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GIVE-VTE-3: a simple three-component score for venous thromboembolism risk stratification in gastrointestinal cancers - a cross- sectional development study GIVE-VTE-3: VTE risk score in GI cancers

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Abstract

Background.

Venous thromboembolism (VTE) is a leading cause of preventable death in patients with cancer. Existing risk scores were derived in Western, mixed-cancer populations and rely on variables (body-mass index, P-selectin, performance status) that are frequently unavailable in low and middle-income countries (LMICs). No simple, gastrointestinal (GI) - specific score exists for these settings. We aimed to develop and internally validate a three-component VTE risk score for GI cancers using only routinely available data.

Methods.

In a cross-sectional study of 207 patients with histologically confirmed GI cancer, we developed GIVE-VTE-3, which assigns one point each for: a high-risk cancer site (pancreas, liver, biliary tract, or gallbladder), D-Dimer ≥ 3,000 ng/mL, and an absolute monocyte count ≥ 0.8 G/L (range 0–3). VTE was confirmed by imaging. Discrimination was quantified by the area under the receiver-operating-characteristic curve (AUC) with bootstrap optimism correction (1,000 iterations) and five-fold cross-validation; calibration by the Hosmer-Lemeshow test; and clinical utility by decision-curve analysis. GIVE-VTE-3 was compared with the Khorana score, an ONKOTEV-like model, and D-Dimer alone. Generalisability was explored in an independent multi-cancer cohort (n = 516).

Results.

The VTE rate was 22.7% (47/207). GIVE-VTE-3 stratified VTE risk across an approximately tenfold gradient: low (score 0) 6.9%, medium (1–2) 25.9%, and high (3) 70.0%. The optimism-corrected AUC was 0.694 (95% CI 0.609–0.777) with good calibration (Hosmer-Lemeshow p = 0.403). At a score of 3, the positive predictive value was 70.0% and the positive likelihood ratio 7.94; at a score of 0, the negative predictive value was 93.1%. GIVE-VTE-3 outperformed the Khorana score (AUC 0.469; ΔAUC + 0.226, p < 0.001), an ONKOTEV-like model (0.608), and D-Dimer alone (0.574). In the exploratory multi-cancer cohort, the integer-score AUC was 0.773 (95% CI 0.718–0.829), with a continuous - model AUC of 0.802, suggesting applicability beyond GI cancers.

Conclusions.

GIVE-VTE-3 is a simple, low-cost score that stratifies VTE risk in GI cancer patients and is immediately deployable in LMIC settings. The inclusion of monocyte count - an inexpensive, routinely measured but seldom-used marker - distinguishes it from existing scores.

Background

Gastrointestinal (GI) cancers account for more than one-third of global cancer mortality (1). Patients with GI malignancies have a four- to sevenfold increased risk of venous thromboembolism (VTE)

compared with the general population (2), and VTE is among the leading causes of death in patients with cancer receiving systemic therapy (3). Pharmacological thromboprophylaxis reduces VTE but carries bleeding risk, so accurate risk stratification is essential to target prophylaxis to those most likely to benefit (4).

Several VTE risk-assessment scores exist. The Khorana score (5) - endorsed by international guidelines (4) - incorporates cancer type, platelet count, hemoglobin, leucocyte count, and body-mass index (BMI), but it was derived in chemotherapy recipients and performs poorly in GI-specific subgroups, with reported AUCs below 0.60 (6). The Vienna CATS (7) and the CATS-MICA model (8) use tumor-site category and D-Dimer (the latter requiring only these two variables), while ONKOTEV (9) adds cancer stage and venous compression. Although well validated, these models were developed predominantly in Western, mixed-cancer populations and depend on variables that are frequently missing in low and middle-income countries (LMICs): BMI is often unrecorded, and P-selectin or soluble biomarkers are unavailable at most district hospitals.

Three considerations motivated the present work. First, no simple, integer-based score has been developed specifically for GI cancers in a resource-limited setting, where the disease burden is high and prophylaxis is not routine. Second, the systemic inflammatory response - and in particular monocyte-lineage activity - has a strong mechanistic link to cancer-associated thrombosis through tumor-associated macrophage polarization, tissue-factor expression, and the formation of neutrophil extracellular traps (10, 11); yet absolute monocyte count, an inexpensive and universally measured parameter, is not used in any established VTE score. Third, the GI cancer landscape in Viet Nam - dominated by hepatitis-B-related hepatocellular carcinoma (HCC), squamous-cell esophageal carcinoma, and mucin-secreting gastric and pancreatic tumors that differs from the Western cohorts in which existing scores were calibrated.

We therefore aimed to develop and internally validate GIVE-VTE-3, a three-component score combining cancer site, D-dimer, and monocyte count, designed for immediate use in LMIC GI-oncology practice, and to explore its generalizability in an independent multi-cancer cohort.

Methods

Study design and population

We performed a cross-sectional study of patients with histologically confirmed GI malignancy managed at the Oncology Center of Viet Tiep Friendship Hospital (campuses Viet Tiep 1 and Viet Tiep 2), Hai Phong, Viet Nam. Although the two campuses share a single institution and the study is therefore not formally multi-center, this dual-campus setting is representative of provincial first- and secondary- level (level I-II) hospitals in Viet Nam. Data were collected retrospectively by extraction of electronic medical records from the hospital information system (HIS) network over the period from January 2024 to January 2026. Because all clinical, laboratory, and imaging information was drawn directly from the

institutional HIS - an online system in which records are stored and archived - data accuracy was high and traceable to source documents. Patients with multiple admission records were deduplicated to one entry per patient, retaining the earliest available laboratory assessment to avoid duplicate enrolment. During the study period, 220 patients with histologically confirmed GI cancer and a first-admission D-Dimer measurement were identified; 13 were excluded due to incomplete histopathological data, leaving 207 unique patients; three patients with a missing monocyte value were excluded from the multivariable model, leaving 204 for model fitting. The study was approved by the institutional ethics committee, which waived individual consent for this retrospective analysis. Reporting follows the TRIPOD statement for prediction-model studies (12).

