 [11.9%]
Stent patency		18.36 ± 2.
N=58		
Time to TACE		5.16 ± 3.29
TACE Dose		30.0 ± 6.93
Results at the end of study	**Stent occlusion**	40 [67.8%]
	Tumor progression	33 [55.9%]
	Death	14 [23.7%]
Repetition of TACE	**N=54**	
	1	10 [18.5%]
	2	13 [24.1%]
	3	10 [18.5%]
	4	1 [1.8%]
	5	1 [1.8%]

Data is presented as mean ± or frequency [%]. TACE: Transarterial Chemoembolization

Table [3]: Survival probability, survival time, and stent patency

		95% [CI]
Survival probability	**1-year**	53.7% [41.9% - 68.8%]
	2-year	33.3% [22.9% - 48.6%]
Median survival time		381 [316 - 661%]
Stent patency probability	**1-year**	42.6% [31.3% - 58.1%]
	2-year	25.9 % [16.5% - 40.7%]
Median stent patency		243 [115- 556%]

Data is presented as median [IQR]. 95% CI: 95% Confidence Interval.

Table [4]: Analysis of predictors for different clinical outcomes

	Univariable			Multivariable		
	HR	**95% CI**	**P value**	**HR**	**95% CI**	**P value**
Predictors associated with survival						
Age	1.01	0.98 - 1.04	0.47	1.01	0.98 - 1.04	0.384
Sex [male vs. female%]	0.79	0.40 - 1.53	0.476	0.96	0.46 - 2.00	0.914
Hepatitis						
[HBV vs. No%]	0.63	0.14 - 2.83	0.547	2.14	0.39 – 11.7	0.379
[HCV vs. No%]	1.18	0.36 - 3.86	0.790	1.53	0.43 – 5.44	0.512
Child-pugh classification [B vs. A%]	1.94	1.02 -3.68	**0.042***	1.79	0.78 -4.10	0.167
Number of TACE procedures [<2 vs. ≥2 TACE%]	2.01	1.04 -3.88	**0.037***	4.01	1.72 -9.33	**<0.001***
Group [group 2 vs. group 1%]	4.87	2.27- 10.4	**<0.001***	5.7	2.16- 15.0	**<0.001***
Predictors associated with stent patency						
Age	1.01	0.97 - 1.04	0.756	1.01	0.98 - 1.05	0.424
Sex [male vs. female%]	0.73	0.38 - 1.42	0.358	0.72	0.34 - 1.50	0.375
Hepatitis						
[HBV vs. No%]	0.13	0.02 - 0.72	**0.020***	0.13	0.02 – 0.77	**0.024***
[HCV vs. No%]	0.64	0.22 - 1.81	0.397	0.53	0.18 – 1.59	0.258
Child-pugh classification [B vs. A%]	1.70	0.90 - 3.23	0.103	1.77	0.77 -4.07	0.182
Number of TACE procedures [<2 vs. ≥2 TACE%]	2.00	1.05 - 3.80	**0.034***	2.99	1.40-6.40	**0.005***
Group [group 2 vs. group 1%]	3.02	1.57 - 5.81	**<0.001***	3.14	1.47- 6.71	**0.003***
Predictors associated with tumor progression						
Age	0.99	0.94-1.04	0.641	0.99	0.93-1.05	0.704
Sex [male vs. female%]	0.63	0.17-2.09	0.457	0.40	0.07-1.91	0.270
Hepatitis						
[HBV vs. No%]	0	NA	0.994	0	NA	0.992
[HCV vs. No%]	0	NA	0.993	0	NA	0.992
Child-pugh classification [B vs. A%]	0.26	0.07-0.84	**0.030***	0.25	0.05-1.12	0.079
Number of TACE procedures [<2 vs. ≥2 TACE%]	0.58	0.18-1.74	0.337	0.23	0.04-1.01	0.061
Group [group 2 vs. group 1%]	0.23	0.06-0.74	**0.018***	0.23	0.04-0.99	0.063

HR: Hazzard ratio. OR: Odds ratio. TACE: Transarterial Chemoembolization 95% CI: 95% Confidence Interval. *: significant as P< 0.05.

The Kaplan-Meier curve for overall survival over a 1000-day follow-up shows a gradual decline in survival from nearly 100% to approximately 23%. The survival probability drops more steeply between days 250-400, from 75% to 50%, then continues to decline more gradually after day 500 [**Figure 3 A].**

Patients with Child-Pugh A demonstrated significantly better survival than those with Child-Pugh B [p=0.04]. Child-Pugh A patients maintained a survival probability of 0.8 until day 400, with a gradual decline to 0.25 by day 1000. In contrast, Child-Pugh B patients experienced a steeper decline to 0.3 by day 400, stabilizing at 0.25 afterward. The number of patients at risk decreased over time for both groups, with 23 for Child-Pugh A and 31 for Child-Pugh B at the start **[Figure 3 B].**

