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Original Article

Predicting venous thromboembolism risk after TACE in hepatocellular carcinoma: a logistic model and nursing protocol development

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Abstract: Objective: To identify risk factors for venous thromboembolism (VTE) after transcatheter arterial chemoembolization (TACE) in patients with hepatocellular carcinoma (HCC), and to establish a personalized risk prediction nomogram. Methods: A single-center retrospective analysis was performed on 322 consecutive HCC patients who received TACE at Baoji Central Hospital from December 2020 to December 2024. Patients were categorized into a VTE group (n=54) and a non-VTE group (n=268) based on the occurrence of VTE within 7 days post-procedure. Demographic, clinical, and laboratory data were gathered. Pearson correlation and variance inflation factor analyses were applied to evaluate multicollinearity, while logistic regression was used to identify independent risk factors. A nomogram and dynamic prediction model were developed from regression coefficients to quantify individualized risk and guide a structured five-phase nursing intervention plan. Results: Multivariate analysis revealed that elevated D-dimer (DD) levels (OR=1.006), age ≥60 years (OR=0.361), Child-Pugh class C (OR=0.371), ECOG performance score 1-2 (OR=0.361), and multiple TACE sessions (OR=2.847) were independent predictors of post-TACE VTE (all P<0.05). The nomogram showed good calibration and strong discrimination (AUC=0.828). The decision-curve analysis also showed that it had a good net clinical benefit. The developed nursing protocol incorporates risk assessment, dynamic DD monitoring, early mobilization, hepatic function support, and patient education to facilitate risk management. Conclusion: D-dimer level, age, Child-Pugh classification, ECOG status, and the frequency of TACE are all important factors affecting post-TACE VTE. The suggested prediction model is accurate and useful in clinical practice, offering valuable insights into early VTE risk stratification and perioperative safety assessment.

Keywords: Hepatocellular carcinoma, transcatheter arterial chemoembolization, venous thromboembolism, logistic regression, nomogram, and nursing intervention

Introduction

Hepatocellular carcinoma (HCC) accounts for most primary liver cancers and remains a major cause of cancer mortality worldwide. The 2022 GLOBOCAN report estimates nearly one million cases and more than 800,000 deaths annually [1]. For patients with intermediate-stage disease under the Barcelona Clinic Liver Cancer framework, and for selected patients with unresectable or recurrent tumors, transarterial chemoembolization (TACE) is widely used as standard locoregional therapy and is also used as a bridge to transplantation or tumor downstaging [2, 3]. Contemporary TACE pairs selective intra-arterial chemotherapy with embolic microspheres delivered through microcatheters to induce ischemic tumor necrosis; next-generation, more flexible embolic platforms and combination strategies such as TACE plus radiofrequency ablation are being explored to enhance intratumoral drug exposure and local control [2, 3]. Despite these advances, post-procedural complications still shape recovery, length of stay, and costs, especially in patients with cirrhosis whose hemostasis is rebalanced rather than autoanticoagulated.

Venous thromboembolism (VTE), including deep vein thrombosis and pulmonary embolism, is a clinically important complication in oncology, associated with recurrence, prolonged hospitalization, and mortality [5, 7]. The VTE risk profile in HCC patients undergoing TACE may

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be distinct. Catheter manipulation of the hepatic artery, procedure-related endothelial injury, transient immobility, central venous access, systemic inflammation, and tumor-derived procoagulant activity can collectively increase thrombotic risk, while portal hypertension and thrombocytopenia raise bleeding concerns [2, 5]. Evidence quantifying VTE specifically after TACE is limited; most prior work addresses perioperative thrombosis or systemic therapy cohorts, or examines patterns of recurrent cancer-associated thrombosis by metastatic site rather than after locoregional interventions [4]. Antithrombotic strategies include low-molecular-weight heparin (LMWH) and direct oral anticoagulants (DOACs). Emerging data support low-dose DOACs for secondary prophylaxis in selected high-risk states, yet their safety and effectiveness in cirrhosis and in the immediate post-TACE period remain uncertain [6, 7].

Methodologic gaps compound this uncertainty. Published studies are often single-center and small, rely predominantly on univariate associations, use heterogeneous at-risk windows, and rarely perform internal validation. Candi date predictors are inconsistently captured, and definitions of clinically relevant VTE - whether symptomatic events, imaging-confirmed thrombosis, or inpatient vs. post-discharge occurrences - vary across reports. As embolic materials and delivery systems evolve [2], it remains unclear whether procedural characteristics exert independent effects on thrombotic risk. Consequently, substantial practice variability persists in post-TACE monitoring and prophylaxis, with no risk-stratified framework currently available to balance thrombosis prevention against bleeding in liver disease.

This retrospective cohort study was conducted to define the burden and determinants of VTE after TACE in patients with HCC. The primary endpoint was symptomatic, imaging-confirmed VTE occurring during the index hospitalization or within 90 days of the procedure, a window aligned with clinical relevance in VTE care [5, 7]. We prespecified clinically plausible predictors - demographics; liver function (Child-Pugh class, ALBI grade); tumor burden and portal vein invasion; prior VTE; performance status; catheterization details and embolic type; and peri-procedural factors including central venous access and immobilization. Using multivariable logistic regression, we identified independent predictors and derived a parsimonious risk score, with internal validation, to support targeted surveillance and prophylaxis pathways in routine care. By anchoring decisions to measurable risk, this work aims to reduce preventable thrombotic events without compromising procedural safety.

Methods and materials

Sample size calculation

Chen [8] and Lei [9] et al. found that the rate of VTE in patients ranges from 10.3% to 18.6%. Using the formula $N=Z^2 \times [P \times (1-P)]/E^2$ for both extreme values, with Z=1.96 and E=0.05, the sample sizes needed was calculated to be 142-232 cases.

Patient information

This single-center retrospective study was conducted at Baoji Central Hospital (Baoji, Shaanxi Province, China), where 322 consecutive patients with HCC who underwent TACE between December 2020 and December 2024 were enrolled. Patients were divided into two groups based on whether or not they had VTE: the VTE group (n=54) and the N-VTE group (n=268). This study was approved by the Ethics Committee of Baoji Central Hospital.