Eligible patients were adults with histologically confirmed gastrointestinal malignancy who underwent D-Dimer testing at the first admission during the study period. Exclusion criteria were: a documented history of anticoagulant or antiplatelet therapy at or before admission; major surgery within the two weeks preceding admission, a recognised transient provoking factor for venous thromboembolism that would bias baseline risk assessment; absence of a first-admission D-Dimer measurement; and duplicate admission records for a patient already enrolled. After screenn, Of 220 patients screened, 13 patients were excluded from the study because accurate histopathological information could not be obtained, yielding a final analytic cohort of 207 unique patients.

Sample size and sampling strategy

No a priori sample-size calculation was performed; instead, we adopted a full-enumeration sampling strategy, consecutively including every eligible patient who received a first-admission D-Dimer measurement during the 25-month study window, with deduplication to prevent repeat enrolment of the same individual. The resulting sample of 207 patients contained 47 venous thromboembolism events. For the three-predictor multivariable model this corresponds to approximately 15.7 events per variable, exceeding the minimum of ten events per variable recommended for logistic prediction models and thereby limiting the risk of overfitting.

Bias

Several measures were taken to limit bias. Selection bias was minimised by consecutively enrolling all eligible first-admission patients rather than a convenience subset, and by deduplicating multiple admissions to a single earliest record. Information and misclassification bias were reduced by defining the outcome exclusively on the basis of imaging confirmation and by extracting all exposure and covariate data directly from the institutional HIS, ensuring traceability to source documents. Optimism (overfitting) bias in performance estimates was addressed by 1,000-iteration bootstrap optimism correction and five-fold cross-validation.

Variables and outcome

Laboratory values were obtained within 72 hours of admission and included D-Dimer (ng/mL fibrinogen-equivalent units), complete blood count with differential, INR, fibrinogen, and albumin. Complete blood counts were measured on a Celltac Alpha automated haematology analyser (Nihon Kohden) using the manufacturer's matched reagents, and D-Dimer was measured on a fully automated SF-8050 coagulation analyser with the manufacturer's matched reagent kit. All clinical, laboratory, and imaging data were extracted from the patients' medical records stored in the institutional HIS online archive, ensuring high accuracy and traceability to the original source documents. The outcome was VTE, defined as at least one imaging-confirmed thromboembolic event (lower-limb deep-vein thrombosis or portal/visceral vein thrombosis on Doppler ultrasonography, or pulmonary embolism on computed tomography). Cancer stage followed the TNM 8th edition. Because predictors were laboratory and pathology values recorded in the HIS during routine care, they were captured before and independently of outcome adjudication, minimising incorporation bias; conversely, imaging to confirm VTE was ordered as part of standard clinical care and was therefore not formally blinded to predictor values, a potential source of verification bias addressed in the Limitations.

GIVE-VTE-3 development

Candidate predictors were pre-specified on the basis of biological plausibility, routine availability in LMIC practice and univariable association with VTE. A high-risk cancer site was defined as pancreas, liver, biliary tract, or gallbladder - anatomical sites with observed VTE rates ≥ 40% and established tissue-factor and portal-vein biology. Synchronous multi-site cancers were not classified as high-risk. The D-Dimer threshold (≥ 3,000 ng/mL) and monocyte threshold (≥ 0.8 G/L) were determined by the Youden index. Each criterion contributes one point, yielding an integer score of 0–3. For full reproducibility, the underlying multivariable logistic model was: logit(P[VTE]) = -2.38 + 1.41×(high-risk site) + 0.77×(D-Dimer ≥ 3,000 ng/mL) + 0.66×(monocyte ≥ 0.8 G/L), where each predictor is coded 1 if present and 0 if absent; the predicted probability for an individual is obtained as P(VTE) = 1 / (1 + e^(− logit)). The regression coefficients (β), corresponding odds ratios, and model intercept are reported in Table 2.

Statistical analysis

Continuous variables are summarized as median [IQR] or mean ± SD, and categorical variables as n (%); groups were compared with the Mann-Whitney U or Fisher exact test. Discrimination was quantified by the AUC, with optimism correction using 1,000 bootstrap iterations (Harrell method) (13) and five-fold cross-validation. Calibration was assessed by the Hosmer-Lemeshow test. The incremental value of adding histopathology, and of each component, was tested by likelihood-ratio tests. Decision-curve analysis quantified net benefit (14) and AUCs were compared with a bootstrap implementation of the DeLong test (15). The Khorana score (BMI component set to 0, as BMI was unavailable - a pre-specified decision), an ONKOTEV-like model (site + stage IV + D-Dimer ≥ 3,000), and D-Dimer alone were computed on the same cohort. Finally, GIVE-VTE-3 was applied, without refitting, to an independent multi-cancer cohort (n = 516, all solid-tumor types, with complete histopathology and D-dimer) to explore

generalisability. Analyses used Python 3.12 (statsmodels 0.14, scikit-learn 1.4, scipy 1.12). A two-sided $p < 0.05$ was considered significant.

Missing data were handled by complete-case analysis. The three GIVE-VTE-3 components (cancer site, D-Dimer, and monocyte count) were essentially complete: monocyte count was missing for three patients (1.4%), who were therefore omitted from multivariable model fitting (204 patients analysed). Albumin, which was not part of the GIVE-VTE-3 score, was missing in 21 patients and was used for descriptive purposes only; its missingness therefore did not affect the primary analysis. No imputation was performed.

