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Screening-detected venous thromboembolism after colorectal cancer surgery in an Asian cohort: incidence, anatomical distribution, and the bleeding burden of therapeutic anticoagulation

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Screening-detected venous thromboembolism after colorectal cancer surgery in an Asian cohort: incidence, anatomical distribution, and the bleeding burden of therapeutic anticoagulation

Running title: Screening-detected VTE in Asian colorectal cancer surgery

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Abstract

Background. Postoperative venous thromboembolism (VTE) after colorectal cancer (CRC) surgery is a leading cause of preventable morbidity, but its true incidence and downstream therapeutic consequences are highly sensitive to the detection strategy employed. Asian populations have historically reported lower symptomatic VTE rates than Western cohorts, yet contemporary screening-based data from Thai surgical populations remain sparse. We sought to quantify the incidence, anatomical distribution, predictors, and bleeding consequences of screening-detected postoperative VTE in a Thai CRC surgical cohort.

Methods. This single-center prospective cohort enrolled consecutive adults with colorectal adenocarcinoma undergoing elective resection at Chulabhorn Hospital (February 2023 to January 2025), all with Caprini score ≥ 5. Prophylaxis was intermittent pneumatic compression (IPC) alone or IPC plus 40 mg of enoxaparin subcutaneous daily. Bilateral lower-limb duplex ultrasonography was performed preoperatively and on postoperative days 7–10. The primary outcome was the cumulative incidence of objectively confirmed VTE within 30 days; safety outcomes.

Results. Of 270 patients, 260 received IPC alone and 10 received IPC plus enoxaparin. Screening-detected DVT occurred in 13 IPC-only patients within 30 days (5.00%), with 76.9% asymptomatic and 61.5% distal. Pulmonary embolism occurred in 2 (0.77%), both symptomatic. Six of 13 (46.2%) received therapeutic anticoagulation; 3 (50.0%) developed major bleeding. Cumulative 90-day VTE incidence was 5.77%. Univariable predictors included splenic-flexure tumor location (OR 21.35; 95% CI 2.75–165.43; p = 0.003), continuous Caprini score (OR 2.55 per 1-unit; p = 0.005), and postoperative small-bowel obstruction (OR 5.46; p = 0.034); operative duration was borderline (OR 1.45 per 120-minute increment; p = 0.066).

Conclusion. In Thai colorectal cancer surgery managed with mechanical prophylaxis alone, systematic screening identified a 5% 30-day DVT incidence, predominantly distal and

asymptomatic. Subsequent therapeutic anticoagulation incurred substantial major-bleeding burden, findings that should inform design of future trials of extended pharmacological thromboprophylaxis in Asian populations.

Trial registration: Thai Clinical Trials Registry, TCTR20230914001 (registered 14 September 2023).

Keywords (5, alphabetical)

anticoagulation; colorectal cancer; deep vein thrombosis; duplex ultrasonography; venous thromboembolism.

Highlights (3–5 bullets, ≤ 85 characters each)

- 30-day duplex-detected DVT incidence was 5.0% under IPC-only prophylaxis (n = 260).
- Over three-quarters of detected DVT were asymptomatic and distal.
- Therapeutic anticoagulation for screening-detected DVT caused major bleeding in 50%.
- Splenic-flexure tumor and Caprini score independently predicted postoperative VTE.
- Bleeding penalty of treating incidental distal DVT may approach the thrombotic burden.

Background

Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), remains a major yet preventable complication after colorectal cancer (CRC) surgery. Patients undergoing CRC resection are particularly vulnerable due to the combined effects of malignancy-associated hypercoagulability, surgical endothelial injury, and postoperative immobility. In a large English population-based cohort, the cumulative incidence of postoperative VTE after CRC resection was three- to four-fold higher than in non-cancer colorectal surgery [1]. Even in the era of routine in-hospital pharmacological prophylaxis, a clinically meaningful proportion of VTE events occurs after hospital discharge: Lewis-Lloyd et al, analyzing more than 165,000 colectomies from English national registry data, reported postdischarge VTE incidence rates that remained elevated for at least 4 weeks after surgery [2], and a contemporary multicenter Chinese prospective cohort study (CRC-VTE) further documented that systematic screening identified VTE in approximately one in nine CRC surgical patients [3].

Although international guidelines recommend extended thromboprophylaxis with low-molecular-weight heparin (LMWH) for up to 28 days following major pelvic or abdominal cancer resection, this strategy is largely based on studies of Western populations [4, 5]. Emerging evidence suggests that Asian patients have a lower baseline risk of postoperative VTE but may be more susceptible to bleeding complications from pharmacological prophylaxis, raising concerns about whether pharmacological prophylaxis is worth the risk of this setting [6–10]. East and Southeast Asian cohorts have historically reported lower baseline incidences of postoperative VTE after CRC surgery than their European counterparts; for exmaple,in a Japanese multicenter study of fondaparinux prophylaxis, symptomatic VTE rates remained well below 2% [7,8]. Conversely, it appears that Asian surgical patients appear to incur higher relative bleeding risks when receiving extended pharmacological prophylaxis

[9,10]. Some researchers have asserted that lower body mass index, distinct inherited thrombophilia profiles, and limited representation of Asians in pivotal anticoagulant trials together justify individualized rather than reflexively guideline-driven thromboprophylaxis decisions in this population [11,12]. The most direct empirical test of this question — a Japanese multicentre randomized trial comparing IPC alone with IPC plus 7-day enoxaparin in laparoscopic gastrointestinal cancer surgery — found no statistically significant between-group difference in 7-day CT-detected VTE (4.8% versus 3.3%; P = 0.453), with bleeding occurring almost exclusively in the enoxaparin arm [13].

Little surgical evidence of VTE prophylaxis has been reported in Thailand-based studies. Real-world data from the GARFIELD-VTE registry, which prospectively enrolled 337 Thai patients alongside cohorts from six other Asian countries, demonstrated meaningful differences from Western populations in term of patient profile and 12-month outcome, despite comparable rates of major bleeding and VTE recurrence [12]. Extended LMWH prophylaxis imposes financial and adherence challenges that compound this evidentiary gap, while current practice therefore varies, reflecting uncertainty rather than consensus. Against this background, we impremented a prospective observational study at Chulabhorn Hospital — a tertiary cancer referral center — to quantify the cumulative incidence of screening-detected postoperative VTE under contemporary mechanical-only prophylaxis; to characterize its anatomical distribution and clinical predictors; and to describe the downstream bleeding consequences of therapeutic anticoagulation initiated for screening-detected events. Because the realized allocation to combined IPC plus enoxaparin was small, we treat between-group comparisons descriptively only and focus on incidence, distribution, and bleeding burden in the larger IPC-only cohort.

Methods

Study design and oversight

This was a single-center prospective observational cohort study conducted at Chulabhorn Hospital, Bangkok, Thailand — a tertiary cancer referral center — between 1 February 2023 and 7 January 2025. The protocol was prospectively registered with the Thai Clinical Trials Registry (TCTR20230914001, registered 14 September 2023) and approved by the Human Research Ethics Committee of the Chulabhorn Royal Academy Institutional Review Board (EC 013/2565). All participants provided written informed consent before enrollment. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cohort studies [14] (Fig.1).

Participants

Consecutive patients undergoing elective colorectal resection between 1 February 2023 and 7 January 2025 were screened for eligibility. Adults (≥18 years) with histologically confirmed colorectal adenocarcinoma scheduled for elective open or laparoscopic resection with curative intent and a Caprini Risk Assessment Model (RAM) score of ≥5 — corresponding to a high preoperative VTE risk stratum [15] — were eligible. Patients were excluded if they had: (i) a preoperative diagnosis of deep vein thrombosis (DVT) on screening duplex ultrasonography; (ii) known hypersensitivity or contraindication to enoxaparin; (iii) severe renal impairment (estimated glomerular filtration rate < 30 mL/min/1.73 m^2); (iv) active major bleeding; or (v) a prior history of VTE.