VTE diagnostic criteria

Ultrasound diagnosis of VTE mainly depends on two-dimensional greyscale imaging and color Doppler flow imaging methods. The Philips EPIQ 7 color Doppler ultrasound diagnostic system was applied, featuring 5-12 MHz high-frequency linear array probes, for an extensive evaluation of the lower extremity deep venous systems, encompassing the femoral, popliteal, and posterior tibial veins. All participants underwent ultrasound screening within 7 days following TACE treatment to assess acute postoperative venous thrombotic events (**Figure 1**). The primary diagnostic criterion was venous non-compressibility, characterized by the inability of venous lumens to fully occlude under compression, signifying thrombus formation. On greyscale imaging, thrombi appeared as either hypoechoic or isoechoic masses that filled lumens and dilated the venous lumen. Color Doppler showed reduced or absent intraluminal flow signals, while spectral Doppler was used to assess changes in blood flow, including

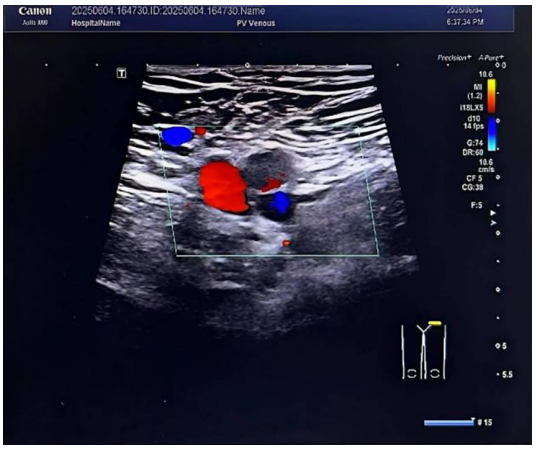

Figure 1. Philips EPIQ 7 color doppler ultrasound system for VTE detection. Note: The lumen of the left femoral vein is indistinct, with low echogenic filling observed inside the lumen, and no significant blood flow signal detected. This suggests the possible presence of thrombus formation within the left femoral vein.

changes in flow waveforms during Valsalva manoeuvres or responses to distal compression.

Inclusion and exclusion criteria

Inclusion criteria: Primary HCC confirmed by imaging and/or pathological diagnosis, meeting relevant standards from "HCC Diagnosis and Treatment Guidelines (2019)" [10]; completion of at least one transcatheter TACE treatment between December 2020 and December 2024; Child-Pugh classification B or C; ECOG performance status 0-2; completion of post-TACE lower extremity venous ultrasonography with complete VTE diagnostic data (limited to lower-extremity deep vein thrombosis); and availability of complete clinical data.

Exclusion criteria: Pre-TACE diagnosis of deep vein thrombosis, pulmonary embolism, or other venous thromboembolic diseases; concurrent active bleeding or use of anticoagulant/antiplatelet medications interfering with thrombosis assessment; coexisting malignancies or severe cardiovascular, cerebrovascular, or respiratory system diseases.

Clinical data collection

All study data were derived from the electronic medical record system and outpatient follow-up records of our hospital. The research team conducted a retrospective analysis of extensive medical records from primary HCC patients receiving TACE treatment between December 2020 and December 2024, collecting essential demographic data, hepatic function status, tumor characteristics, treatment details, and thrombosis-related indicators. Two or more researchers reviewed all materials to ensure data accuracy and comprehensiveness. The primary data collected included: general information such as age, sex, body mass index (BMI), smoking history, alcohol consumption, diabetes mellitus, and hypertension. Liver functional reserve was assessed using the Child-Pugh classification (grades B or C). Tumor-related variables included maximum dimension, the quantity of nodules, and the presence of a portal vein tumor thrombus. The ECOG scale was used to evaluate performance status. The treatment protocol encompassed TACE sessions and the duration of postoperative bed rest. Thrombosis-related indicators included postoperative D-dimer levels. The incidence of post-TACE venous thromboembolism was evaluated using Philips EPIQ 7 system.

Outcome measurements

The primary outcome was the occurrence of VTE within 7 days of TACE. With VTE occurrence being taken as the dependent variable, logistic regression analysis was performed to identify independent variables for post-TACE VTE. VTE nursing protocols were developed utilizing outcome variables from logistic regression models.

Secondary outcomes: The correlations among baseline characteristics were evaluated, and a nomogram predictive model was established, with its predictive performance validated.

Nursing protocol construction

This study developed a nursing intervention program to prevent VTE, based on independent risk factors identified through logistic regression analysis: DD levels, age, Child-Pugh classification, ECOG score, and TACE frequency. The protocol incorporates individual patient risk assessment and evidence-based nursing principles, establishing a management process that includes risk identification, stratified intervention, dynamic monitoring, and quality checks. This study aims to enhance effectiveness of postoperative nursing care. The protocol consists of five main parts: 1) initial assess-

Table 1. Structure of post-TACE VTE nursing intervention protocol based on risk factors

Phase	Module Name	Content Description
Phase I	Initial Assessment	Collect patient baseline data (age, gender, diagnosis type, etc.) and conduct VTE risk screening within 1 week post-operatively.
Phase II	Risk Factor Stratification Assessment	Target five validated independent risk factors (elevated D-dimer, ≥60 years, Child-Pugh grade C, ECOG score 1-2, multiple TACE procedures) for individual scoring and grading, identifying high-risk populations.
Phase III	Individualized Nursing Intervention Measures	Establish intervention priorities according to different risk characteristics, including: ▪ Motor function intervention (encouraging early ambulation) ▪ Medication observation and compliance assessment ▪ Dynamic D-dimer monitoring ▪ Nutritional support and hepatic function management ▪ Individualized education and psychological intervention.
Phase IV	Continuous Dynamic Monitoring and Adjustment	Daily ward monitoring + post-discharge follow-up: Focus on observing thrombotic symptoms, behavioral compliance, laboratory indicators, post-discharge medication adherence, etc., with dynamic intervention strategy adjustments.
Phase V	Nursing Process Quality Control and Evaluation Summary	Establish nursing quality assessment indicator systems, monthly evaluation of VTE incidence, nursing compliance rates, patient satisfaction, etc., serving as performance assessment criteria.

Note: VTE: Venous Thromboembolism, TACE: Transarterial Chemoembolization, BMI: Body Mass Index, ECOG: Eastern Cooperative Oncology Group.

ment, 2) risk factor stratification, 3) nursing intervention measures, 4) continuous monitoring and adjustment, and 5) quality control and performance evaluation. **Tables 1** and S1 provide information about structural diagrams and implementation processes.

Statistical analysis

R language (version 4.3.3) was used for statistical analyses and figure illustration. The main R packages used included *dplyr, readxl, openxlsx, car, pROC, rms, dcurves, ggplot2, cowplot, ggtext, GGally, broom, forestplot, and tibble*. *readxl* and *openxlsx* were first used to import electronic medical records and follow-up data. Then, *dplyr* and *tibble* were employed to classify, record, and handle missing values. For descriptive statistics, continuous variables were represented as means ± standard deviations or medians with interquartile ranges, whereas categorical variables were displayed as frequencies and percentages. Inter-group comparisons utilized t-tests, Mann-Whitney U tests, chi-square tests, or Fisher's exact tests, depending on data distribution characteristics. *GGally* analysis showed the correlations between different variables, and *car::vif()* was used to check for multicollinearity among the independent variables. Logistic regression analysis employed *glm()* functions, with regression results obtained via broom for odds ratios (OR) and confidence intervals (CI), while forest plots were created to illustrate multivariate analysis outcomes. Nomograms were created from regression models using the *rms* package to predict VTE risk for each person. Model discrimination was tested using receiver operating characteristic (ROC) curves and AUC calculations from pROC, and goodness-of-fit was tested using Bootstrap calibration curves. The clinical applicability of the model was assessed via decision curve analysis (DCA) utilizing the *dcurves* package. *ggplot2* and its extension packages were used to customize all of the statistical visualizations. $P<0.05$ indicated statistical significance.