Results

Patient characteristics

Among these 207 patients, the mean age was 65.9 ± 10.4 years and 148 (71.5%) were male (Table 1). The most frequent tumors were colorectal (19.3%), HCC (19.3%), gastric (18.8%), and oesophageal (16.4%). Most patients had advanced disease (62.3% stage IV; 57.0% with distant metastasis), and 64 (30.9%) had a high-risk cancer site. VTE was confirmed in 47 patients (22.7%), with the highest rates in pancreatic (46.2%) and hepatocellular (42.5%) cancers.

Table 1
Baseline characteristics (n = 207).

Characteristic	n	%	Detail
Age, mean ± SD (years)	65.9 ± 10.4	-	Range 36–95
Male sex	148	71.5	M:F ≈ 2.5:1
Colorectal cancer	40	19.3	
Hepatocellular carcinoma	40	19.3	VTE 42.5%
Gastric cancer	39	18.8	
Oesophageal cancer	34	16.4	SCC predominant
Pancreatic cancer	13	6.3	VTE 46.2%
Biliary tract / others	41	19.8	
Stage IV	129	62.3	Metastatic 57.0%
High-risk cancer site	64	30.9	Pancreas/liver/biliary/gallbladder
Venous thromboembolism (VTE)	47	22.7	Primary outcome

SCC, squamous cell carcinoma; VTE, venous thromboembolism. Median [IQR]: D-Dimer 2,259 [1,113-5,224] ng/mL; monocyte 0.65 [0.46–0.90] G/L; albumin 34.7 [30.5–39.0] g/L. Missing data: monocyte n = 3 (1.4%);

albumin n = 21 (10.1%); all other variables complete. Albumin was not a component of GIVE-VTE-3 and was used for description only.

Biomarker comparisons

D-Dimer was higher in patients with VTE (median 3,815 vs 2,202 ng/mL; p = 0.134), and monocyte count was significantly higher (p = 0.036; Fig. 1). INR was higher in the VTE group (1.17 vs 1.09; p = 0.026), whereas the inflammatory indices NLR and SIRI tracked disease stage rather than VTE (both p < 0.05 for stage IV vs I-III).

GIVE-VTE-3 development and component contribution

On univariable analysis, all three components were associated with VTE (cancer site OR 3.96, 95% CI 2.00-7.86; D-Dimer ≥ 3,000 ng/mL OR 2.23, 95% CI 1.15–4.33; monocyte ≥ 0.8 G/L OR 1.73, 95% CI 0.90–3.34). In the multivariable model, cancer site was the strongest predictor (OR 4.10, 95% CI 2.01–8.35, p < 0.001), followed by D-Dimer ≥ 3,000 ng/mL (OR 2.17, 95% CI 1.11–4.25, p = 0.025) and monocyte ≥ 0.8 G/L (OR 1.93, 95% CI 0.83–4.49, p = 0.128; Table 2). Adding histopathological subtype did not improve discrimination once cancer site was included (likelihood-ratio p = 0.95), indicating that anatomical site is a sufficient proxy for the prothrombotic biology - an advantage where pathology is delayed.

Table 2
GIVE-VTE-3 components, regression coefficients, and univariable and multivariable odds ratios.

Component	Criterion	Points	β	Univariable OR (95% CI)	Adjusted OR (95% CI), p
Cancer site (G)	Pancreas / liver / biliary tract / gallbladder	+ 1	1.41	3.96 (2.00-7.86)	4.10 (2.01–8.35), p < 0.001
D-Dimer (I)	≥ 3,000 ng/mL	+ 1	0.77	2.23 (1.15–4.33)	2.17 (1.11–4.25), p = 0.025
Monocyte (VE)	≥ 0.8 G/L	+ 1	0.66	1.73 (0.90–3.34)	1.93 (0.83–4.49), p = 0.128
Intercept	—	—	−2.38	—	—
Total	Sum of items	0–3	—	—	Higher = greater risk

β, logistic-regression coefficient (log-odds); OR, odds ratio; CI, confidence interval. Univariable OR, unadjusted association of each component with VTE; Adjusted OR, mutually adjusted estimate from the three-predictor multivariable logistic model. The model intercept (− 2.38) and β coefficients permit calculation of individual predicted probabilities: P(VTE) = 1 / (1 + e^{−[− 2.38 + 1.41×site + 0.77×D-Dimer + 0.66×monocyte]}), each predictor coded 1 (present) or 0 (absent). GIVE-VTE-3: G, GI site; I, inflammation/coagulation (D-dimer); VE, vessel/monocyte.

Risk stratification and performance

VTE rates rose monotonically across integer scores (0: 6.9%; 1: 18.8%; 2: 31.5%; 3: 70.0%), and the three-tier scheme spanned an approximately tenfold gradient (Table 3, Fig. 2). The optimism-corrected AUC was 0.694 (95% CI 0.609–0.777), the five-fold cross-validated AUC 0.683 ± 0.037, and calibration was good (Hosmer-Lemeshow p = 0.403). GIVE-VTE-3 significantly outperformed the Khorana score (AUC 0.469; ΔAUC + 0.226, p < 0.0001), an ONKOTEV-like model (0.608; ΔAUC + 0.087), and D-Dimer alone (0.574). Importantly, the cancer-site component added discrimination beyond D-Dimer alone (likelihood-ratio χ^2 = 27.9, p < 0.0001; AUC 0.752 → 0.797), and decision-curve analysis showed positive net benefit across the 10–45% threshold range. At a score of 3, the positive predictive value was 70.0% and the positive likelihood ratio 7.94; at a score of 0, the negative predictive value was 93.1%.

Table 3
Risk stratification and model comparison.