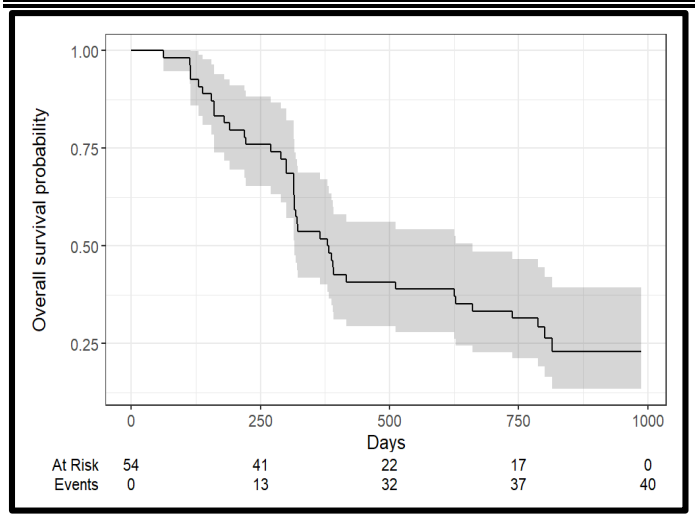
Regarding TACE procedures, there was a significant survival difference between patients with more than 2 TACE procedures [TACE ≥ 2] and those with 2 or fewer [TACE < 2] [p=0.034]. Patients with TACE ≥ 2 had better survival, maintaining a probability of 0.45 at 1000 days, while those with TACE < 2 showed a survival probability of 0.1 by 1000 days. Both groups showed a decrease in the number of patients at risk over time, with 25 in the TACE ≥ 2 group and 29 in the TACE < 2 group initially **[Figure 3 C].**

The Kaplan-Meier curve for stent patency over an 800-day follow-up shows an initial rapid decline within the first 100 days, followed by a more gradual decrease. Starting with nearly 100% patency, the probability drops to about 75% by day 100 and continues to decline steadily to approximately 25% by day 800 **[Figure 4 A].**

Significant differences in stent patency probability were observed among patients with different hepatitis statuses [p=0.032]. Hepatitis B patients demonstrated the best stent patency, maintaining a high probability [0.75-1.0] throughout the observation period. Hepatitis C patients had intermediate patency rates, while patients without hepatitis [NO] exhibited the poorest outcomes, with patency dropping to 0 by day 600. The number of patients at risk decreased over time for all groups, starting with 4 for NO, 7 for Hepatitis B, and 43 for Hepatitis C **[Figure 4 B].**

A significant difference in stent patency was also found between patients who underwent more than 2 TACE procedures [TACE ≥ 2] and those with 2 or fewer [TACE < 2] [p=0.033]. Patients with TACE ≥ 2 demonstrated better stent patency, maintaining a probability of around 0.4 at 800 days. In contrast, patients with TACE < 2 showed a decline in patency to about 0.15 by 800 days. The initial number at risk was 25 for TACE ≥ 2 and 29 for TACE < 2, with both groups showing a decrease over the follow-up period **[Figure 4 C].**

The Kaplan-Meier curve also revealed a highly significant difference in stent patency between Group 1 and Group 2 [p=0.00058]. Group 1 exhibited better stent patency, maintaining a probability of approximately 0.4 at 800 days. In contrast, Group 2 experienced a rapid decline in patency within the first 100 days, stabilizing at about 0.2 thereafter. The number of patients at risk started at 24 for Group 1 and 30 for Group 2, with Group 1 retaining more patients throughout the follow-up [13 at 600 days] compared to Group 2 [5 at 600 days] **[Figure 4 D].**



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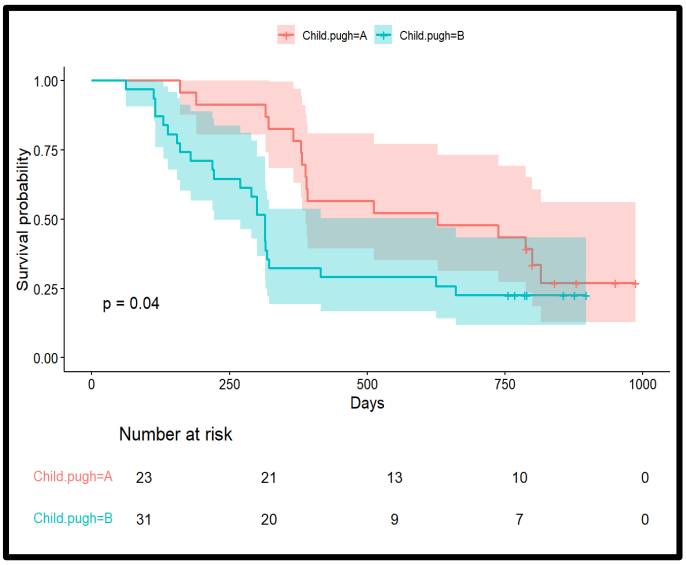