Allocation and prophylactic interventions

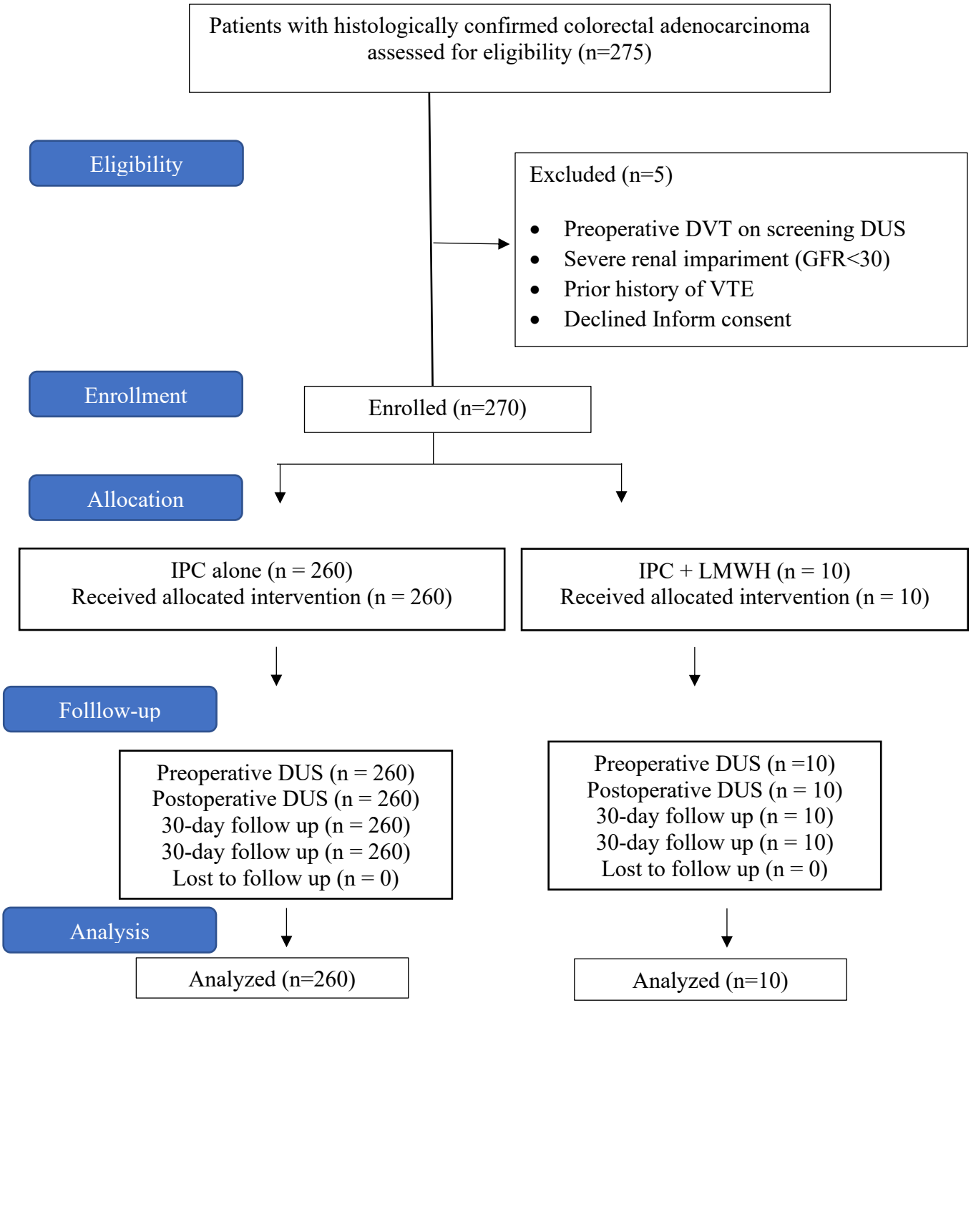
Group allocation was non-randomized and reflected real-world practice: Each treating surgeon, consistent with the institutional protocol informed by ACCP and ASCO guidance [4,6], assigned patients prospectively to either mechanical prophylaxis alone (IPC group) or

combined mechanical and pharmacological prophylaxis (IPC + enoxaparin group). Both arms received standardized perioperative care within the institutional Enhanced Recovery After Surgery (ERAS) pathway, including early mobilization, multimodal analgesia, normothermia maintenance, and prophylactic antibiotics.

In the IPC group, intermittent pneumatic compression was delivered using the Kendall SCD™ Express system (Cardinal Health) in sequential mode with bilateral calf–thigh sleeves. Compression was initiated immediately before the induction of anesthesia, continued throughout the operative period, and maintained postoperatively for ≥18 hours per day until full ambulation.

In the IPC + enoxaparin group, identical IPC was combined with subcutaneous 40 mg of enoxaparin subcutaneously once daily, with the first dose administered postoperatively once the attending surgeon confirmed adequate hemostasis (typically within 12–24 hours after skin closure). Enoxaparin was prescribed for a planned duration of 28 days postoperatively. However, treatment could be discontinued earlier at the discretion of the treating physician in cases of intolerance or bleeding. The actual duration of enoxaparin use, including any premature discontinuation and its underlying reasons (e.g., intolerance, non-adherence, or bleeding), was prospectively recorded for all patients.

Figure 1. Study conduction flowchart according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.



Surveillance and assessments

Bilateral lower-extremity compression duplex ultrasonography (DUS) was performed at two prespecified time points: within 1 day before surgery (preoperative DUS) and between postoperative day 7 and day 10 (postoperative DUS). Examinations were performed by board-certified vascular surgeons using B-mode imaging with augmentation maneuvers and color Doppler flow analysis. The protocol systematically interrogated the common femoral, femoral, popliteal, posterior tibial, peroneal, and intramuscular (soleal and gastrocnemius) veins. DVT was defined as non-compressibility on B-mode imaging, with or without absence of color Doppler flow, and was categorized as proximal (femoral or popliteal) or distal (calf or intramuscular). Sonographers were blinded to the patient's prophylaxis assignment whenever practicable. Suspected pulmonary embolism (PE) was investigated using computed tomography pulmonary angiography (CTPA) or, when contraindicated, ventilation–perfusion scintigraphy. Patients found to have preoperative DVT were withdrawn before surgery and managed in accordance with to the institutional thrombosis pathway.

Demographic, clinical, and operative variables were collected prospectively using a standardized case-report form. Recorded variables included age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) physical status, tumor location and TNM stage, histological differentiation, presence of synchronous tumors or distant metastases, surgical approach (open versus laparoscopic), operative duration, estimated intraoperative blood loss, and perioperative transfusion requirement. Postoperative variables included surgical complications (postoperative ileus, small-bowel obstruction and chyle leak), prophylaxis adherence (total enoxaparin days, dropout and reason for dropping out) and length of hospital stay.

Outcomes

The primary outcome was the cumulative incidence of VTE within 30 days of surgery, defined as a composite of objectively confirmed DVT (proximal or distal, identified on protocol or symptom-driven DUS) or PE confirmed by CTPA or ventilation–perfusion scintigraphy. Secondary outcomes were: (i) overall, proximal, and distal DVT incidence within 30 days; (ii) symptomatic DVT within 30 days; (iii) total and symptomatic PE within 30 days; (iv) cumulative VTE incidence at 90 days; (v) 30-day all-cause mortality; and (vi) length of hospital stay.