Results

Baseline characteristics of patients with and without post-TACE VTE

Among patients with HCC, several demographic and clinical indicators differed between those who developed VTE and those who did not. Individuals aged 60 years or older accounted for a higher proportion of the VTE group (P=0.006). Patients with Child-Pugh grade B disease were more frequent in the VTE group than those with grade C (P=0.004). Similarly, cases with an Eastern Cooperative Oncology Group (ECOG) performance status of 1-2 were more likely to experience VTE than patients scoring 0 (P=0.013). Prolonged bed rest of 12 hours or more after TACE was also associated with a higher rate of VTE (P=0.011). Patients

Table 2. Comparison of baseline characteristics and clinical factors between VTE and N-VTE groups

Factor	Total	VTE (n=54)	N-VTE (n=268)	Statistical Value	*P*-value
Age					
≥60 years	166 (51.55%)	37 (68.52%)	129 (48.13%)	7.477	0.006
<60 years	156 (48.45%)	17 (31.48%)	139 (51.87%)		
Gender					
Male	257 (79.81%)	40 (74.07%)	217 (80.97%)	1.327	0.249
Female	65 (20.19%)	14 (25.93%)	51 (19.03%)		
BMI					
≥24	85 (26.40%)	13 (24.07%)	72 (26.87%)	0.180	0.671
<24	237 (73.60%)	41 (75.93%)	196 (73.13%)		
Smoking History					
Yes	272 (84.47%)	44 (81.48%)	228 (85.07%)	0.442	0.506
No	50 (15.53%)	10 (18.52%)	40 (14.93%)		
Alcohol Consumption History					
Yes	98 (30.43%)	15 (27.78%)	83 (30.97%)	0.216	0.642
No	224 (69.57%)	39 (72.22%)	185 (69.03%)		
Diabetes History					
Yes	41 (12.73%)	9 (16.67%)	32 (11.94%)	0.904	0.342
No	281 (87.27%)	45 (83.33%)	236 (88.06%)		
Hypertension History					
Yes	86 (26.71%)	14 (25.93%)	72 (26.87%)	0.020	0.887
No	236 (73.29%)	40 (74.07%)	196 (73.13%)		
Child-Pugh Classification					
B	220 (68.32%)	46 (85.19%)	174 (64.93%)	8.524	0.004
C	102 (31.68%)	8 (14.81%)	94 (35.07%)		
ECOG Score					
1-2	87 (27.02%)	22 (40.74%)	65 (24.25%)	6.196	0.013
0	235 (72.98%)	32 (59.26%)	203 (75.75%)		
Tumor Size					
≥5 cm	113 (35.09%)	17 (31.48%)	96 (35.82%)	0.372	0.542
<5 cm	209 (64.91%)	37 (68.52%)	172 (64.18%)		
Portal Vein Tumor Thrombus					
Yes	117 (36.34%)	18 (33.33%)	99 (36.94%)	0.253	0.615
No	205 (63.66%)	36 (66.67%)	169 (63.06%)		
Number of Nodules					
<2	222 (68.94%)	40 (74.07%)	182 (67.91%)	0.797	0.372
≥2	100 (31.06%)	14 (25.93%)	86 (32.09%)		
Post-operative Bed Rest Duration					
≥12 h	81 (25.16%)	21 (38.89%)	60 (22.39%)	6.500	0.011
<12 h	241 (74.84%)	33 (61.11%)	208 (77.61%)		
TACE Frequency					
Single	110 (34.16%)	11 (20.37%)	99 (36.94%)	5.487	0.019
Multiple	212 (65.84%)	43 (79.63%)	169 (63.06%)		
D-dimer (μg/L)	781.53±218.58	963.30±209.97	745.58±202.03	7.122	<0.001

Note: VTE: Venous Thromboembolism, TACE: Transarterial Chemoembolization, BMI: Body Mass Index, ECOG: Eastern Cooperative Oncology Group.

who had undergone multiple TACE sessions were more prone to VTE than those treated once (P=0.019). In addition, DD levels were markedly elevated in VTE patients (P<0.001). Other variables, such as gender, BMI, smoking or alcohol consumption history, diabetes, hypertension, tumor size, presence of portal vein tumor thrombus, and the number of nodules, showed no significant differences between VTE and non-VTE groups (P>0.05) (**Table 2**).