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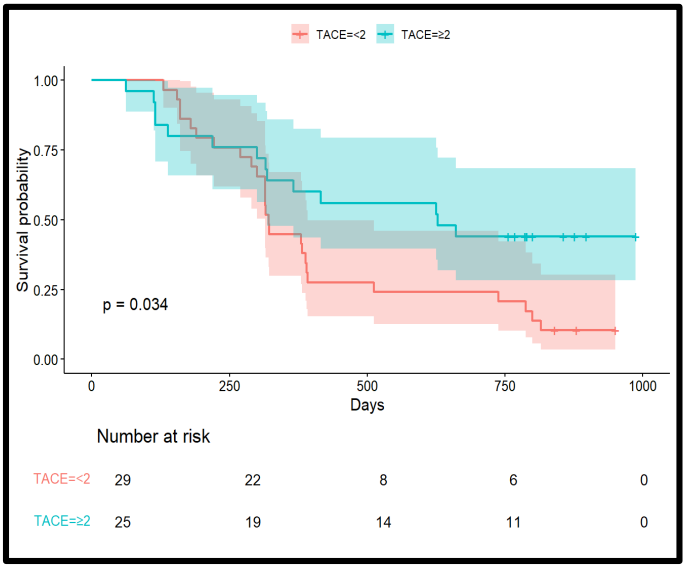
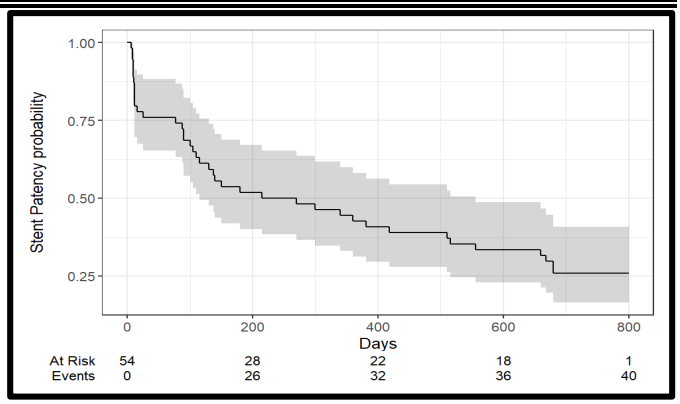


[C]

Figure [3]: Kaplan-Meier Curves for: [A] Overall Survival Rate, [B] Survival Probability by Child-Pugh Classification, and [C] Survival Probability According to Number of TACE Procedures



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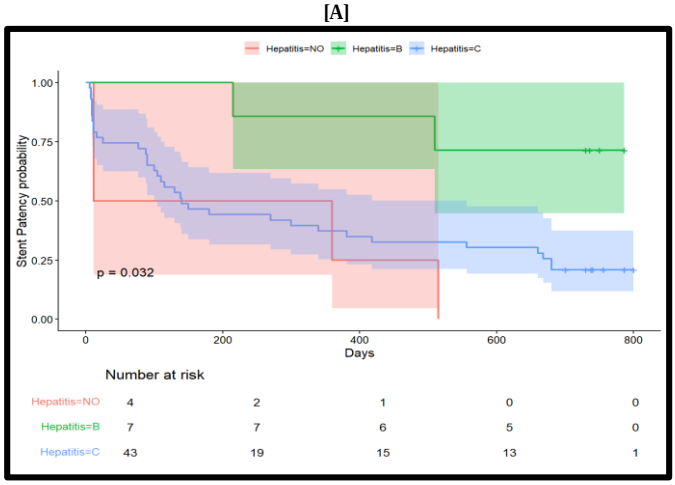

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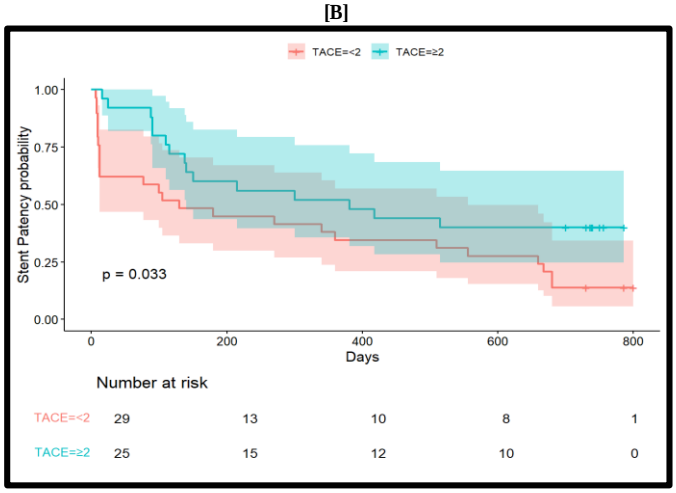

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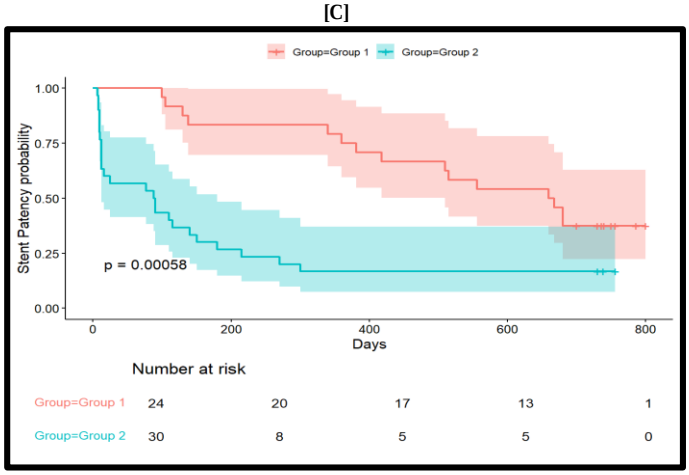

[D]

Figure [4]: Kaplan-Meier Curves for [A] Overall Stent Patency, [B] Stent Patency according to hepatitis virus, [C] Survival Probability according to Number of TACE Procedures, and [D] Survival Probability according to group.