Safety outcomes were defined according to the International Society on Thrombosis and Haemostasis (ISTH) criteria [16]. Major bleeding was defined as followed: fatal bleeding; symptomatic bleeding in a critical organ (intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial); bleeding causing a drop in hemoglobin of ≥20 g/L; or bleeding requiring transfusion of ≥2 units of whole blood or red blood cells. Clinically relevant non-major bleeding (CRNMB) was defined as overt bleeding not meeting the criteria for major bleeding but requiring medical intervention, unscheduled contact with a clinician, interruption of prophylaxis, or impaired daily activity. Reoperation for bleeding and perioperative transfusion requirement were also recorded.

Sample size

Based on prior evidence from a Japanese randomized trial comparing IPC alone with IPC plus enoxaparin, which reported 30-day VTE incidences of 4.8% and 3.3%, respectively [13], we estimated that approximately 113 patients per group would be required to detect a 3% absolute risk difference with 80% power at a two-sided alpha of 0.05. After inflating by 5% for anticipated loss to follow-up, the planned recruitment target was 120 patients per arm (total N = 240).

However, owing to the observational design and treatment allocation based on physician preference, actual group sizes were not controlled and were markedly imbalanced. Therefore, this study should be interpreted as exploratory and not powered for definitive between-group comparisons.

Statistical analysis

Continuous variables are presented as mean ± standard deviation or median (interquartile range), as appropriate; categorical variables are presented as frequencies and percentages. Between-group comparisons were performed using Student's t test or the Mann–Whitney U test for continuous variables and the χ^2 test or Fisher's exact test for categorical variables, with standardized mean differences (SMDs) reported and SMD < 0.20 considered indicative of acceptable balance. Because of the large difference in group sizes (260 vs 10), causal estimation by propensity-score adjustment was not feasible — kernel-density inspection of the estimated propensity score showed minimal common support, violating the assumption of positivity[44]. Between-group comparisons are therefore presented descriptively only.

The principal analytical effort was directed at the IPC-only cohort (n = 260; 13 events). Univariable associations between candidate predictors and 30-day VTE were estimated using Firth's penalized maximum-likelihood logistic regression, which mitigates small-sample bias and quasi-complete separation arising from rare exposures and limited events. Continuous predictors were rescaled to clinically interpretable units (operative duration per 120-min increment; Caprini score per 1-unit increment). Effect estimates are reported as odds ratios (ORs) with profile-likelihood 95% confidence intervals. The discriminative ability of operative duration as a continuous predictor of 30-day VTE was further explored using receiver-operating-characteristic (ROC) analysis, with optimal threshold identification by Youden's J statistic and sensitivity analyses using the closest-to-(0,1) and Liu's index methods. The 95% confidence interval for the area under the curve was derived from 2,000 nonparametric

bootstrap. Given the limited number of events (n = 13), all reported associations should be interpreted as hypothesis-generating. Missing data were minimal and handled by complete-case analysis. All tests were two-sided with significance threshold of $p < 0.05$. Analyses were performed in Stata version 17 (StataCorp LLC, College Station, TX, USA).

Results

Study population and baseline characteristics

Between 1 February 2023 and 7 January 2025, 270 patients with colorectal cancer undergoing elective surgery were enrolled and analyzed (Fig.1); 260 (96.3%) received IPC alone and 10 (3.7%) received IPC plus enoxaparin. Mean age was 64.8 ± 10.7 years, 171 patients (63.3%) were male, and mean BMI was 23.1 ± 3.5 kg/m². All patients had a Caprini score ≥5 (overall mean 5.96 ± 0.76), classifying the entire cohort as being at high VTE risk. Baseline comorbidities, ASA class, tumor stage, and tumor location were broadly similar between the groups, although the small size of the IPC + enoxaparin group precluded meaningful inference (Table 1).

Regarding tumor characteristics, the most common tumor locations were the rectum (47.78%, n = 129) and sigmoid colon (30.74%, n = 83) as shown in Table 1. TNM stage III was the most prevalent (39.26%, n = 106), followed by stage IV (24.44%, n = 66), stage II (23.70%, n = 64), and stage I (12.59%, n = 34). Distant metastasis was present in 23.33% of patients (n = 63), predominantly to the liver (14.07%) and lung (6.67%). Synchronous tumors were identified in 5.00% of patients (n = 13). No significant differences in tumor location, TNM stage, pathological grade, or pattern of metastasis were observed between groups. Regarding high bleeding risk in the IPC-only group, 13 patients (5.0%) were receiving concomitant anticoagulant or antiplatelet therapy, and 51 patients (19.6%) underwent procedures associated with a high bleeding risk according to the ACCP guidelines (Table 1).

293 **Table 1.** Baseline characteristics of the study cohort, by venous thromboembolism

294 prophylaxis assignment.

Variable	IPC only (n=260)	IPC+LMWH (n=10)	Standardized mean difference (SMD)
Age, mean ± SD (years)	64.7 ± 10.8	68.0 ± 8.3	0.34
Male sex, n (%)	164 (63.1)	7 (70.0)	0.15
BMI, mean ± SD	23.1 ± 3.5	24.0 ± 3.6	0.25
ASA ≥3, n (%)	80 (30.8)	3 (30.0)	0.02
Caprini score	5.95 ± 0.76	6.10 ± 0.74	0.20
Location of tumor			
- Cecum	9 (3.46)	1 (10.00)	0.2632
- Ascending colon	21 (8.08)	0 (0.00)	0.4192
- Hepatic flexure	10 (3.85)	1 (10.00)	0.2442
- Transverse colon	9 (3.46)	0 (0.00)	0.2678
- Splenic flexure	4 (1.54)	0 (0.00)	0.1768
- Sigmoid colon	79 (30.38)	4 (40.00)	0.2024
- Descending colon	12 (4.6)	1 (10.0)	0.208
- Rectum	125 (48.08)	4 (40.00)	0.1632
Synchronous tumor	13 (5.00)	1 (10.00)	0.1907
Pre-op CEA, ng/mL, median (IQR)	2.8 (1.5–9.1)	4.0 (2.1–9.7)	0.518
TNM staging - 1 - 2	 32 (12.31) 63 (24.23)	 2 (20.00) 1 (10.00)	0.4497

- 3 - 4	101 (38.85) 64 (24.62)	5 (50.00) 2 (20.00)	
Liver metastasis	37 (14.23)	1 (10.00)	0.1299
Lung metastasis	18 (6.92)	0 (0.00)	0.3857
Peritoneal metastasis	8 (3.08)	1 (10.00)	0.2828
Simultaneous metastatectomy	13 (5.00)	0 (0.00)	0.3244
Pathology - Well differentiation - Moderate differentiation - Poorly differentiation	 33 (12.69) 220 (84.62) 7 (2.69)	 1 (10.00) 9 (90.00) 0 (0.00)	0.2541
Mucinous component	15 (5.77)	1 (10.00)	0.1575
High bleeding risk			
- Concomitant use of anticoagulant, antiplatelet	13 (5.00)	1 (10.00)	0.1907
- Procedure-specific risk	51 (19.62)	2 (20.00)	0.0097
Laparoscopic surgery	73 (28.08)	2 (20.00)	0.1899
Operation			
- Right hemicolectomy	30 (11.54)	2 (20.00)	0.2338

- Sigmoidectomy	52 (20.00)	4 (40.00)	0.4472
- Low anterior resection	31 (11.92)	0 (0.00)	0.5203
- Abdominoperineal resection	96 (36.92)	3 (30.00)	0.1471
- Adjacent organ resection	10 (3.85)	0 (0.00)	0.2828
- Metastatectomy	7 (2.69)	0 (0.00)	0.2352
Duration of surgery (min) Mean +/- SD	312.57 (156.73)	269.90 (162.46)	0.2673
- <2 hours - 2-6 hours - >6 hours	23 (8.85) 147 (56.54) 90 (34.62)	3 (30.00) 3 (30.00) 4 (40.00)	0.6675
Estimated blood loss (ml) Mean +/- SD	323.55 (973.63)	132.00 (139.90)	0.2754
Perioperative blood transfusion	28 (10.77)	0 (0.00)	0.4913
Postoperative complication			
- Postoperative ileus	34 (13.08)	0 (0.00)	0.5485
- Post op small bowel obstruction	11 (4.23)	1 (10.00)	0.2258
- Chyle leak	9 (3.46)	0 (0.00)	0.2678