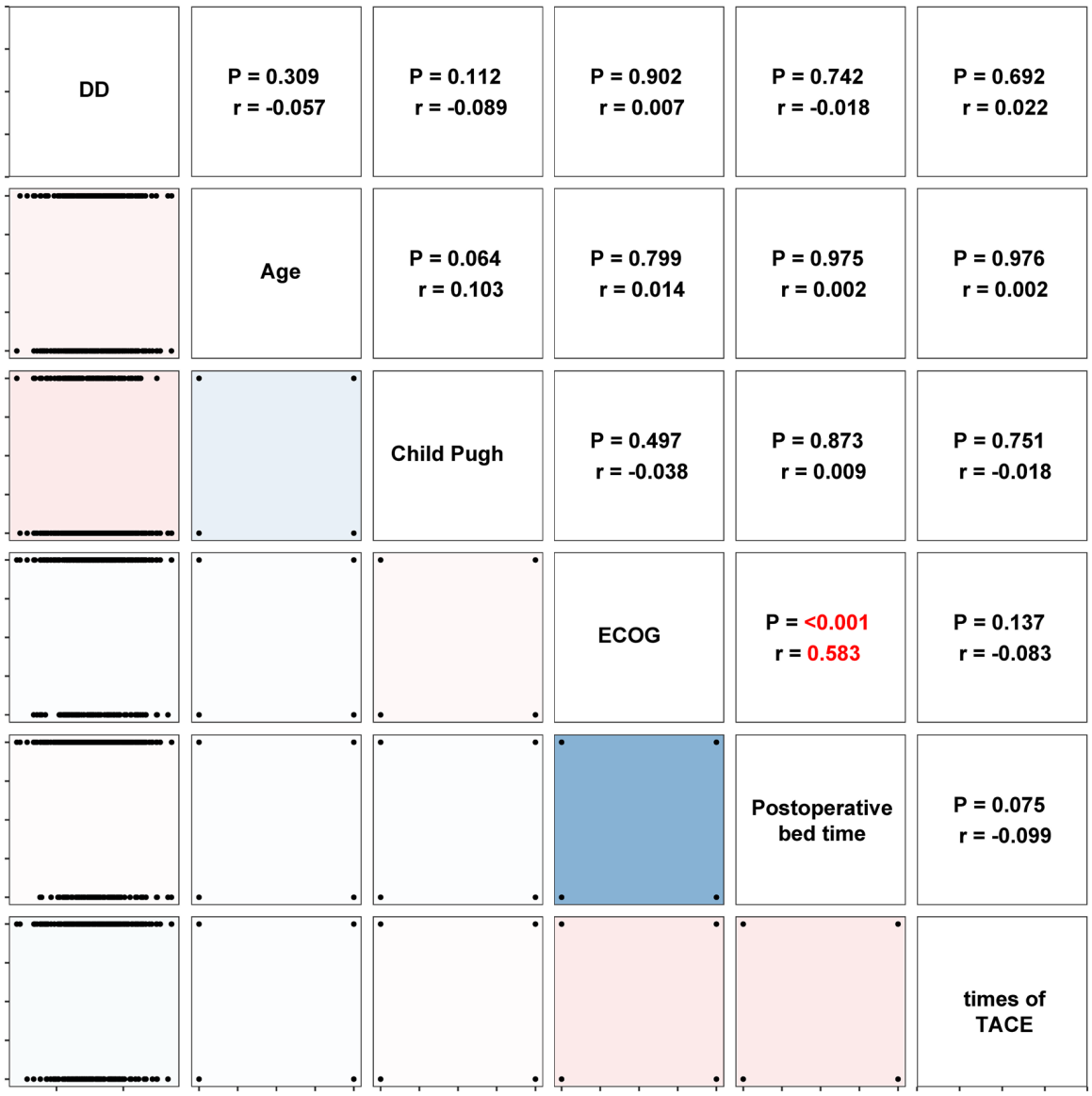

Figure 2. Pearson correlation analysis among factors associated with post-TACE VTE. Note: ECOG: Eastern Cooperative Oncology Group, TACE: Transarterial Chemoembolization, DD: D-dimer; VTE: Venous Thromboembolism.

Pearson correlation analysis

Correlation analysis demonstrated a significant positive correlation between ECOG score and bed rest duration (r=0.583, P<0.001), suggesting an interaction between these variables. Other factors, such as age, the Child-Pugh classification, the frequency of TACE, and DD, did not show any significant pairwise associations (P>0.05). To avert potential collinearity in the regression model, the duration of postoperative bed rest was excluded from the subsequent analysis (**Figure 2**).

Univariate and multivariate logistic regression

Table 3 summarizes variable assignments and multicollinearity tests, with the occurrence of VTE designated as dependent variable (1= presence, 0= absence). The VIF values ranged from 1.014 to 1.575, indicating no significant multicollinearity between the predictors. The univariate logistic regression analysis showed that multiple factors were related to post-TACE VTE, including elevated DD levels (OR=1.005, P<0.001), age ≥60 years (OR=0.415, P=0.005), Child-Pugh C

Table 3. Variable assignment and multicollinearity testing in logistic regression analysis

Variable	VIF	Variable Type	Assignment Content
DD	1.088	(X)	Continuous variable using original data
Age	1.056	(X)	≥60 years = 1, <60 years = 0
Child-Pugh Classification	1.014	(X)	C = 1, B = 0
ECOG Score	1.530	(X)	1-2 = 1, 0 = 0
Post-operative Bed Rest Duration	1.575	(X)	≥12 h = 1, <12 h = 0
TACE Frequency	1.039	(X)	Multiple = 1, Single = 0
VTE		(Y)	Yes = 1, No = 0

Note: VIF: Variance Inflation Factor, DD: D-dimer, TACE: Transarterial Chemoembolization, ECOG: Eastern Cooperative Oncology Group, VTE: Venous Thromboembolism.

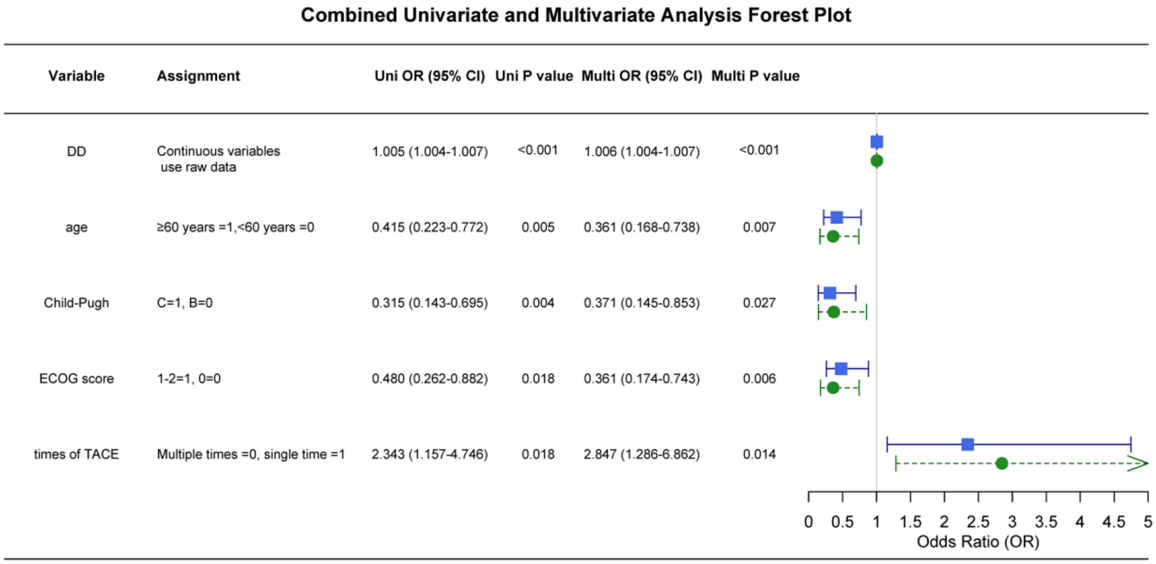

Figure 3. Univariate and multivariate logistic regression analysis of risk factors for post-TACE VTE in hepatocellular carcinoma patients. Note: DD: D-dimer, TACE: Transarterial Chemoembolization, ECOG: Eastern Cooperative Oncology Group, VTE: Venous Thromboembolism, OR: Odds Ratio, CI: Confidence Interval.

classification (OR=0.315, P=0.004), ECOG 1-2 (OR=0.480, P=0.018), and multiple TACE sessions (OR=2.343, P=0.018). In the multivariate model, these variables remained independently related to VTE risk: DD (OR=1.006, P<0.001), age ≥60 years (OR=0.361, P=0.007), Child-Pugh C (OR=0.371, P=0.027), ECOG 1-2 (OR=0.361, P=0.006), and multiple TACE treatments (OR=2.847, P=0.014) (**Figure 3**).