Tier / model	n (%)	VTE rate / AUC	Key metric
Score 0 - Low	58 (28)	6.9% (2.7–16.4)	NPV 93.1%
Score 1–2 - Medium	139 (67.2)	25.9% (19.3–33.8)	LR + 2.04
Score 3 - High	10 (4.8)	70.0% (39.7–89.2)	PPV 70.0%, LR + 7.94
GIVE-VTE-3 (AUC)	-	0.694 (0.609–0.777)*	HL p = 0.403
ONKOTEV-like	-	0.608	ΔAUC + 0.087
D-Dimer alone	-	0.574	ΔAUC + 0.138
Khorana score	-	0.469	ΔAUC + 0.226

**Optimism-corrected (1,000-iteration bootstrap). VTE rates with 95% Wilson CI. AUC, area under ROC curve; HL, Hosmer-Lemeshow; LR+, positive likelihood ratio; NPV/PPV, negative/positive predictive value. ΔAUC versus GIVE-VTE-3, all p < 0.05 (DeLong bootstrap).*

Biomarker profiles by histology

D-Dimer differed significantly across histological subtypes (Kruskal-Wallis p < 0.001; Fig. 4): it was highest in signet-ring-cell carcinoma (median 3,847 ng/mL) and cholangiocarcinoma (3,655 ng/mL), and lowest in squamous-cell carcinoma (1,120 ng/mL), which conversely showed the highest inflammatory indices. HCC was characterized by low albumin and platelet counts, reflecting cirrhosis rather than tumor-driven coagulopathy.

Exploratory analysis in an independent multi-cancer cohort

To probe generalizability, GIVE-VTE-3 was applied without modification to an independent cohort of 516 patients spanning all solid-tumor types (VTE rate 13.4%). The integer score retained strong discrimination (AUC 0.773, 95% CI 0.718–0.829), with a continuous-model AUC of 0.802, and again markedly outperformed the Khorana score (0.472) and Vienna CATS (0.527) calculated in the same

dataset. Risk rose monotonically (score 0: 2.8%; 1: 10.5%; 2: 33.3%; 3: 72.7%). Performance was similar in the non-GI subset (n = 324; AUC 0.758), suggesting that the score - and particularly its D-Dimer and cancer-site components - may generalize beyond GI cancers, although the monocyte component contributed less in this broader population (p = 0.18). These findings are hypothesis-generating and require dedicated external validation.

Discussion

In one sentence, this study asks whether venous thromboembolism (VTE) risk in gastrointestinal (GI) cancer can be stratified using only what a district hospital already measures on the day of admission, and answers it with GIVE-VTE-3, a three-item integer score (high-risk cancer site, D-dimer ≥ 3,000 ng/mL, monocyte ≥ 0.8 G/L) that separates patients across an approximately tenfold risk gradient (6.9% → 25.9% → 70.0%; Table 3, Fig. 2, Fig. 3), reaches an optimism-corrected AUC of 0.694 with good calibration, and substantially outperforms the Khorana score (ΔAUC + 0.226, p < 0.0001; Table 3, Fig. 2). The single contribution we want the reader to remember is this: three routinely available variables, costing roughly US$3–5 per patient, are enough to build a clinically actionable VTE score for GI cancer in a resource-limited setting and doing so requires elevating one marker, absolute monocyte count, that established scores have overlooked.

This matters because existing VTE risk models - the Khorana score, Vienna CATS, CATS-MICA, ONKOTEV that were derived in Western, mixed-cancer, chemotherapy-treated populations, and depend on variables (BMI, P-selectin, performance status, continuous biomarkers) that are frequently unrecorded or unavailable in low- and middle-income countries (LMICs), where the burden of GI cancer is heaviest and thromboprophylaxis is not routine. GIVE-VTE-3 is, to our knowledge, the first simple integer score developed explicitly for GI cancer in an LMIC setting, and its performance in this population meaningfully exceeds that of the guideline-endorsed Khorana score, which was near-random in our cohort (AUC 0.469). The score card, integer-to-risk mapping, and recommended clinical actions are summarized in Fig. 3, and the implementation toolkit (nomogram, four-step pathway, benefit–harm profile) in Fig. 5.

The novel ingredient is absolute monocyte count. There is a strong mechanistic case for its inclusion — tumor-associated macrophages, tissue-factor expression, and neutrophil-extracellular-trap formation all link monocyte-lineage activity to cancer-associated thrombosis (10, 11) — yet monocyte count appears in no established VTE score. In our GI cohort, monocyte count was significantly higher in patients with VTE (p = 0.036; Fig. 1) and added incremental risk stratification at essentially zero cost. Its adjusted effect was statistically modest (OR 1.93, 95% CI 0.83–4.49) and it contributed less in the exploratory multi-cancer cohort (p = 0.18), so we present it as a mechanistically grounded, inexpensive addition worth prospective evaluation rather than as a fully established predictor.

A reader may reasonably ask whether GIVE-VTE-3 offers more than D-dimer alone. Two findings say it does. Cancer site added significant discrimination beyond D-dimer (likelihood-ratio $\chi^2 = 27.9$, p < 0.0001; AUC 0.752 → 0.797), and converting a continuous laboratory value into four integer tiers (score 0 to 3)

yields a bedside instrument that maps directly onto a prophylaxis decision — a step D-dimer alone does not take (16). The high-risk tier (score 3) carried a 70.0% VTE rate and a positive likelihood ratio of 7.94, and the low-risk tier (score 0) a negative predictive value of 93.1% (Fig. 3), figures a clinician can act on.

The histology-specific biomarker profiles (Fig. 4) are mechanistically coherent and reinforce the choice of anatomical site as an anchor: mucin-secreting signet-ring-cell and biliary tumors showed the highest D-dimer, consistent with mucin-mediated coagulation activation and tissue-factor expression (17, 18); squamous-cell carcinoma displayed an inflammation-predominant profile; and the low albumin and platelet count in hepatocellular carcinoma reflect cirrhosis, a reminder that inflammatory ratios must be interpreted with the underlying liver disease in mind.