Length of hospital stay (days)	10.41 (4.55)	14.10 (17.21)	-0.2934
Post op immobilization (day)	2.35 (1.24)	1.90 (0.74)	
Contraindication for IPC	2 (0.77)	0 (0.00)	0.1245
Postoperative LMWH	0 (0)	10 (100.00)	2.2975
- Intolerance	0 (0.00)	1 (10.00)	
- Bleeding complication	0 (0.00)	0 (0.00)	
Dutation of LMWH (days)	0 (0.00)	24.2 (10.78)	

Continuous variables are presented as median (interquartile range) or mean ± standard deviation, as appropriate based on Shapiro–Wilk normality testing. IPC: Intermittent pneumatic compression; LMWH: Low molecular weight heparin; BMI, body mass index; ASA, American Society of Anesthesiologists physical status classification; CEA, carcinoembryonic antigen; TNM, Tumor–Node–Metastasis staging system.

Procedure-specific bleeding risk was defined according to ACCP guidance [4]. Duration of postoperative immobilization was defined as the number of days with restricted ambulation following surgery. Length of hospital stay was calculated from the day of operation to discharge.

Operative characteristics

The most frequently performed operations were abdominoperineal resection (APR, 36.92%, n = 96), sigmoidectomy (20%, n = 52), and low anterior resection (11.92%, n = 31).

Open surgery was performed in 72.22% of patients (n = 195) and laparoscopic surgery in 27.78% (n = 75).

The mean operative duration was 312.57 ± 156.73 minutes overall. As shown in Table 1, operations lasting 2–6 hours accounted for 150 cases (55.6%), while those exceeding 6 h numbered 94 (34.8%), indicating a complex surgical case-mix. Mean estimated blood loss was 316.45 ± 956.39 mL, and approximately one in ten patients required perioperative blood transfusion. No statistically significant differences in surgical approach, operative duration, or blood loss were observed between the IPC-only and IPC + enoxaparin groups (Table 1).

VTE prophylaxis exposure and adherence

IPC was applied in nearly all patients, with contraindications to mechanical prophylaxis documented only rarely, as shown in Table 1. Among patients who received enoxaparin, the mean duration of enoxaparin administration was 24.20 ± 10.78 days. The timing of the first enoxaparin dose was 23.29 ± 20.02. Treatment dropout occurred in 1 patients overall (10% of LMWH recipients) which was due to intolerance (Table 1).

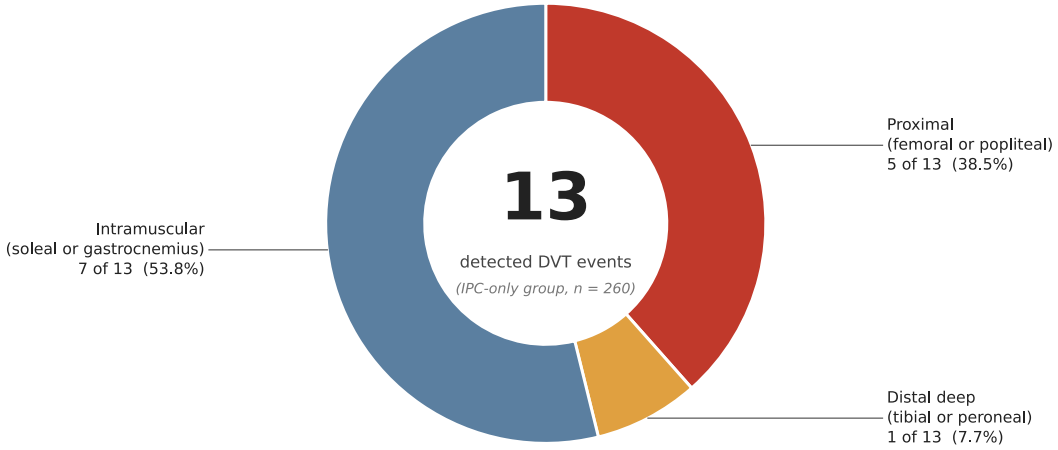
Primary outcome: 30-day VTE incidence

Within 30 days of surgery, screening-detected DVT occurred in 13 patients, all in the IPC-only group, corresponding to an incidence of 5.00% (13/260) within then IPC-only group and 4.81% (13/270) across the total cohort. No DVT events occurred in the IPC + enoxaparin group (0/10). The 30-day composite VTE incidence (DVT or PE) was therefore 5.00% in IPC-only and 0% in IPC + enoxaparin. Of the 13 detected DVT events, 10 (76.9%) were asymptomatic and identified solely by protocol screening, and 3 (23.1%) were symptomatic with clinical features such as lower-limb swelling, calf tenderness, or pain. By anatomical level, 8 of 13 (61.5%) events were distal (involving the tibial, peroneal, or intramuscular veins) and

5 of 13 (38.5%) were proximal (femoral or popliteal) (Fig.2). Limb involvement was right-sided in 4 of 13 (30.8%), left-sided in 6 of 13 (46.2%), and bilateral in 3 of 13 (23.1%) (Table 2).

Pulmonary embolism was diagnosed in 2 IPC-only patients (0.77%) and in no IPC + enoxaparin patients; both PE events were symptomatic. The 30-day all-cause mortality was 0.77% (2/260) in the IPC-only group and 0% in the IPC + enoxaparin group. By 90 days, two additional events were captured in the IPC-only group, yielding a cumulative VTE incidence of 5.77% (15/260) in IPC-only and 0% in IPC + enoxaparin.

Figure 2. Anatomical distribution of screening-detected DVT events



Anatomical distribution of screening-detected deep vein thrombosis events within 30 days of colorectal cancer surgery. Lower-extremity venous segments are categorized as proximal (femoral or popliteal) or distal (calf or intramuscular).

Table 2: Characteristics and clinical course of postoperative venous thromboembolism in patients receiving mechanical prophylaxis alone

Preoperative ultrasound parameter	Number	IPC only
Overall DVT	13	13 (5.00)
Location		
- Femoral	4	4 (1.54)
- Popliteal	1	1 (0.38)
- Tibial vein	1	1 (0.38)
- Intramuscular	8	8 (3.08)
Location		
- Proximal	5	5 (38.46)
- Distal	8	8 (61.54)
Limb involvement		
- Rt leg	4	4 (30.77)
- Lt leg	6	6 (46.15)
- Both	3	3 (23.08)
Symptomatic DVT	3	3 (23.08)
Treatment		
- Full dose anticoagulant	6	6 (46.15)
- Surveillance	7	7 (53.8)
Bleeding complication after anticoagulant	3	3 (50)
Symptomatic PE	2	2 (66.67)
VTE at 4 weeks	13	13 (5.00)
VTE at 3 months	15	15 (5.77)

Preoperative ultrasound parameter	Number	IPC only
30-day mortality (all cause)	2	2 (0.77)

Sum of vessel-level rows exceeds the 13 patient-level DVT events because one patient had multi-segment involvement.