Nursing model development

Based on the five independent risk factors (DD level, age, Child-Pugh classification, ECOG score, and TACE frequency), a targeted nursing protocol was developed to prevent VTE after TACE. The framework prioritizes patients at high risk, specifically those with older age, Child-Pugh C cirrhosis, diminished performance status, recurrent TACE exposure, and elevated DD levels, aiming to lower the incidence of thromboembolic events and support post-TACE recovery (**Figure 4**).

Nomogram for risk prediction

A nomogram was developed to illustrate personalized VTE risk following TACE, utilizing the five predictors. Continuous variables, including DD level, age, and total calculated score were plotted on continuous scales, and categorical variables of Child-Pugh grade, ECOG status, and TACE frequency were presented as categorical scales. Each item corresponds to a specific point value, and the total represents an

VTE Prevention Nursing Intervention Protocol

Personalized Nursing Intervention System Based on Five Risk Factors

Phase 1: Initial Assessment

Step	Action	Requirements	Assessment Criteria	Responsible
1.1	Collect Basic Information	• Gather patient age, gender, disease type • Record past medical & family history • Assess lifestyle & mobility status	Completeness: 100% Complete Required Accuracy: Information Verified	Primary Nurse
1.2	VTE Risk Assessment	• Document Child-Pugh classification • Evaluate ECOG performance score • Measure D-dimer levels • Count TACE treatment sessions	High Risk: Risk Score ≥ Cut-off Value Low Risk: Risk Score < Cut-off Value	Attending Physician Primary Nurse

Phase 2: Five Risk Factors Assessment

Risk Factor	Assessment Criteria	Monitoring Frequency	Interventions	Target Value
DD D-Dimer	High Risk: ≥860μg/L Low Risk: <860μg/L	Daily Monitoring	• Increase anticoagulation frequency • Adjust monitoring schedule • Monitor for bleeding tendencies	<860μg/L
Age Patient Age	High Risk: ≥60 years Low Risk: <60 years	Initial Assessment	• Enhance early mobilization • Encourage moderate leg exercises • Reduce bed rest time	Improved Activity Tolerance
Child-Pugh Liver Function Grade	High Risk: Grade C Low Risk: Grade B	Weekly Assessment	• Enhanced anticoagulation monitoring • Regular liver function testing • Adjust treatment protocols	Maintain Grade B
ECOG Performance Status	High Risk: 1-2 points Low Risk: 0 points	Daily Assessment	• Provide personalized care • Arrange rehabilitation training • Encourage physical activity	0 points
TACE Treatment Sessions	High Risk: Multiple sessions Low Risk: Single session	Pre/Post Treatment	• Increase monitoring frequency • Prophylactic anticoagulation • Minimize excessive bed rest	No Thrombosis Formation

Phase 3: Nursing Intervention Measures

Intervention Type	Specific Measures	Implementation Frequency	Outcome Indicators
Anticoagulation Therapy	• Adjust drug type & dosage based on risk factors • Regular coagulation function monitoring • Observe for bleeding complications	Administration: Daily Monitoring: Every 2-3 days	• PT/APTT within target range • No bleeding complications • No thrombotic events
Exercise Intervention	• Early mobilization in bed • Active/passive lower limb exercises • Compression stockings application • Intermittent pneumatic compression	Exercise: Every 2 hours Assessment: Every shift	• Reduced lower limb swelling • Improved activity tolerance • No lower limb varicose veins
Dynamic Monitoring	• D-dimer level tracking • Regular liver function assessment • Lower limb vascular ultrasound • Vital signs monitoring	D-dimer: Daily Liver Function: Weekly Ultrasound: As needed	• Parameters trending to normal • No signs of thrombosis • Early detection of abnormalities
Health Education	• VTE prevention knowledge education • Importance of early mobilization • Medication adherence guidance • Family involvement in care	Admission: Initial Education During Stay: Reinforcement Discharge: Summary Guidance	• Patient knowledge rate >90% • Good medication adherence • High family cooperation

Phase 4: Continuous Monitoring & Adjustment

Monitoring Content	Monitoring Frequency	Adjustment Criteria	Expected Outcomes
Daily Monitoring	Daily	• D-dimer trend changes • ECOG score improvement • Treatment tolerance assessment	• Timely detection of risk changes • Dynamic adjustment of intervention intensity
Post-Discharge Follow-up	1 week post-discharge 1 month post-discharge 3 months post-discharge	• Phone or in-person follow-up • Assess home care adherence • Monitor VTE occurrence	• Continuous care quality assurance • Timely problem identification & resolution
Outcome Evaluation	At Discharge Follow-up Period	• VTE incidence rate statistics • Post-operative recovery status • Patient satisfaction survey	• VTE incidence rate <5% • Patient satisfaction >95% • Good post-operative recovery

Nursing Process Flow

Admission Assessment → Risk Factor Screening → Personalized Intervention → Continuous Monitoring → Outcome Evaluation → Quality Improvement

Key Performance Indicators Summary

Indicator Category	Specific Indicator	Target Value	Monitoring Frequency	Responsible Department
Safety Indicators	VTE Incidence Rate	<5%	Monthly Statistics	Nursing Department
	Bleeding Complication Rate	<2%	Monthly Statistics	Nursing Department
Quality Indicators	Nursing Compliance Rate	>95%	Weekly Review	Nursing Department
	Patient Satisfaction	>95%	Discharge Survey	Nursing Department
Efficiency Indicators	Average Length of Stay	10% reduction from baseline	Monthly Statistics	Medical Affairs
	Nursing Workload	Optimal allocation	Weekly Assessment	Nursing Department

Print Instructions:
This table is optimized for A4 paper printing and can be used as a clinical nursing guideline manual for VTE prevention. Press Ctrl+P to print.

Figure 4. Nursing model schematic based on post-TACE VTE risk factors. Note: DD: D-dimer, TACE: Transarterial Chemoembolization, ECOG: Eastern Cooperative Oncology Group, VTE: Venous Thromboembolism.