Applied without modification to an independent 516-patient multi-cancer cohort, GIVE-VTE-3 retained strong discrimination (integer-score AUC 0.773; continuous-model AUC 0.802; Fig. 5), again outperforming the Khorana score (0.472) and Vienna CATS (0.527) in that dataset, with monotonic rise in risk across integer scores. Performance was similar in the non-GI subset (AUC 0.758), although the monocyte component contributed less ($p = 0.18$). These results are hypothesis-generating; a dedicated external validation, ideally prospective and multicentre, is the necessary next step.

Our study has limitations. First, although data were drawn from two campuses of a single institution, the study is not formally multi-centre; the setting is nonetheless representative of provincial level I–II hospitals in Viet Nam, which supports applicability to comparable resource-limited settings but may limit generalisability to primary-care or Western tertiary populations. Second, the cross-sectional design captured prevalent rather than incident VTE, so temporal precedence between biomarker elevation and thrombus formation cannot be established and prospective validation is required. Third, BMI was unavailable, which is likely to have biased the apparent performance of the Khorana score downward; because BMI is frequently missing in real-world LMIC practice, however, this reflects the conditions under which the score would actually be used. Fourth, some histological subgroups were small, reducing the precision of subtype-specific estimates, and the multi-cancer analysis was exploratory and cannot substitute for independent external validation. Finally, the optimism-corrected AUC of 0.694, while comparable to established scores, leaves room for improvement and underscores the inherently stochastic nature of cancer-associated VTE.

Conclusions

GIVE-VTE-3 shows that VTE risk in GI cancer can be usefully stratified with three variables that every LMIC district hospital already obtains as part of routine admission work-up: cancer site, D-dimer, and absolute monocyte count - all of which are basic tests covered by national health insurance and therefore incur no additional cost to the patient, separating patients across an approximately tenfold risk gradient. Its key contribution is bringing monocyte count - a biologically relevant but overlooked marker - into a practical bedside VTE score for LMIC GI-oncology. Prospective multicentre validation is the next step.

Declarations

Ethics approval and consent to participate.

The study was approved by the Ethics Committee in Biomedical Research of Hai Phong University of Medicine and Pharmacy (Approval number: 13_IRB/HPMU, dated September 15, 2023). The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication.

Written informed consent for participation was obtained from all participants or waived by the Institutional Review Board due to the retrospective study design.

Competing interests.

The authors declare that they have no competing interests.

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Author Contribution

PHV and HND conceived and designed the study. HND, DLV, TLH and KLV performed clinical data acquisition. ADNM, CVM and HNX carried out data analysis, and PHV, HND and LPT contributed to data interpretation. PHV drafted the manuscript. TPV and KNV critically revised the manuscript for important intellectual content. LPT supervised the project and coordinated manuscript preparation. All authors read and approved the final manuscript.

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Data Availability

The de-identified dataset and the analysis code supporting the findings are available from the corresponding author on reasonable request. The full model specification (intercept and β coefficients, Table 2), the score card, the nomogram (Fig. 5A), and the participant flow diagram (Fig. S1) are provided to enable independent calculation of predicted probabilities and external validation.