The cumulative incidence curve demonstrates the local tumor progression rate over a 20-month follow-up period. The curve shows a gradual increase in tumor progression, starting at approximately 5 months. Initially, there were 58 patients at risk with no events. By 10 months, 46 patients remained at risk with 3 events recorded. At 15 months, the number at risk decreased to 24 patients with 10 events, and by 20 months, 10 patients remained at risk with 15 events total. The cumulative tumor progression rate reached approximately 45% by the end of the follow-up period, with the grey shading representing the 95% confidence interval. The curve suggests a steady increase in tumor progression risk over time, with the steepest rise occurring between 10-20 months **[Figure 5].**

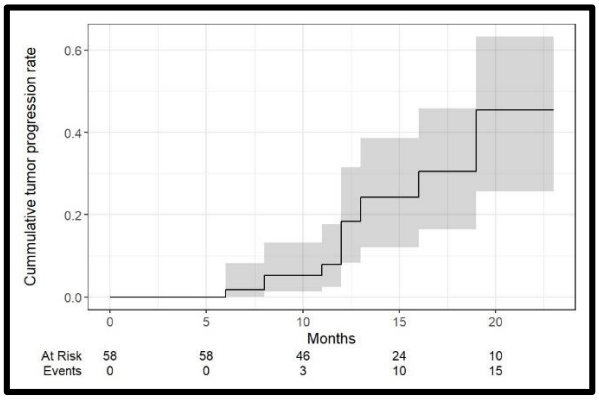

Figure [5]: Cumulative incidence curve for the local tumor progression rate.

DISCUSSION

TACE is widely regarded as the standard first-line treatment for unresectable HCC. However, PVTT significantly reduces its therapeutic efficacy. PVTT exacerbates the obstruction of the portal vein, which can compromise hepatic blood flow and elevate the risk of liver failure **[10].** The treatment of unresectable HCC with TACE is aided by the fact that, unlike normal liver tissue, HCC tumors primarily receive their blood supply from the HA, while the normal liver is supplied by both the HA and the PV **[11].** This unique blood supply characteristic allows for selective targeting of the tumor during TACE. However, the presence of PVTT in HCC patients can serve as a predictive factor for acute hepatic failure following TACE, as it exacerbates PV obstruction and reduces liver function **[12, 13].** PVS placement is a promising therapeutic option for HCC patients with main PVTT, as it helps restore portal flow and alleviate portal hypertension. This approach addresses the difficulties of treating advanced HCC with MVI, where conventional therapies typically provide limited success. When combined with other treatments, PVS has been linked to improved survival outcomes **[14].**

In the present analysis, the mean stent diameter was 10.54 ± 1.22 mm, and the mean length was 10 ± 0 mm. Consistent with our findings, **Yu *et al.*** **[15]** reported that, in group-A patients, an average of 16.1 ± 5.3 Iodine-125 seeds [range: 6–26] were implanted in the MP. As part of this study, the mean portal vein pressure was 30.10 ± 4.83 mmHg before stenting, which significantly decreased to 18.42 ± 2.56 mmHg after stenting [P < 0.001]. Consistent with our findings, Yu et al. [15] demonstrated that, following stent placement, the mean pressure in the MPV decreased from 40.6 ± 5.2 cm H_2O [range 28–55 cm H_2O] to 34.5 ± 5.0 cm H_2O [range 25–44 cm H2O] [P < 0.001] in group A, and from 41.8 ± 5.8 cm H_2O [range 31–57 cm H_2O] to 35.3 ± 4.9 cm H_2O [range 26–45 cm H_2O] [P < 0.001] in group B. In addition, Zhang et al. [16] reported that portal vein pressure in 55 patients was measured before [42.73 ± 8.25 cm H_2O] and after stent implantation [36.73 ± 8.14 cm H_2O], showing a significant decrease in mean portal venous pressure by 6.00 ± 4.63 cm H_2O [P < 0.001].