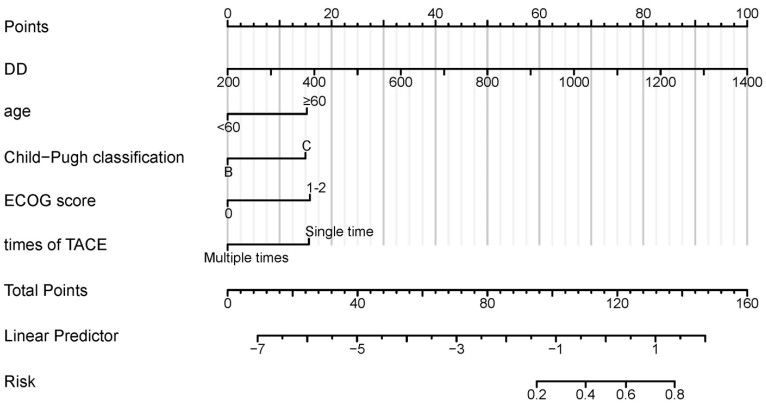

Figure 5. Nomogram model for Post-TACE VTE risk prediction. Note: DD: D-dimer, TACE: Transarterial Chemoembolization, ECOG: Eastern Cooperative Oncology Group, VTE: Venous Thromboembolism.

estimated probability of developing VTE. This graph-based tool helps doctors quickly figure out a patient's VTE risk and plan early treatments (**Figure 5**).

Internal validation of the risk model

Internal validation demonstrated effective discrimination and calibration of the predictive model. The ROC curve produced an AUC of 0.828 (**Figure 6A**). One thousand bootstrap resamples were applied for calibration analysis, yielding a mean squared error of 0.00029 and a mean absolute error of 0.014. The Hosmer-Lemeshow test produced a *P* value of 0.478 (**Figure 6B**), signifying a satisfactory

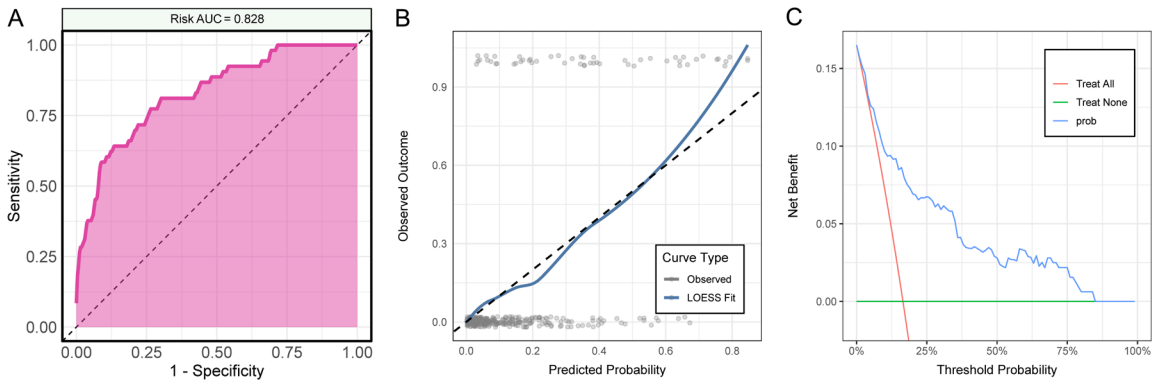

Figure 6. ROC curve, calibration curve, and decision curve analysis for post-TACE VTE risk prediction model. Note: ROC: Receiver Operating Characteristic, AUC: Area Under the Curve, VTE: Venous Thromboembolism, TACE: Transarterial Chemoembolization, DCA: Decision Curve Analysis.

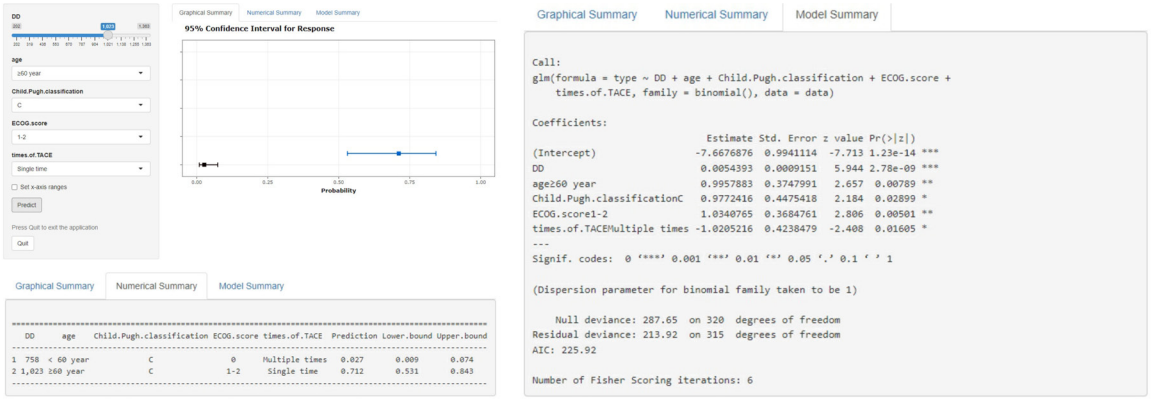

Figure 7. Dynamic nomogram example for post-TACE VTE risk assessment. Note: DD: D-dimer, TACE: Transarterial Chemoembolization, ECOG: Eastern Cooperative Oncology Group, VTE: Venous Thromboembolism.

model fit. DCA analysis indicated a net clinical advantage at thresholds of 85% or greater, with the maximum benefit observed at 16.77% (**Figure 6C**), supporting its practical uses. Additionally, an interactive dynamic nomogram based on the same five predictors was established to allow real-time bedside risk calculation and individualized management (**Figure 7**).

Discussion

D-dimer: D-dimer shows the breakdown products of cross-linked fibrin and serves as a marker of abnormal coagulation and fibrinolysis. After TACE, D-dimer levels often rise and have been consistently identified as an independent predictor of VTE [11]. In a nomogram study by Lei et al. [9], D-dimer levels above 1.44 mg/L were strongly associated with an elevated risk of VTE in patients with primary liver cancer. The pathophysiological mechanisms underlying post-TACE hypercoagulability involves arterial embolization-induced local ischemia and inflammation, which activate the coagulation cascade. Additionally, chemotherapeutic agents may irritate the vascular endothelium, thereby heightening the risk of thrombosis. A prior study indicated that the incidence of VTE in HCC was 2.8%, with a continual annual increase [12]. In HCC, compromised hepatic synthesis of coagulation factors often disturbs the balance between coagulation and anticoagulation pathways, resulting in an aberrant increase in D-dimer levels. Pastori et al. [13] emphasized that D-dimer elevation signifies a common mechanism of thrombus development across different cancers. These results elucidate the high sensitivity of D-dimer for predicting VTE risk in patients undergoing TACE.

Nursing implications: Targeted nursing for patients with elevated DD level is effective.

Regular postoperative monitoring, threshold-based alerts, and color Doppler ultrasound enable early thrombosis detection. Integrating DD thresholds into risk models has been shown to enhance DVT prediction [14]. For patients with persistently elevated DD, nursing priorities should include ensuring anticoagulant adherence, correct LMWH administration, and vigilant bleeding surveillance. The integration of D-dimer-based algorithms into EMRs can automatically adjust lab frequency and nursing intensity according to patient status, enabling more responsive care than fixed schedules. It is also essential to provide education on the significance of elevated DD and early symptoms (limb swelling, pain). Combining digital monitoring with education may support earlier VTE identification, improving surgical safety and accelerating recovery.