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Figures

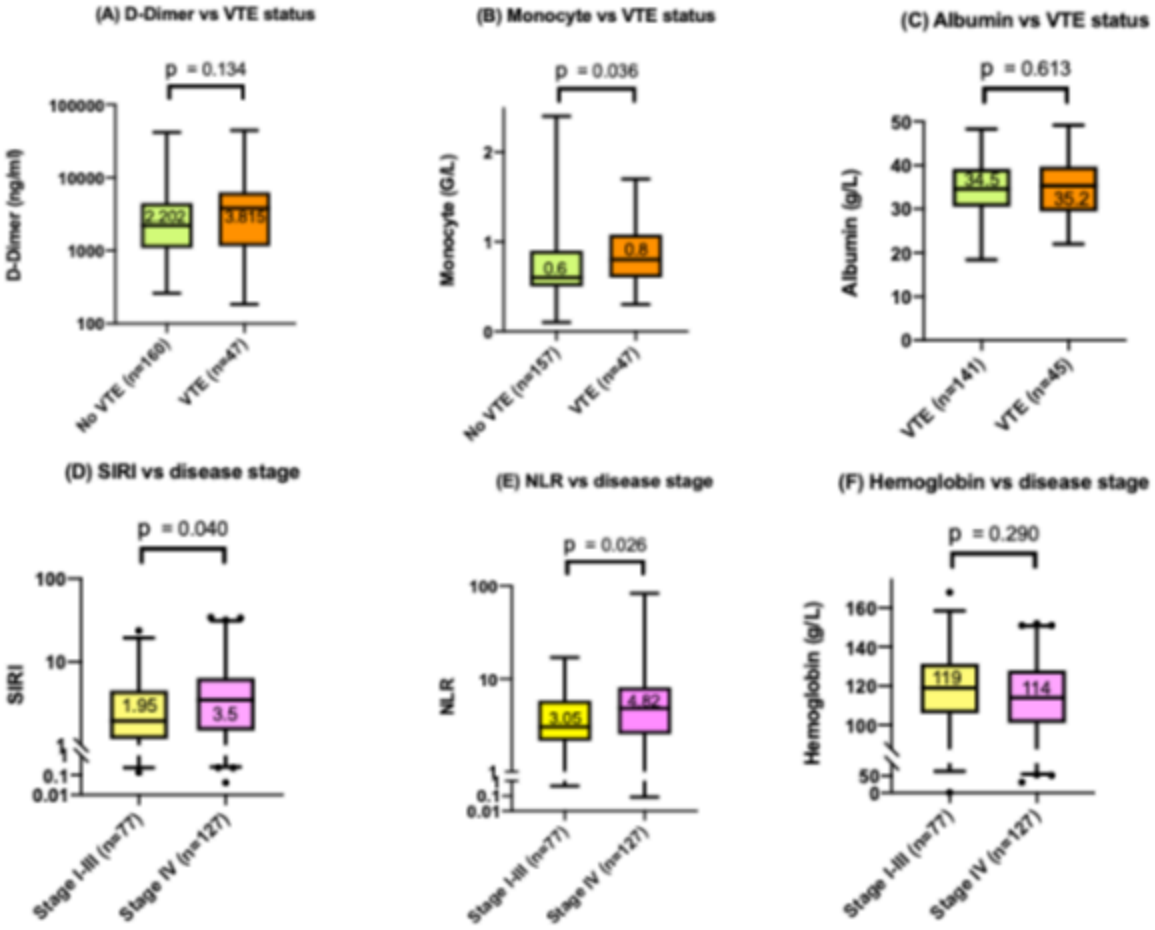


Figure 1

*Biomarker comparison between outcome groups (Mann-Whitney U test; *p < 0.05). (A-B-C) D-Dimer, monocyte and albumin by VTE status; (D-E-F) SIRI, NLR and hemoglobin by disease stage.*

Figure 2. Discrimination, calibration, and decision curve analysis of GIVE-VTE-3

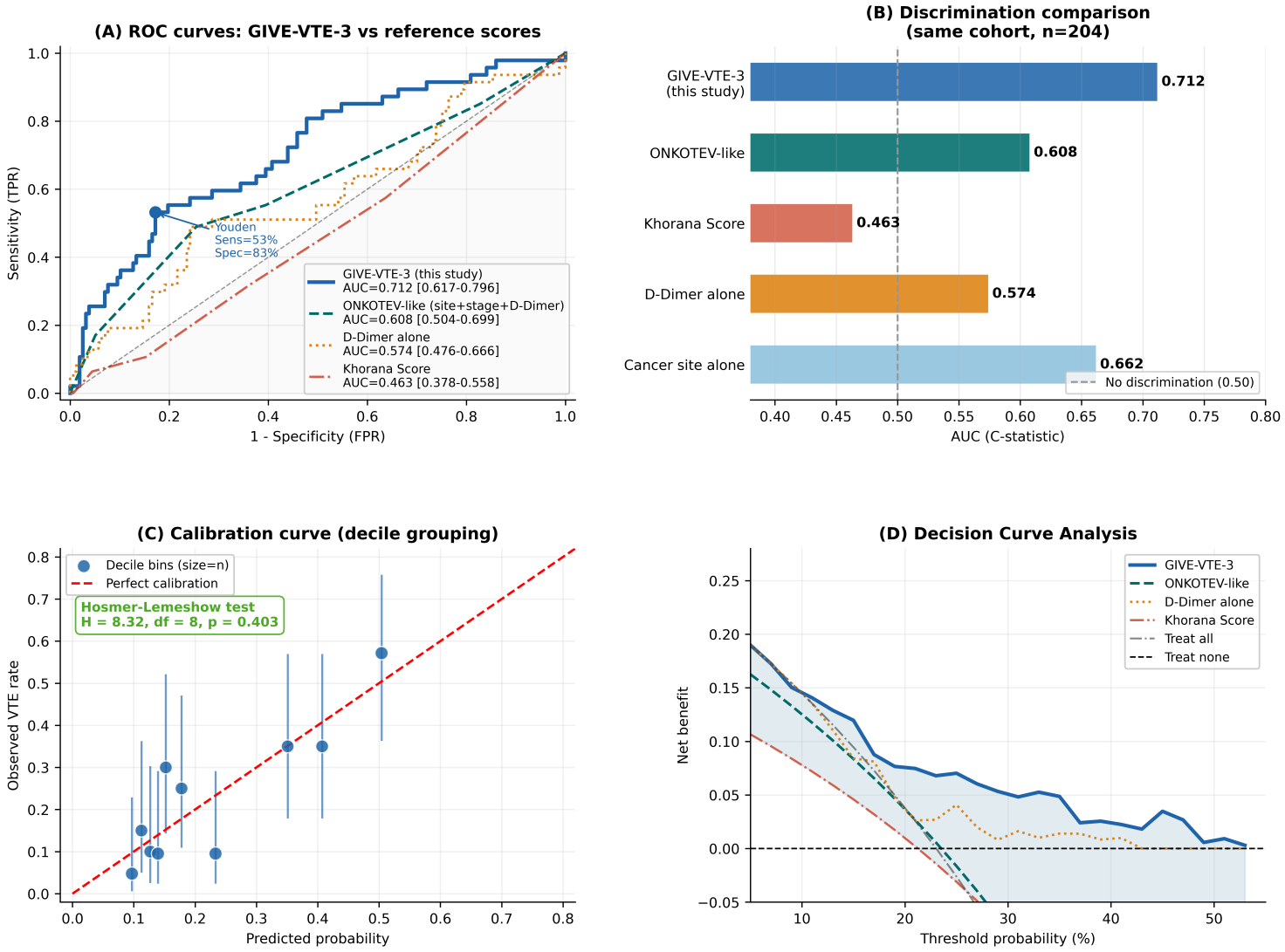


Figure 2

Discrimination, calibration, and decision-curve analysis. (a) ROC curves for GIVE-VTE-3 versus reference models; (b) AUC comparison (same cohort); (c) calibration curve (Hosmer-Lemeshow p = 0.403); (d) decision-curve analysis, with the shaded area indicating net-benefit advantage over the Khorana score. FPR, false-positive rate; NB, net benefit; TPR, true-positive rate.