Data are presented as n (%) or mean standard deviation unless stated otherwise. IPC: Intermittent pneumatic compression; DVT: Deep vein thrombosis; PE: Pulmonary Embolism; VTE: Venous thromboembolism

Management of detected DVT and downstream bleeding

Of the 13 patients with screening-detected DVT, 6 (46.2%) received full-dose therapeutic anticoagulation and 7 (53.8%) were managed with surveillance ultrasonography alone, in accordance with anatomical extent and clinical judgment. Among the 6 patients who commenced on therapeutic anticoagulation, 3 (50.0%) developed major bleeding, all in the early postoperative period and requiring transfusion or interventional management. By contrast, no major bleeding event was attributable to prophylactic-dose enoxaparin in the IPC + enoxaparin group; given the small denominator (n = 10), the corresponding upper 95% binomial confidence bound for any major-bleeding event in that group is approximately 30.8%, preventing us from drawing any definitive conclusions about the safety of prophylactic enoxaparin from these data alone. Reoperation for bleeding occurred in 2 IPC-only patients (0.77%) and in no IPC + enoxaparin patients. Median length of hospital stay was 9 days (IQR 8–11) in IPC-only and 9 days (IQR 8–10) in IPC + enoxaparin.

Univariable analysis of risk factors for postoperative VTE

Among 260 patients receiving IPC-only prophylaxis, 13 (5.0%) developed objectively confirmed venous thromboembolism within 30 days of surgery. Univariable Firth's-penalized logistic regression identified five predictors significantly associated with postoperative VTE (Table 3; Figure 3). Splenic-flexure tumor location showed the strongest univariable association (OR 21.35; 95% CI 2.75–165.43; p = 0.003), followed by extended left hemicolectomy and preoperative leg swelling, both with identical odds ratios reflecting their near-perfect overlap in this cohort (OR 19.72; 95% CI 1.16–334.07; p = 0.039 for both). Postoperative small-bowel obstruction was also associated with VTE (OR 5.46; 95% CI 1.13–26.27; p = 0.034). Notably, the continuous Caprini score emerged as a significant univariable predictor (OR 2.55 per 1-unit increment; 95% CI 1.32–4.93; p = 0.006), despite all patients in the cohort being categorized as Caprini high-risk (≥ 5). Operative duration achieved only borderline univariable significance

(OR 1.45 per 120-minute increment; 95% CI 0.98–2.15; p = 0.066). Wide confidence intervals across binary predictors reflect rare exposures (n ≤ 4 affected patients) and should be interpreted as hypothesis-generating.

Table 3. Univariable predictors of 30-day postoperative venous thromboembolism in the IPC-only cohort (n = 260; 13 events).

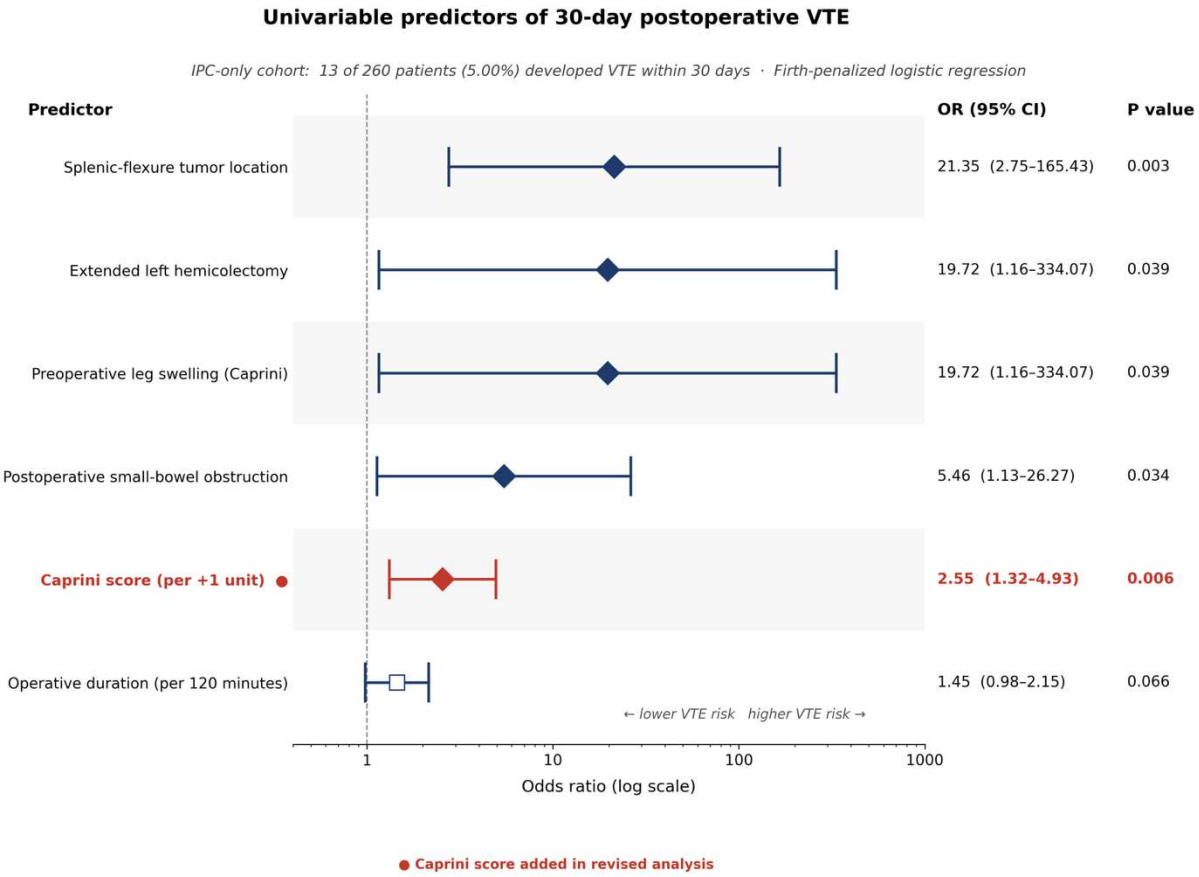
Variable	**Non-VTE (n = 247)**	**VTE (n = 13)**	**OR (95% CI)**	**P value**
Body mass index, kg/m², mean ± SD	23.05 ± 3.51	24.02 ± 4.28	1.08 (0.93–1.25)	0.306
Caprini score, mean ± SD	5.92 ± 0.74	6.54 ± 0.97	**2.55 (1.32–4.93)**	**0.005**
Preoperative leg swelling (Caprini item), n (%)	1 (0.40)	1 (7.69)	**19.72 (1.16–334.07)**	**0.039**

Splenic-flexure tumor location, n (%)	2 (0.81)	2 (15.38)	**21.35 (2.75–165.43)**	**0.003**
Extended left hemicolectomy, n (%)	1 (0.40)	1 (7.69)	**19.72 (1.16–334.07)**	**0.039**
Operative duration, min, mean ± SD	308.4 ± 154.5	391.8 ± 183.3	1.45 (0.98–2.15)	0.066
per 120-min (2-hour) increment				
Operative duration category, n (%)				
< 2 hours (reference)	23 (9.31)	0 (0.00)	1 (reference)	—
2–6 hours	140 (56.68)	6 (46.15)	0.66 (0.22–1.96)	0.458
> 6 hours	84 (34.01)	7 (53.85)	2.23 (0.75–6.62)	0.148
Postoperative small-bowel obstruction, n (%)	9 (3.64)	2 (15.38)	**5.46 (1.13–26.27)**	**0.034**

Data are presented as mean ± standard deviation or n (%) unless stated otherwise. Operative duration odds ratio refers to a continuous per-120-minute (2-hour) increment. Effect estimates and 95% confidence intervals are derived from Firth's penalized maximum-likelihood logistic regression to mitigate small-sample bias and quasi-complete separation given the limited number of events. Wide confidence intervals reflect the small absolute number of events (n = 13) and rare exposures (n ≤ 4 affected patients for several binary predictors); these