Age: Multivariate analysis identified that age ≥60 was associated with lower post-TACE VTE (OR=0.361, P=0.007), suggesting a protective effect. Likely contributors include less intensive TACE, more conservative anticoagulation, and closer perioperative supervision in older adults; younger patients often receive more intensive therapy and mobilize earlier, transiently increasing coagulation activation and endothelial stress [15]. Despite this inverse association, vigilance remains essential in older adults given vascular stiffness, impaired venous return, and comorbidities. Nursing priorities should emphasize early ambulation, individualized exercise guidance, and fall-prevention education [16].

Child-Pugh classification: In this study, Child-Pugh class C (OR=0.371, P=0.027) exhibited an inverse relationship with the incidence of VTE, indicating a statistically significant "protective" impact relative to class B. This unanticipated result is probably due to variations in clinical care instead of an actual biological benefit. Patients who are classified as Child-Pugh C usually have severe liver damage, have fewer TACE procedures, and have to follow stricter bed-rest rules, anticoagulant evaluations, and liver function monitoring. These care patterns may collectively reduce the incidence of thrombosis even though the liver reserve is low [17, 18]. In contrast, individuals with Child-Pugh class B disease may undergo more treatments or have prolonged TACE procedures, both of which can raise the risk of VTE [19]. Nursing interventions for Child-Pugh C patients should continue to prioritize optimization of hepatic function and nutritional support. Regular monitoring of serum albumin, liver enzymes (ALT, AST, TBIL), and coagulation indicators remains essential. Additionally, educating patients and their families about the connection between liver disease and thrombosis can enhance adherence to medications and follow-up appointments. So, even though the statistics show a negative correlation, clinical nursing should still treat severe hepatic dysfunction as a high-risk background that needs constant monitoring and personalized care.

ECOG score: Similarly, patients with ECOG scores of 1-2 demonstrated a significantly lower likelihood of developing VTE compared with those with ECOG 0 (OR=0.361). This may be due to more structured postoperative care and a more organized rehabilitation process. In clinical practice, patients with mild performance impairment often receive intensive assistance with early mobilization, pain management, and nursing surveillance, whereas those with ECOG 0 might resume activity autonomously with less oversight, increasing the chance of unnoticed thrombus formation [20-22]. So, even though the regression result shows a protective effect, nursing teams should interpret this finding cautiously. Practical experience indicates that reduced functional status inherently predisposes individuals to venous stasis and thrombotic risk. Consequently, early assisted mobilization, pain management, and physiotherapist-guided rehabilitation remain essential elements in the prevention of VTE.

TACE treatment frequency: Multiple TACE treatments (OR=2.847, P=0.014) remained an independent risk factor for VTE, aligning with existing evidence. Repeated manipulation of blood vessels can cause cumulative endothelial injury, provoke local inflammation, and alter regional hemodynamics, all of which raise the risk of thrombosis [8, 23]. Nursing interventions should prioritize pre-procedural coagulation screening, baseline D-dimer testing, and prophylactic anticoagulation when indicated. Color Doppler ultrasound examinations on days 7 and 14 are recommended to facilitate early detection of thrombosis, as well as compression therapy or intermittent pneumatic compression. Strengthening patient education re-

garding the thrombosis risks associated with repeated TACE is essential for ensuring adherence to preventive measures and improving long-term clinical outcomes [24, 25].

Innovative nursing intervention strategies: Prior studies have demonstrated that comprehensive nursing models substantially reduce postoperative DVT in patients with spinal fractures [26]. Xiang et al. [27] developed a DVT risk-prediction nomogram, demonstrating utility of individualized risk assessment in clinical decision-making. Modern nursing interventions incorporates multiple approaches, such as risk stratification, digital monitoring, and structured patient education, to optimize patient outcomes. The literature corroborates [28] that extensive protocolized nursing interventions hold significant clinical importance for preventing postoperative lower extremity DVT. Ma et al. [29] developed thrombosis risk-prediction models for cancer patients, providing support for precision nursing. These studies collectively validate the efficacy of multidimensional, individualized nursing interventions in the prevention of VTE despite the inverse OR patterns observed in our analysis - likely attributable to differences in the sample and treatment - our results still support integrating risk prediction and personalized nursing pathways. This comprehensive nursing model offers a robust, evidence-based framework for post-TACE VTE prevention and patient-centered management.

This retrospective study has a limited sample size and is subject to potential selection or information bias. The exclusion of patients with pre-operative confirmed VTE and those receiving anticoagulants/antiplatelets likely shifts the cohort towards a lower baseline thrombotic risk, potentially underestimating the true incidence of VTE. While this reduces treatment-confounding for internal validity, it limits generalizability of our findings to higher-risk, on-therapy populations. Additionally, we did not include inflammatory or genetic markers in our analysis, and the length of bed rest after surgery was excluded from the multivariable model due to its correlation with the ECOG status, which could reduce the model's completeness. The nomogram showed good internal performance (AUC=0.828) with good calibration and net benefit. However, its external validity remains untested. The implementation of the dynamic nomogram may be hindered by the complexity of data entry and the necessity for staff training. Additionally, the feasibility of the nursing protocol can be affected by available resources, patient adherence, and staff workload. Furthermore, limited follow-up restricts the evaluation of long-term effectiveness. To address these limitations, future research will include supplementary stability assessments (such as temporal and key subgroup analyses), compare cohort characteristics with external data to contextualize the findings, and make analysis code and variable definitions accessible. Future research should implement multicenter prospective validation - including primary hospitals, high-volume centers, and cohorts with prior VTE or anticoagulation therapy - to evaluate the model's generalizability and recalibration needs. Additionally, future investigations should consider incorporating inflammatory and coagulation biomarkers alongside TACE medication dosing, and utilizing machine learning techniques to enhance predictive accuracy.

Conclusion

D-dimer, age, Child-Pugh classification, ECOG scores, and TACE frequency are important risk factors for post-TACE VTE. The constructed nomogram model provides scientific evidence for predicting VTE risk. Nursing intervention protocols, tailored to these risk factors, provide both theoretical and practical guidance for enhancing postoperative safety in patients with HCC.

Disclosure of conflict of interest

None.