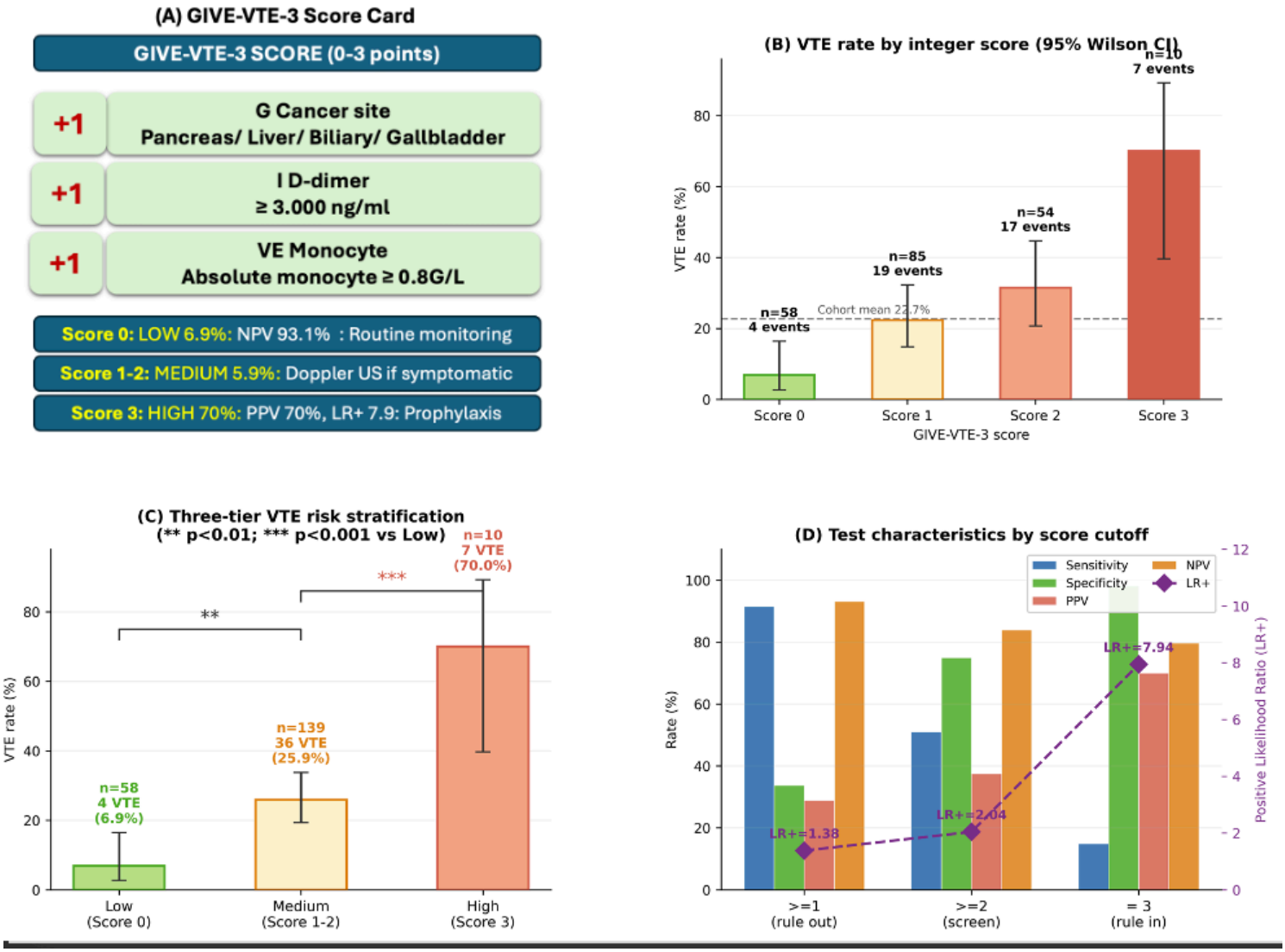


Figure 3

*GIVE-VTE-3 score card and clinical performance. (a) Score card with risk tiers and recommended actions; (b) VTE rate by integer score (95% Wilson CI); (c) three-tier stratification (**p < 0.01, ***p < 0.001 vs low); (d) test characteristics at three cut-offs. DOAC, direct oral anticoagulant; LMWH, low-molecular-weight heparin.*

Figure 4. VTE rates by cancer site, D-Dimer profiles, and biomarker heatmap by histological subtype