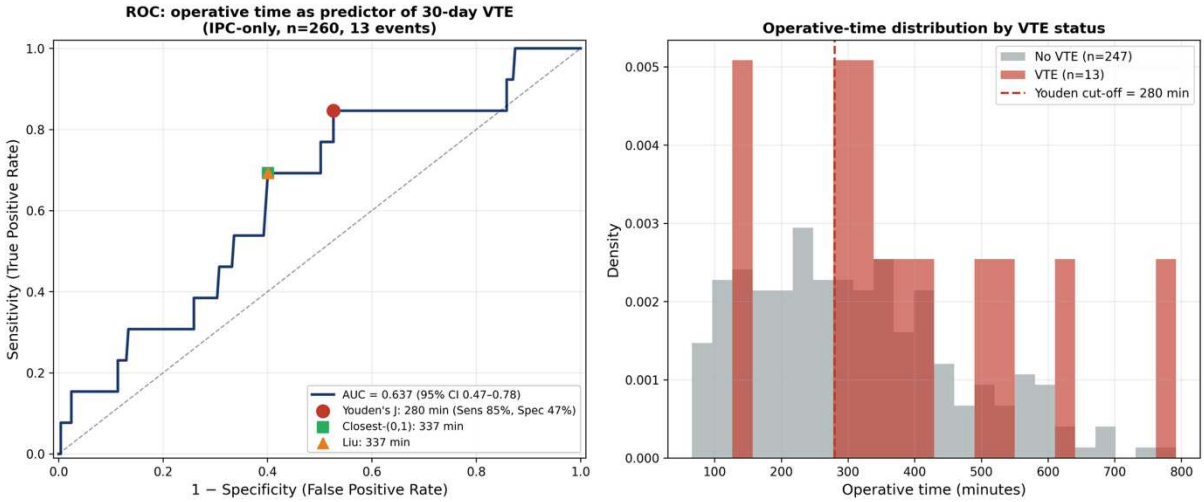
associations should be interpreted as hypothesis-generating. CI, confidence interval; OR, odds ratio; SD, standard deviation; VTE, venous thromboembolism.

Figure 3. Forest plot of univariable predictors of 30-day VTE in the IPC-only cohort, with odds ratios and 95% confidence intervals.



Univariable predictors of 30-day postoperative venous thromboembolism in the IPC-only cohort (n = 260; 13 events). Filled diamonds denote predictors with 95% confidence intervals not overlapping with the null value of 1; horizontal bars represent 95% confidence intervals. Operative duration is rescaled per 120-min (2-hour) increment; the Caprini score is presented per 1-unit increment. CI, confidence interval; OR, odds ratio.

Figure 4: Discrimination of operative duration as a sole predictor of 30-day postoperative venous thromboembolism.



Discrimination of operative duration as a sole predictor of 30-day postoperative venous thromboembolism. (A) Receiver-operating-characteristic curve with bootstrap-derived 95% confidence interval for the area under the curve (AUC = 0.64; 95% CI 0.47–0.78). The Youden's optimal threshold of 280 minutes (filled red circle) yielded a sensitivity of 85% and specificity of 47%, with three convergent cut-off methods (Youden's J, closest-to-(0,1), and Liu's index) shown for sensitivity analysis. (B) Density distribution of operative time stratified by VTE status, illustrating substantial overlap between groups (median 363 min in events vs 294 min in non-events; Mann–Whitney p = 0.097). The dashed vertical line marks the Youden cut-off. AUC, area under the curve; CI, confidence interval; VTE, venous thromboembolism.

The discriminative ability of operative duration as an isolated predictor of 30-day VTE was modest (**Figure 4A**). The area under the receiver-operating-characteristic curve was 0.64 (95% bootstrap 95% CI 0.47–0.78), indicating limited but non-trivial discrimination. Patients who developed VTE underwent significantly longer procedures (median 363 minutes; IQR 251–451) than those who did not (median 294 minutes; IQR 192–404), although the between-

group difference reached only borderline significance on Mann–Whitney testing (U = 2,095; p = 0.097), reflecting substantial overlap in operative-time distributions (**Figure 4B**). Three convergent threshold-selection methods identified an optimal cut-off in the range of 280–337 minutes. The Youden-optimal threshold of 280 minutes (≈ 4.7 hours) yielded a sensitivity of 84.6%, specificity of 47.4%, positive predictive value of 7.8%, and negative predictive value of 98.3%, supporting operative duration's utility as a rule-out criterion rather than a screen-in tool. Bootstrap 95% confidence intervals for the optimal threshold were wide (280–618 minutes), reflecting estimator instability with limited events.

Discussion

In this prospective single-center cohort of 270 Thai adults undergoing elective colorectal cancer surgery within an enhanced recovery pathway, systematic duplex screening detected postoperative DVT in 5.00% of patients managed with IPC alone. Three observations from these data warrant particular emphasis here. First, more than three-quarters of detected thrombi were asymptomatic and almost two-thirds were anatomically distal — a phenotype defined by the screening protocol itself rather than by clinical presentation. Second, the screening-detected rate exceeded the symptom-triggered VTE incidence reported at our own institution in a previous cohort of 2,462 abdomino-pelvic surgeries by approximately tenfold (5.00% vs 0.48%) [17], reflecting the methodological gulf between active surveillance and clinically driven detection. Third, therapeutic anticoagulation initiated in response to these screening-detected thrombi precipitated major bleeding in half of those treated — a hazard exceeding the findings for prophylactic-dose bleeding reported in contemporary trials [18]. Together, these findings expose an unresolved tension at the heart of postoperative VTE management: Detection sensitivity, treatment escalation, and bleeding risk are not independent levers but linked elements of the same risk–benefit calculus.

Quantitative comparisons across the postoperative VTE literature must be calibrated to the detection strategy. English population-based registry data indicated that colorectal cancer resection confers a postoperative VTE risk three- to four-fold higher than non-cancer colorectal surgery, with a clinically relevant proportion of events accruing after hospital discharge [1,2]. The Chinese CRC-VTE prospective cohort, employing protocolized surveillance, identified postoperative VTE in roughly one in nine patients [3]. By contrast, a Japanese colorectal series using pharmacological prophylaxis and clinical endpoints have, by contrast, reported symptomatic VTE rates below 2% [7,8]. Thai data span an analogous methodological range — symptom-triggered surveillance has yielded incidences below 1% [18], whereas duplex-based detection has consistently identified rates in the 3%–7% range [19,20]. Our 5.00% screening-detected DVT rate is therefore broadly aligned with prior Thai imaging-based estimates and roughly an order of magnitude higher than symptom-triggered rates at the same institution. The implication of this is methodological rather than biological: estimates of postoperative VTE burden are governed less by the underlying thrombotic risk of the population than by how aggressively that risk is interrogated [3,7,13,17,19,20].

The clinical centerpiece of this study is not the absolute event rate but the asymmetry between thrombus detection and the harm of treating what is detected. Of 13 DVT events, 8 (61.5%) were anatomically distal and 10 (76.9%) were asymptomatic at the time of duplex screening — a phenotype broadly congruent with imaging-based postoperative cancer cohorts [3,7,11,18,20]. Chinese surveillance-based series in patients without pharmacological prophylaxis have documented asymptomatic distal DVT rates of 38%–42% after open and laparoscopic colorectal resection [21,22], and a multicenter United Kingdom duplex-surveillance study identified asymptomatic below-knee DVT in 6.3% of patients at 6 weeks despite extended prophylaxis in selected cases [23]. A Korean prospective cohort similarly identified that approximately 3% of colorectal cancer patients developed postoperative VTE,

predominantly asymptomatic distal calf-vein thrombosis detected on screening ultrasonography [24]. The natural history of these screening-detected events remains unclear. Outside the perioperative setting, several reviews suggest that selected low-risk patients with isolated distal DVT may be safely managed with serial ultrasonographic surveillance rather than immediate anticoagulation [26,27]. However, active malignancy, recent major abdominal surgery, perioperative immobility, and systemic inflammatory activation collectively place colorectal surgical patients in a substantially higher thrombotic-risk category, and contemporary cancer-thrombosis reviews continue to debate whether small, asymptomatic, or distal thrombi warrant the same anticoagulation intensity as proximal DVT [28]. Ongoing uncertainty rather than established consensus characterizes this clinical space.