In this research, the mean time to TACE was 5.16 ± 3.29 weeks, and the mean dose administered was 30.0 ± 6.93. **Tan *et al.*** **[17]** reported that an average of 3.1 ± 1.4 sessions of TACE in the PVIS plus TACE group, which is slightly lower than ours. Also, Yu et al. [15] showed that a mean number of 3.3 ± 1.9 sessions of TACE [range 1–9] were performed in Group A and 3.6 ± 2.2 [range 1–10] in Group B [P = 0.231] patients. The mean dose of epirubicin and iodized oil used in the TACE procedure was 26.7 ± 7.1mg [range 10–40 mg], 9.5± 4.1ml [range 2–20 ml] in Group A and 26.0 ± 7.9mg [range 10–40 mg], 9.3 ± 4.3 [range 3–16 ml] in Group B [P = 0.557 and 0.771], respectively

As part of this study, the 1-year survival probability for patients was 53.7% [95% CI: 41.9% - 68.8%], while the 2-year survival probability was 33.3% [95% CI: 22.9% - 48.6%]. The median survival time for patients was 381 days [95% CI: 316 - 661%]. The Kaplan-Meier curve for overall survival over a 1000-day follow-up shows a gradual decline in survival from nearly 100% to approximately 23%. The survival probability drops more steeply between days 250-400, from 75% to 50%, then continues to decline more gradually after day 500.

Consistent with our findings, **Tan *et al.*** **[17]** reported that at a median follow-up of 14.3 [range, 1.2-60] months, the median OS was 13.1 [95% CI: 9.8 -16.4] months. In accordance with our observations, Liang et al. [18] found that the Kaplan–Meier survival curve analysis indicated that the median survival time was 8.3 months [95% confidence interval, 95% CI, 4.3–11.0]. Survival rate at 6, 12, 18 and 24 months was 56.6%, 31.5%, 21.9% and 13.1%, respectively. However, Sun et al. [19] noted that the 90-, 180-, and 360-day cumulative survival rates were 94.1%, 61.8%, and 32.4%. The median survival time was 147 days. While both studies report significant survival declines, the exact survival rates and median survival times differ, likely due to differences in follow-up duration, treatment approaches, or patient characteristics.

In this research, in univariate analysis, Child-Pugh classification, the number of TACE procedures, and group were significant predictors for better survival outcomes. Other variables that did not show significant associations include age, sex, and hepatitis status [HBV or HCV]. Consistent with our findings, **Jeong *et al.*** **[20]** found that Child-Pugh classification [HR, 1.606; 95% CI, 1.130 to 2.283; p=0.008], was significant predictors for better survival outcomes. Other variables that did not show significant associations include age, sex, and hepatitis status [HBV or HCV]. **Yu *et al.*** **[15]** demonstrated that in univariate analysis, the number of TACE procedures, and group were significant predictors for better survival outcomes. Other variables that did not show significant associations include age, and sex.

In the present analysis, the Kaplan-Meier curve demonstrates that patients with Child-Pugh A showed significantly better survival compared to Child-Pugh B [p=0.04]. Patients with Child-Pugh A showed better survival outcomes, maintaining a probability of approximately 0.8 until 400 days and gradually declining to 0.25 by 1000 days. In contrast, Child-Pugh B patients exhibited poorer survival, with a steeper decline to about 0.3 by 400 days and stabilizing around 0.25 thereafter. The initial number at risk was 23 for Child-Pugh A and 31 for Child-Pugh B, with both groups showing a progressive decrease over time [Child-Pugh A: 21 at 250 days, 13 at 500 days, 10 at 750 days; Child-Pugh B: 20 at 250 days, 9 at 500 days, 7 at 750 days]. Consistent with our findings, Lv et al. [21] noted that Child-Pugh A patients had higher cumulative survival rates [e.g., 6-month survival of 63.4% vs. 44.5% for Group A and B, respectively] and longer median survival times [e.g., 8.79 vs. 5.44 months for Group A and Group B]. In alignment with our results, Zhang et al. [16] stated that the Kaplan-Meier survival curve shows a significant difference [P<0.01] in survival between Child-Pugh A and B patients after PTPVS-TACE treatment. Child-Pugh A patients [n=37] demonstrated better survival rates, maintaining around 20% survival even at 1000 days' post-treatment. In

contrast, Child-Pugh B patients [n=21] showed poorer outcomes, with survival dropping rapidly within the first 200 days and reaching 0% by approximately 400 days. Child-Pugh classification is a prognostic factor for survival outcomes in patients receiving this treatment.