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Table S1. Implementation process of the five-phase post-TACE VTE nursing intervention protocol

Phase	Core objective	Key implementation steps	Specific measures	Monitoring frequency and indicators	Responsible staff
Phase I Initial Assessment (within 1 week after TACE)	Collect complete baseline data and complete early VTE risk screening to define the nursing baseline before individualized intervention.	1. Collect baseline demographic and clinical data. 2. Evaluate hepatic function reserve, tumor burden and performance status. 3. Perform lower-extremity venous ultrasound screening within 7 days after TACE. 4. Document the risk profile and the preliminary nursing plan in the electronic record.	Baseline data: age, sex, BMI, smoking and alcohol history, diabetes and hypertension. Hepatic function: Child-Pugh class (B or C) with albumin, bilirubin and coagulation indicators. Tumor status: maximum tumor dimension, number of nodules and portal vein tumor thrombus. Performance and treatment: ECOG score, number of TACE sessions and duration of post-operative bed rest. Laboratory: post-operative D-dimer (DD) level. VTE screening: color Doppler ultrasound of the lower extremities (femoral, popliteal and posterior tibial veins), assessing venous compressibility, intraluminal echogenicity and color/spectral Doppler flow (Philips EPIQ 7 system).	Screening completed within 7 days after TACE; findings entered into the nursing record before risk stratification.	Primary nurse; attending physician.
Phase II Risk Factor Stratification Assessment	Score the five validated independent risk factors, quantify individual VTE risk and identify high-risk patients to set nursing priority.	1. Score each of the five independent risk factors (elevated DD, age ≥60 years, Child-Pugh class C, ECOG score 1-2, multiple TACE sessions). 2. Convert the factor scores into an individual risk probability using the nomogram. 3. Grade patients into low-, moderate- and high-risk levels. 4. Link the risk level to the corresponding surveillance and intervention intensity (Phases III-IV).	Continuous DD contributes to the total score according to its measured value. Each categorical factor is assigned 1 point when present (age ≥60 years, Child-Pugh C, ECOG 1-2, multiple TACE) and 0 otherwise. The nomogram total score is translated into a predicted VTE probability for the individual patient. Risk level and recommended nursing grade are documented in the nursing plan and re-assessed before each subsequent TACE cycle.	Performed at admission and re-assessed before and after each TACE session.	Attending physician; primary nurse (validated by the nurse in charge).
Phase III Individualized Nursing Intervention Measures	Deliver stratified interventions covering motor function, medication observation, dynamic DD monitoring, hepatic function and nutritional support, and education and psychological care.	1. Motor function intervention: promote early mobilization and instruct active/passive lower-limb exercises (e.g., ankle pump) from the early post-operative period; minimize bed rest where clinically appropriate; provide graduated sit-to-stand and ambulation programs. 2. Medication observation and compliance: ensure correct low-molecular-weight heparin (LMWH) administration (dose, timing and technique); initiate prophylactic anticoagulation when indicated, particularly before repeated TACE; assess medication adherence at each shift. 3. Dynamic DD monitoring: monitor DD daily after TACE; rising or persistently elevated DD triggers physician notification, threshold-based alerting and repeat color Doppler ultrasound. 4. Hepatic function support and nutrition: monitor serum albumin, ALT, AST, TBIL and coagulation indicators; provide nutritional and hepatoprotective support, especially in Child-Pugh class C patients. 5. Education and psychological intervention: teach patients and families to recognize VTE warning symptoms (lower-limb swelling or pain, chest pain, dyspnea) and the importance of early mobilization and medication adherence; address activity-related anxiety and fear to improve compliance.	• Motor function: early ambulation; ankle-pump and passive/active limb exercise; assisted ambulation and physiotherapist-guided rehabilitation for patients with ECOG 1-2 or reduced mobility; fall-prevention education. • Medication: LMWH administration and prophylactic anticoagulation when indicated; adherence assessment each shift; bleeding surveillance (skin/mucous membranes, puncture sites, stool color). • Monitoring: daily DD; repeat ultrasound when DD is persistently elevated or symptoms appear. • Hepatic/nutritional: albumin, ALT/AST/TBIL and coagulation monitoring; nutritional and hepatoprotective support for Child-Pugh class C. • Education/psychology: symptom recognition, early-mobilization and adherence teaching; family involvement; psychological support to relieve activity-related anxiety.	DD daily; coagulation and hepatic panel per physician orders; ultrasound repeated when DD is persistently elevated or thrombotic symptoms occur.	Primary nurse; physician, physiotherapist and dietitian as needed.

Phase IV Continuous Dynamic Monitoring and Adjustment	Maintain a closed loop of monitoring and adjustment during hospitalization and after discharge so that intervention intensity is adapted to the patient's evolving risk.	1. Daily ward monitoring of thrombotic symptoms (lower-limb swelling or pain, chest pain, dyspnea), behavioral compliance, laboratory trends and medication adherence. 2. Scheduled ultrasound re-examination on post-TACE days 7 and 14 in high-risk patients (e.g., multiple TACE sessions or persistently elevated DD). 3. Dynamic adjustment of prophylaxis, monitoring frequency and nursing measures according to DD trends and clinical status. 4. Post-discharge follow-up by telephone or outpatient visit to review symptoms, adherence and laboratory results, with timely referral when abnormalities are detected.	• Daily ward monitoring: symptoms, compliance, laboratory indicators and post-discharge medication adherence. • Ultrasound re-examination on post-TACE days 7 and 14 for high-risk patients. • Dynamic adjustment of intervention strategies according to risk changes. • Scheduled post-discharge follow-up (telephone or outpatient) with continuous care handover.	Daily during hospitalization; ultrasound on post-TACE days 7 and/or 14; scheduled post-discharge follow-up.	Primary nurse; designated follow-up nurse.
Phase V Nursing Process Quality Control and Evaluation Summary	Audit the implementation of the protocol and use outcome indicators for continuous quality improvement.	1. Establish a nursing quality indicator system covering VTE incidence, nursing compliance rate, patient satisfaction and anticoagulation-related adverse events. 2. Collect and review indicators monthly, comparing results with the previous cycle. 3. Provide feedback to the nursing team and adjust the protocol, training content and resource allocation accordingly. 4. Incorporate the evaluation results into nursing performance assessment.	• Indicator system: VTE incidence, nursing compliance rate, patient satisfaction and adverse events. • Monthly statistics and review of the quality indicators. • Feedback loop for protocol adjustment, staff training and resource allocation. • Performance assessment of the nursing team based on the evaluation results.	Monthly statistics and quality review.	Head nurse; nursing quality control group.

Note: VTE, venous thromboembolism; TACE, transarterial chemoembolization; BMI, body mass index; DD, D-dimer; ECOG, Eastern Cooperative Oncology Group; LMWH, low-molecular-weight heparin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin. The five phases correspond to the structure shown in **Table 1**; the risk factors and nursing measures are derived from the multivariable logistic regression analysis and the nursing recommendations described in the main text. As stated in the Methods, all patients underwent lower-extremity venous ultrasound screening within 7 days after TACE, and repeated color Doppler ultrasound examinations on post-TACE days 7 and 14 are recommended for high-risk patients (e.g., those with multiple TACE sessions or persistently elevated D-dimer).