That uncertainty was empirically demonstrated in our cohort. Of six patients in whom therapeutic anticoagulation was initiated for screening-detected DVT, three (50.0%) developed major bleeding — almost two orders of magnitude higher than the 0.7% major-bleeding rate observed under prophylactic-dose rivaroxaban in PRO-LAPS II [17] and substantially exceeding the 2–3-fold bleeding excess reported in cancer-patient therapeutic anticoagulation cohorts relative to counterparts undergoing cancer-unrelated surgery [28,29]. CRC-specific VTE registries have likewise documented substantial major and clinically relevant non-major bleeding, driven by age, frailty, anemia, thrombocytopenia, and antiplatelet exposure rather than by surgery alone [30, 31]. The early postoperative window introduces additional asymmetry: fresh anastomoses, raw pelvic dissection planes, and unstable hemostasis recalibrate the threshold at which therapeutic-dose anticoagulation becomes safe. This finding is not an indictment of distal DVT as a clinical entity. Rather, it is a quantitative reminder that the act of detecting subclinical thrombi early after surgery may trigger interventions whose immediate harm rivals or exceeds the short-term threat posed by the thrombus itself. For colorectal surgeons, the practical question therefore shifts from whether duplex screening

increases sensitivity — it self-evidently does — to whether all screening-detected distal events warrant equal weight in treatment algorithms, trial endpoints, and quality benchmarks.

Univariable analysis identified four risk factors significantly associated with 30-day postoperative VTE: splenic-flexure tumor location (OR 21.35; 95% CI 2.75–165.43), extended left hemicolectomy (OR 19.72; 95% CI 1.16–334.07), the continuous Caprini score (OR 2.55 per 1-unit increment; 95% CI 1.32–4.93), and postoperative small-bowel obstruction (OR 5.46; 95% CI 1.13–26.27). Operative duration achieved only borderline univariable significance (OR 1.45 per 120-min increment; 95% CI 0.98–2.15; $p = 0.066$), although VTE patients underwent surgery on for an average of 83 minutes longer than non-VTE patients (mean 391.8 vs 308.4 minutes). The direction and magnitude of the operative-duration effect align with prior large-scale registry-based analyses identifying prolonged operative duration as an independent VTE risk factor in colorectal surgery — including a NSQIP analysis of 51,139 CRC resections in which operative time of 4–6 hours and beyond 6 hours conferred odds ratios of 1.56 and 1.85, respectively, relative to procedures under 2 hours [36], a Chinese multicenter prospective cohort in which anesthesia time ≥ 180 minutes independently elevated 28-day VTE risk [25], and a Bangladeshi prospective study identifying prolonged operative duration as an independent 90-day VTE predictor [37]. The biological coherence is well-established: prolonged operations amplify lower-limb venous stasis, intensify tissue injury, and serve as a surrogate for technical complexity, multivisceral resection, and pelvic dissection [3,7–9].

To translate this borderline univariable signal into a clinically interpretable threshold, an exploratory receiver-operating-characteristic analysis identified a Youden-optimal operative-time cut-off of 280 minutes (approximately 4.7 hours; AUC 0.64; 95% CI 0.47–0.78; sensitivity 85%; specificity 47%; negative predictive value 98%) (Figure 4). Operative time below this threshold reliably identified patients at low absolute risk of 30-day VTE, supporting its utility as a rule-out criterion rather than a screen-in tool. This cut-off sits intermediate

between the thresholds most commonly invoked in the postoperative-VTE literature. The Caprini Risk Assessment Model uses a 3-hour benchmark, assigning additional points to procedures exceeding 180 minutes [15]; the CRC-VTE risk score incorporates anesthesia time ≥ 180 minutes as a discrete predictor [25]; and the NSQIP CRC analysis of Schlick and colleagues stratifies operative time at 2-hour, 4-hour, and 6-hour boundaries, with each successive stratum conferring approximately 1.5- and 1.85-fold elevations in odds, respectively [36]. Our cohort-derived threshold of 280 minutes (4.7 hours) is higher than the 3-hour benchmark used in Caprini and CRC-VTE — plausibly reflecting the technical complexity of the predominantly oncologic resections at our tertiary referral center, where median operative time was 294 minutes (interquartile range 192–406) — and lower than the 6-hour boundary used in the NSQIP CRC stratification used by Schlick and colleagues [36]. The 95% bootstrap confidence interval for the optimal threshold was wide (280–618 minutes), reflecting estimator instability with limited events, and convergent sensitivity-analysis methods (closest-to-(0,1) and Liu's index) identified an alternative threshold of 337 minutes (5.6 hours), suggesting that a clinically meaningful 'prolonged-surgery' boundary for this population likely lies between 4 and 6 hours rather than at the conventional 3-hour benchmark. Whether a population-specific threshold derived from Asian colorectal cohorts ultimately serves clinical practice better than the existing literature-derived benchmarks remains a question for prospective multicenter validation.

Tumor location and procedure-type signals — particularly splenic-flexure tumors and extended left hemicolectomy — are more difficult to interpret. Confidence intervals span two to three orders of magnitude, and the apparent over-representation of splenic-flexure tumors among VTE events (2 of 4 affected patients) may reflect the technical demands of splenic-flexure mobilization, often associated with prolonged operative time and extensive dissection, rather than an intrinsic anatomical effect. These associations should be regarded as

hypothesis-generating until replicated in larger cohorts. Notably, our results differ from larger colorectal surgery series. A retrospective study of 6,844 CRC resections by McKenna et al. found that distal tumor location, especially rectal cancer, was associated with increased postoperative VTE risk, with extensive pelvic surgery further amplifying this risk [38]. Similar observations were reported in a multicenter randomized trial, where rectal resection emerged as a significant VTE risk factor [9]. In contrast, the signal in our cohort was primarily associated with splenic-flexure tumors rather than rectal lesions.

The Caprini score retained meaningful within-cohort discrimination in univariable analysis despite the constraint that every patient was scored ≥ 5 for the enrollment criteria. Prespecified subgroup analyses (Supplementary Table S1) revealed a dose-response gradient: Patients with Caprini scores ≥ 7 and ≥ 8 had approximately four- and seven-fold higher odds of 30-day VTE, respectively, than those at the lower end of the high-risk spectrum. This signal is biologically consistent with the Caprini framework but unexpected given the well-described ceiling effect of Caprini in uniformly high-risk surgical populations [25,32,33]. Recent CRC-specific work has highlighted modest discriminative performance of the Caprini score (AUC 0.59 in a large Chinese cohort), with CRC-tailored models such as CRC-VTE outperforming Caprini-based prediction (AUC 0.72) [25,32]. Composite approaches integrating Caprini with postoperative D-dimer and procedure-specific variables (operative duration, blood loss, surgical complexity) have shown improved discrimination [33,34], supporting a broader principle that thrombosis risk prediction after CRC surgery may benefit from integrating patient-level risk factors with procedure-specific operative characteristics. In elderly Korean colorectal cancer patients managed within an ERAS pathway, an age-adjusted modification of the Caprini score similarly outperformed the standard instrument for postoperative VTE prediction, reinforcing the case for population- and procedure-specific calibration — particularly given the significant excess VTE risk observed among patients ≥ 70 years in our

subgroup analysis (Supplementary Table S1) [34,35]**.** These developments — together with our own findings — do not refute the value of the Caprini score but rather suggest the need for its supplementation with perioperative variables in future Asian-adapted risk-stratification models.