Study	Sample Size	Publication Year	Treatment Protocol	Key Outcomes
Yu et al. [15]	176 [Group A: 133, Group B: 43]	2017	Combination of PVS placement and TACE with Iodine-125 seed implantation in the Main Portal Vein [MPV]	- **Portal Vein Pressure:** Decreased from 40.6 ± 5.2 cm H_2O to 34.5 ± 5.0 cm H_2O in Group A and from 41.8 ± 5.8 cm H_2O to 35.3 ± 4.9 cm H_2O in Group B post-stenting [P < 0.001]. - **Stent Patency:** Mean stent patency was 14.7 ± 1.0 months in Group A and 9.6 ± 0.8 months in Group B. - **TACE Procedures:** Average of 3.3 ± 1.9 sessions in Group A and 3.6 ± 2.2 sessions in Group B [P = 0.231].
Tan et al. [17]	105	2021	PVIS plus TACE	- **Survival:** Median Overall Survival [OS] was 13.1 months [95% CI: 9.8 - 16.4 months] with a median follow-up of 14.3 months. - **Stent Patency:** Blood flow of the PVIS remained patent throughout the survival period in 42 patients [40 deceased, 2 alive]; stent occlusion occurred in 11 patients.
Zhang et al. [16]	55	2009	Stent implantation followed by TACE	- **Portal Vein Pressure:** Decreased from 42.73 ± 8.25 cm H_2O before stenting to 36.73 ± 8.14 cm H_2O after stenting [P < 0.001]. - **Survival:** Median survival time was 8.3 months [95% CI: 4.3–11.0 months]. - **Stent Patency:** Significant difference in survival between Child-Pugh A and B patients [P < 0.01].
Jeong et al. [20]	200	2017	TACE with or without PVS	- **Survival Predictors:** Child-Pugh classification was a significant predictor for better survival outcomes [HR, 1.606; 95% CI: 1.130 to 2.283; p=0.008]. - **Non-Significant Factors:** Age, sex, and hepatitis status [HBV or HCV] were not significant predictors.
Liang et al. [18]	100	2017	PVS followed by TACE	- **Survival:** Median survival time was 8.3 months [95% CI: 4.3–11.0 months]. - **Kaplan-Meier Survival Rates:** 6-month: 56.6%, 12-month: 31.5%, 18-month: 21.9%, 24-month: 13.1%.
Sun et al. [19]	80	2016	TACE alone vs. TACE with lenvatinib and PD-1 blockades	- **Survival Rates:** 90-day: 94.1%, 180-day: 61.8%, 360-day: 32.4%. - **Median Survival Time:** 147 days. - **Comparison:** TACE combined with lenvatinib and PD-1 blockades showed better survival rates compared to TACE alone.
Lv et al. [21]	150	2018	TACE combined with PVS	- **Survival Rates:** 6-month survival of 63.4% [Group A] vs. 44.5% [Group B]. - **Median Survival Times:** 8.79 months [Group A] vs. 5.44 months [Group B].
Kim et al. [26]	120	2009	Repeated TACE in patients with portal vein invasion	- **Survival:** Median survival reached 10.2 months with repeated TACE compared to 2.3 months with conservative management. - **Outcome:** Repeated TACE associated with substantial survival benefits.
Herber et al. [27]	130	2007	Sequential TACE treatments	- **Prognostic Factors:** Number of TACE procedures performed was an independent prognostic factor for survival. - **Analysis:** Used Cox Proportional Hazard Model to identify prognostic factors.
Li et al. [28]	30	2020	PVS combined with [125]I particle chain implantation followed by as[2]o[3]	- **Tumor Progression:** 53.3% with progression vs. 46.7% without progression. - **Survival:** 40% mortality rate, 23.7% survival rate. - **Comparison:** Differences in outcomes attributed to treatment approaches and patient characteristics.
Ren et al. [22]	[Not Specified]	2019	TACE combined with radiofrequency ablation	- **Clinical Outcome:** Improved clinical outcomes using TACE combined with radiofrequency ablation for patients in Barcelona Clinic Liver Cancer stage A or B regardless of tumor size. - **Study Type:** Single-center retrospective case-control study.

In the course of this work, patients with Child-Pugh A demonstrated significantly better survival than those with Child-Pugh B [p=0.04]. Child-Pugh A patients maintained a survival probability of 0.8 until day 400, with a gradual decline to 0.25 by day 1000. In contrast, Child-Pugh B patients experienced a steeper decline to 0.3 by day 400, stabilizing at 0.25 afterward. The number of patients at risk decreased over time for both groups, with 23 for Child-Pugh A and 31 for Child-Pugh B at the start. Consistent with our findings, **Liang *et al.*** [18] demonstrated that the median survival time was 3.4 months for subjects with progressive response and 11.0 months for subjects with disappeared or stable disease. Result of log-rank test showed significant differences in survival rate between two groups [P <0.001]. Additionally, **Kim *et al.*** [26] exhibited that repeated TACE has been associated with substantial survival benefits, particularly in patients with portal vein invasion, where median survival reached 10.2 months compared to 2.3 months for conservative management Moreover, **Herber *et al.*** [27] analyzed the course of disease of patients treated with sequential TACE and to evaluate the dependent and independent prognostic factors for patient survival using the Cox Proportional Hazard Model. They indicated that independent prognostic factors for survival include the number of TACE procedures performed.

At the end of the study, stent occlusion was observed in 40 [67.8%] patients, while 14 [23.7%] patients did not experience occlusion. Tumor progression occurred in 33 [55.9%] patients, and 21 [35.6%] showed no progression. Forty [67.8%] patients died, with 14 [23.7%] surviving. The 1-year probability of stent patency is 42.6% [95% CI: 31.3% - 58.1%], while the 2-year probability decreases to 25.9% [95% CI: 16.5% - 40.7%]. The median stent patency time was 243 days [95% CI: 115-556 days]. The mean stent patency duration was 18.36 ± 2.53 months.