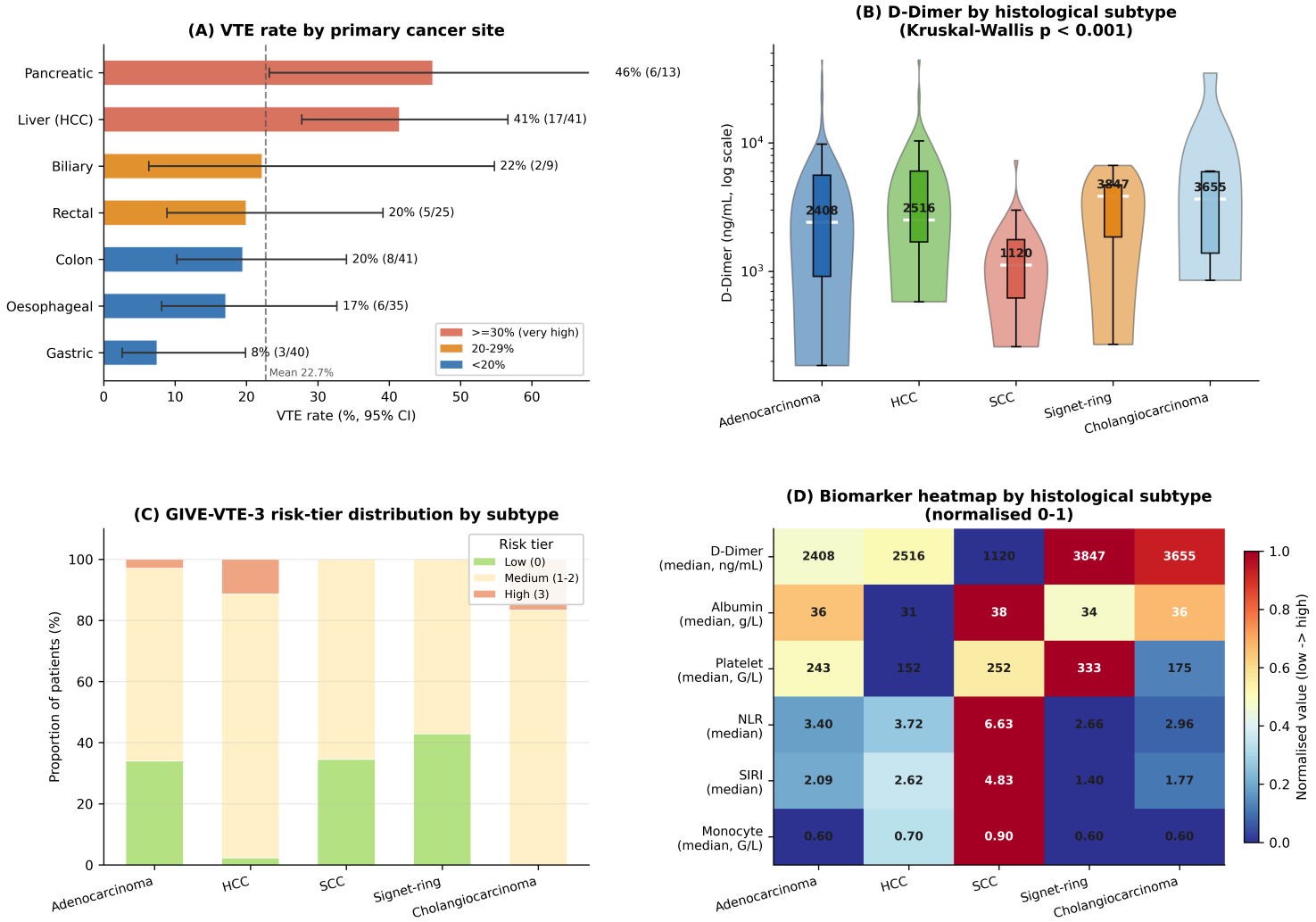


Figure 4

VTE rates by cancer site and biomarker profiles by histological subtype. (a) VTE rate by site (95% Wilson CI); (b) D-Dimer by subtype (Kruskal-Wallis p < 0.001); (c) GIVE-VTE-3 tier distribution by subtype; (d) biomarker heatmap. HCC, hepatocellular carcinoma; SCC, squamous-cell carcinoma.

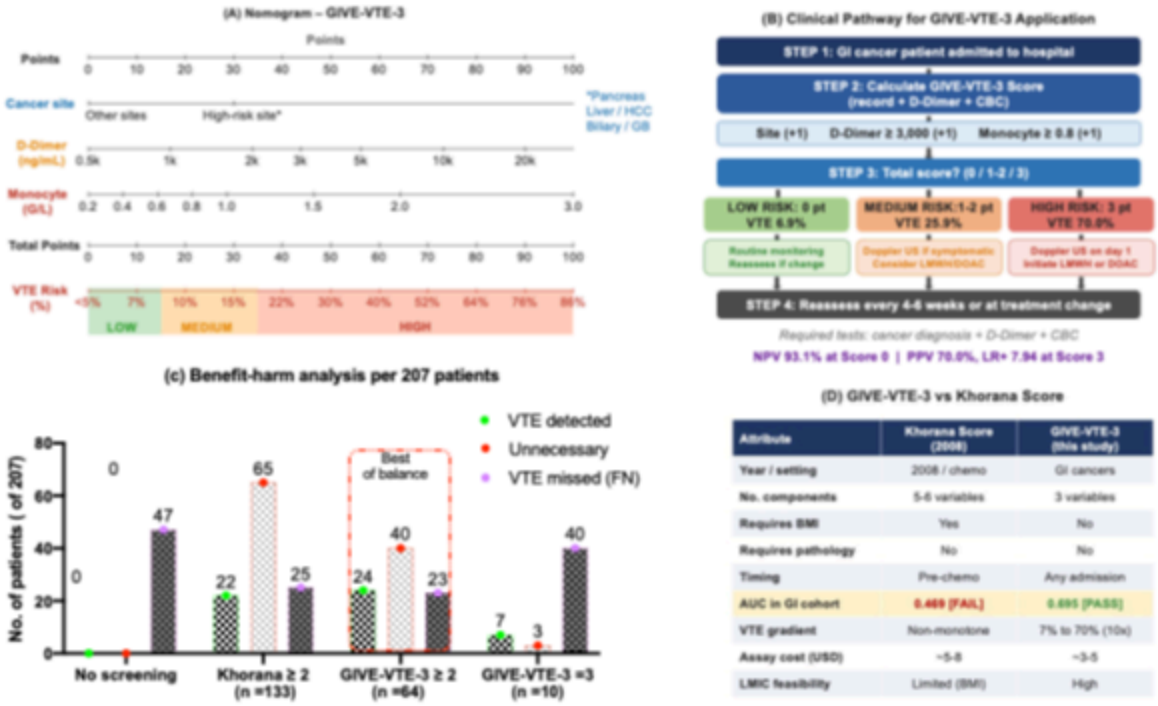


Figure 5

Clinical implementation toolkit. (a) Nomogram; (b) four-step clinical pathway; (c) benefit-harm analysis per 207 patients; (d) attribute comparison with the Khorana score (ΔAUC +0.226, p < 0.0001). LMWH, low-molecular-weight heparin.