In alignment with our results, **Tan *et al.*** [17] reported that by the end of the follow-up period, the blood flow of the PVIS remained patent throughout the survival period in 42 patients [40 dead, 2 living]. Stent occlusion was observed in 11 patients. Also, **Yu *et al.*** [15] stated that stenosis and occlusion of the MPV were found in 133 [75.6%] and 43 [24.4%] patients, respectively. The mean and median stent patency period were 14.7 ± 1.0 months [95 % CI 12.7–16.8 months], 10.3 ± 1.1 months [95 % CI 8.1–12.5 months] in group A and 9.6 ± 0.8 months [95 %CI 8.1–11.2 months], 8.7 ± 0.7 months [95 % CI 7.4 –10.0 months] in group B, respectively. The 12- and 24-month cumulative stent patency rates were 46.5%, 25.7 % in group A and 29.8%, 0% in group B, respectively.

Opposing our investigations, **Li *et al.*** [28] noticed that tumor progression occurred in 16 [53.3%] patients, and 14 [46.7%] showed no progression. Forty [67.8%] patients died, with 14 [23.7%] surviving. The survival outcomes showed that 40% [12/30] of the patients died, and 23.7% [14/30] survived. The differences in tumor progression and survival rates could be attributed to variations in treatment approaches, patient characteristics, or the stage of disease at the time of treatment.

This study is the first to identify through univariate analysis that HBV status, the number of TACE procedures, and group were significant predictors of better stent patency outcomes. However, other variables such as age, sex, HCV status, and Child-Pugh classification did not show significant associations with stent patency.

Notably, HBV status emerged as a critical factor, with patients exhibiting HBV positivity showing improved stent patency. Additionally, the number of TACE procedures performed was positively associated with stent patency, suggesting that repeated interventions may enhance vascular outcomes [29]. Furthermore, the grouping of patients based on treatment protocols also influenced stent patency, indicating that tailored treatment strategies could optimize results [30].

Within this investigation, the Kaplan-Meier curve illustrates the overall stent patency probability over an 800-day follow-up period. The curve shows a rapid initial decline in the first 100 days, followed by a more gradual decrease thereafter. Starting at nearly 100% patency, the probability drops to approximately 75% by day 100, then continues to decline steadily to about 25% by day 800.

This trend likely reflects the interplay between early thrombotic or tumor-related occlusion and the gradual development of treatment resistance or complications over time. Li et al. [28] reported that the Kaplan-Meier curve showed an overall stent patency probability over a 20-month follow-up period, with a mean stent patency duration of 8.4 ± 4.2 months [range, 2–17 months], and cumulative stent patency rates at 3, 6, 9, and 12 months of 83.1%, 69.2%, 43.7%, and 31.2%, respectively.

In the present analysis, the Kaplan-Meier curve shows significant differences in stent patency probability among patients with different hepatitis statuses [p=0.032]. Hepatitis B patients demonstrated the best stent patency over time, maintaining a higher probability [around 0.75-1.0] throughout the observation period. Hepatitis C patients showed intermediate patency rates, while patients without hepatitis [NO] had the poorest stent patency outcomes, dropping to 0 by 600 days. The number of patients at risk decreased over time in all groups, with initial numbers being 4 [NO], 7 [Hepatitis B], and 43 [Hepatitis C] patients respectively.

Several studies [31, 32] have suggested that hepatitis B-related cirrhosis tends to have better vascular integrity, which could contribute to prolonged stent patency. On the other hand, hepatitis C-related cirrhosis is often associated with more severe fibrosis and portal hypertension, which could lead to poorer outcomes after PVS [33]. The poorest outcomes in non-hepatitis patients could reflect the lack of an inflammatory or viral component, leading to a different pathophysiology of the liver parenchyma, which may not respond well to stent implantation [34].

In the course of this work, the Kaplan-Meier curve demonstrates a statistically significant difference in stent patency between patients with TACE ≥ 2 versus TACE<2 [p=0.033]. Patients who underwent more than or equal 2 TACE procedures [TACE ≥ 2] showed better stent patency, maintaining a probability of approximately 0.4 at 800 days. In contrast, patients with TACE < 2 exhibited poorer stent patency, declining to around 0.15 by 800 days. The initial number of patients at risk was 25 for TACE ≥ 2 and 29 for TACE < 2, which gradually decreased over the follow-up period. These findings align with previous research [35, 36], which suggests that multiple TACE sessions are associated with better local tumor control and longer stent patency.

As part of this study, the Kaplan-Meier curve demonstrates a highly significant difference in stent patency between Group 1 and Group 2 [p=0.00058]. Group 1 showed markedly better stent patency, maintaining a probability of approximately 0.4 at 800 days, while Group 2 exhibited a rapid decline in patency within the first 100 days, stabilizing at around 0.2 thereafter. The number of patients at risk started at 24 for Group 1 and 30 for Group 2, with Group 1 retaining more patients throughout follow-up [13 at 600 days] compared to Group 2 [5 at 600 days].

Studies indicate that a longer interval between TACE sessions associated with improved OS in patients with unresectable HCC, with median OS extending from 8.7 months in short-interval groups to 12.1 months in long-interval groups [19, 37]. Additionally, combining PVS with TACE has shown promising results, with stent patency rates remaining high and significant survival benefits observed in patients with PVTT [17].

In this study, the cumulative incidence curve demonstrates the local tumor progression rate over a 20-month follow-up period. The curve shows a gradual increase in tumor progression, starting at approximately 5 months. Initially, there were 58 patients at risk with no events. By 10 months, 46 patients remained at risk with 3 events recorded. At 15 months, the number at risk decreased to 24 patients with 10 events, and by 20 months, 10 patients remained at risk with 15 events total. The cumulative tumor progression rate reached approximately 45% by the end of the follow-up period, with the grey shading representing the 95% confidence interval. The curve suggests a steady increase in tumor progression risk over time, with the steepest rise occurring between 10-20 months.

The findings regarding PVTT as a significant determinant of HCC prognosis are well-supported in the literature. PVTT is associated with advanced disease stages and poor OS, with median OS varying significantly based on the extent of PVTT, as shown in a Western cohort where patients with more limited PVTT had better outcome [38]. The classification of PVTT into four categories [Vp1 to Vp4] associated closely with prognosis, influencing treatment decisions and outcomes across various therapeutic modalities [39,40]. Systemic therapies, particularly sorafenib and lenvatinib, have demonstrated improved survival rates in patients with macrovascular invasion, yet the effectiveness of combined treatment approaches, such as TACE with systemic therapy, has shown promise in enhancing survival [41, 42].

This study is the first to report that, in univariate analysis, Child-Pugh classification, treatment group [timing of PVS and TACE], and the number of TACE procedures are significant predictors of tumor progression in patients with HCC and PVTT.

The Child-Pugh classification is crucial in managing HCC as it directly influences treatment tolerance and outcomes. Patients classified as Child-Pugh B exhibit poorer liver function, which associated with reduced overall survival and response rates to treatments like TACE and PVS [43, 44]. Specifically, a two-week interval between PVS and TACE allows for recovery, enhancing treatment efficacy and potentially improving tumor control [19]. Moreover, the frequency of TACE procedures significantly affects tumor progression, with multiple sessions providing better control than a single treatment [16]. In contrast, demographic factors such as age, sex, and hepatitis status did not significantly impact tumor progression, suggesting that liver function and disease stage are more critical determinants of treatment outcomes [44, 45].

This study has several limitations: it was a single-center, small-sample study with a short follow-up period, which may limit its generalizability and long-term outcome assessment. The inclusion of only Child-Pugh Class A or B patients may overestimate the treatment's feasibility and therapeutic value, excluding those with more advanced liver disease.

Our findings indicated that performing two or more TACE procedures and extending the interval between PVS and TACE beyond two weeks are

significant predictors of improved survival and prolonged stent patency. Specifically, patients receiving multiple TACE treatments exhibited markedly better survival [HR = 4.01, P < 0.001] and extended stent functionality [HR = 2.99, P = 0.005]. Additionally, those classified in Group 2, with a longer interval between PVS and TACE, demonstrated enhanced survival [HR = 5.7, P < 0.001] and better stent outcomes [HR = 3.14, P = 0.003] compared to Group 1.

These results align with previous studies that emphasize the importance of repeated TACE sessions in managing HCC with PVTT. Multiple TACE procedures have been associated with sustained tumor control and delayed disease progression, contributing to improved survival rates [22, 23]. The timing of TACE relative to PVS appears to play a crucial role in optimizing clinical outcomes. A longer interval between PVS and TACE may allow for better stabilization of portal hemodynamics and enhanced efficacy of subsequent embolization **[24].**

Our multivariate analysis did not identify age, sex, hepatitis status [HBV or HCV], or Child-Pugh classification as significant predictors of survival or stent patency. This suggests that the therapeutic interventions of TACE and PVS may mitigate the impact of these demographic and clinical variables on patient outcomes. However, in the univariate analysis, factors such as Child-Pugh classification and group classification were significant predictors of tumor progression, although they did not retain significance in the multivariate model.

The lack of significant predictors for tumor progression in the multivariate analysis may be attributable to the relatively small sample size, which limits the statistical power to detect subtle associations. Additionally, tumor biology and molecular characteristics, which were not assessed in this study, likely play pivotal roles in disease progression and could confound the observed outcomes **[25].**

In conclusion, PVS significantly reduced portal vein pressure and improved the effectiveness of subsequent TACE, with generally low complication rates. The 1-year survival probability was 53.7%, and the 2-year probability was 33.3%, with better outcomes seen in patients with Child-Pugh Class A liver function and those undergoing more than two TACE procedures. However, tumor progression occurred in 55.9% of patients, and stent patency declined over time, with a 1-year patency probability of 42.6%. Hepatitis B patients had the best stent patency, and frequent TACE procedures were linked to better survival and stent outcomes. Key survival and stent patency predictors included liver function [Child-Pugh classification] and the number of TACE procedures.

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