The most striking observation independent of any comparative claim is the asymmetry of prophylaxis allocation: 96.3% of patients received IPC alone, while only 3.7% received combined IPC plus enoxaparin. This pattern reflects more than individual clinician discretion. The Thailand subgroup of the multinational ENDORSE survey documented that, although 56.1% of hospitalized patients met VTE-risk criteria, only 1.8% received guideline-concordant prophylaxis [40]. Even after structured multidisciplinary protocol implementation at a major Thai academic center, pharmacological prophylaxis was administered to fewer than one in six high-risk surgical patients, despite a measurable reduction in symptomatic VTE (from 1.20% to 0.37%) and VTE-related 30-day mortality (from 0.11% to 0.02%) [39]. A complementary Korean experience embedding a structured venous thromboembolism prophylaxis program within an established Enhanced Recovery After Surgery protocol demonstrated improved adherence to guideline-concordant thromboprophylaxis without disrupting enhanced-recovery milestones, illustrating that delivery-pathway redesign — rather than guideline revision alone — can narrow the implementation gap [35]. The allocation pattern in our cohort is therefore less an outlier than the natural extension of a long-standing implementation gap [17,39,40] — driven by clinician concern about early postoperative bleeding, ambiguity about timing of the first dose, outpatient injection burden, cost, adherence, and the residual perception that Asian patients face lower thrombotic risk [6,11,12]. Whether universal Caprini high-risk classification justifies universal pharmacological prophylaxis or supports individualized de-escalation is a question that can not be answer by the present study. What this work does establish is that improving postoperative thromboprophylaxis in CRC surgery requires not only sharper

comparative evidence but also delivery models calibrated to the workflow, economics, and patient-acceptability constraints of routine Asian surgical practice [39].

Strengths

Various methodological strengths of this work support the validity of these findings. For example, the cohort was prospectively assembled with a high rate of standardized preoperative and postoperative bilateral whole-leg duplex screening, eliminating the ascertainment bias common to retrospective registry analyses and complementing prior Thai cohorts that relied on symptom-triggered diagnosis [18,19] or proximal-vein-only imaging [20]. Moreover, univariable risk-factor estimation used Firth's penalized maximum-likelihood logistic regression [42,43], providing bias-corrected coefficients that remain interpretable under quasi-complete separation arising from rare exposures and limited events — a methodological choice rarely applied in surgical VTE risk-factor analyses. Granular ascertainment of tumor characteristics, operative variables, prophylaxis exposure, thrombus anatomy, and downstream bleeding collectively yields a contemporary, clinically rich description of postoperative VTE in a Thai oncological surgical population.

Limitations

Despite the above strength, the study also has subject to several important limitations. The first and most critical is the severe imbalance in group allocation: 260 patients (96.3%) received IPC alone and only 10 patients (3.7%) received IPC plus enoxaparin. This imbalance precludes statistically meaningful between-group comparison, renders propensity-score adjustment numerically unreliable owing to violation of the positivity assumption, and makes causal inference from group contrasts impossible. The absence of VTE events in the IPC plus enoxaparin group, while directionally encouraging, cannot be attributed to prophylaxis strategy with statistical confidence given the small denominator (upper 95% binomial confidence bound

for any major-bleeding event approximately 30.8%). Second, the non-randomized observational design is inherently susceptible to confounding by indication. Third, the study was conducted at a single institution, limiting its generalizability to other contexts. Fourth, the absolute number of VTE events (n = 13) is small, yielding wide confidence intervals around all effect estimates and making univariable analyses underpowered to detect modest effects; reported associations should accordingly be interpreted as hypothesis-generating. Fifth, the 3-month follow-up window, while capturing most clinically relevant postoperative VTE, may miss late events in patients receiving adjuvant systemic therapy that independently elevates VTE risk. Finally, the Caprini score's universal high-risk classification (all patients ≥ 5) compressed its distribution within the cohort and limited within-cohort discrimination, although subgroup analyses suggested preserved signal at higher thresholds (Caprini ≥ 7 and ≥ 8).

Implications and future directions

First, a multicenter prospective trial with balanced allocation — randomized or pragmatically comparative — is required to evaluate extended pharmacological prophylaxis against optimized mechanical-only care, using endpoints calibrated to clinical importance: symptomatic VTE, proximal DVT, pulmonary embolism, and major bleeding. Existing meta-analyses of prolonged LMWH after abdomino-pelvic cancer surgery [4,5] and the favorable efficacy–safety profile of extended rivaroxaban in PRO-LAPS II [17] establish a credible evidence base from which to design such a study. Second, future protocols must prespecify the management of screening-detected distal DVT, because the present cohort demonstrates that reflexive therapeutic anticoagulation in the early postoperative window can carry an unacceptably high bleeding penalty. Distinguishing biological signal from patient-important benefit is essential to trial endpoint selection — a methodological clarification with implications well beyond Thai practice. Third, Asian-adapted CRC-specific risk stratification and implementation research should advance in parallel. The ceiling effect of the Caprini score in

our cohort, mirrored in earlier Thai surgical cohorts [18,19], indicates room for context-sensitive risk models incorporating perioperative variables; the persistence of an implementation gap across two decades of Thai data [18,39,40] indicates that delivery science — addressing bleeding concerns, post-discharge injection logistics, adherence, and clinician risk perception — must accompany any new pharmacological prophylaxis recommendation [6,11,12,39,40]. Mixed-methods studies embedded within colorectal surgical pathways may therefore prove as consequential as further efficacy trials in narrowing the gap between guideline and practice.

Conclusions

Routine duplex screening after elective colorectal cancer surgery uncovers a substantial burden of predominantly distal, asymptomatic thrombosis under mechanical-only prophylaxis — approximately tenfold higher than the symptom-triggered rate observed at our own institution. Treating these incidental events with therapeutic anticoagulation in the early postoperative window incurred major bleeding in half of those treated. The central question for postoperative VTE prevention in Asian colorectal cancer surgery is therefore not whether more thrombosis can be detected, but which detected thrombi are clinically meaningful, and how prophylactic intensity should be calibrated to the balance of thrombotic and hemorrhagic risk in routine practice.

Declarations

Ethics approval and consent to participate

This study was approved by the Human Research Ethics Committee of the Chulabhorn Royal Academy Institutional Review Board (EC 013/2565) and prospectively registered with the Thai Clinical Trials Registry (TCTR20230914001). Written informed consent was obtained from all

752 participants prior to enrollment, and confidentiality was maintained throughout data collection
753 and analysis.
754 **Note:** Guarantor: Nawaphan Taengsakul

755 **Consent for publication**

756 Not applicable.

757 **Availability of data and materials**

758 The dataset generated and analyzed during this study is not publicly available due to the data
759 protection policy governed by the Human Research Ethics Committee of Chulabhorn
760 Research Institute. However, the data may be made available from the corresponding author
761 upon reasonable request and subject to ethical approval.

762 **Competing interests**

763 The authors declare that they have no competing interests.

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766 involvement in the study design or collection, analysis, and interpretation of data. Chulabhorn
767 Hospital was not involved in the decision to submit the manuscript for publication.

768 **Authors' contributions**

769 All listed authors contributed to study design, data collection, and critical revision of the
770 manuscript. NT conceived the study, supervised data collection, performed the principal
771 analyses, and drafted the manuscript. CT contributed hematological expertise and critical
772 review. AB, SK, and NS contributed to patient enrollment, clinical care, and data acquisition.

All authors read and approved the final manuscript and accept public responsibility for its content.

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Figures + figure legends:

Figure 1. Study conduction flowchart according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

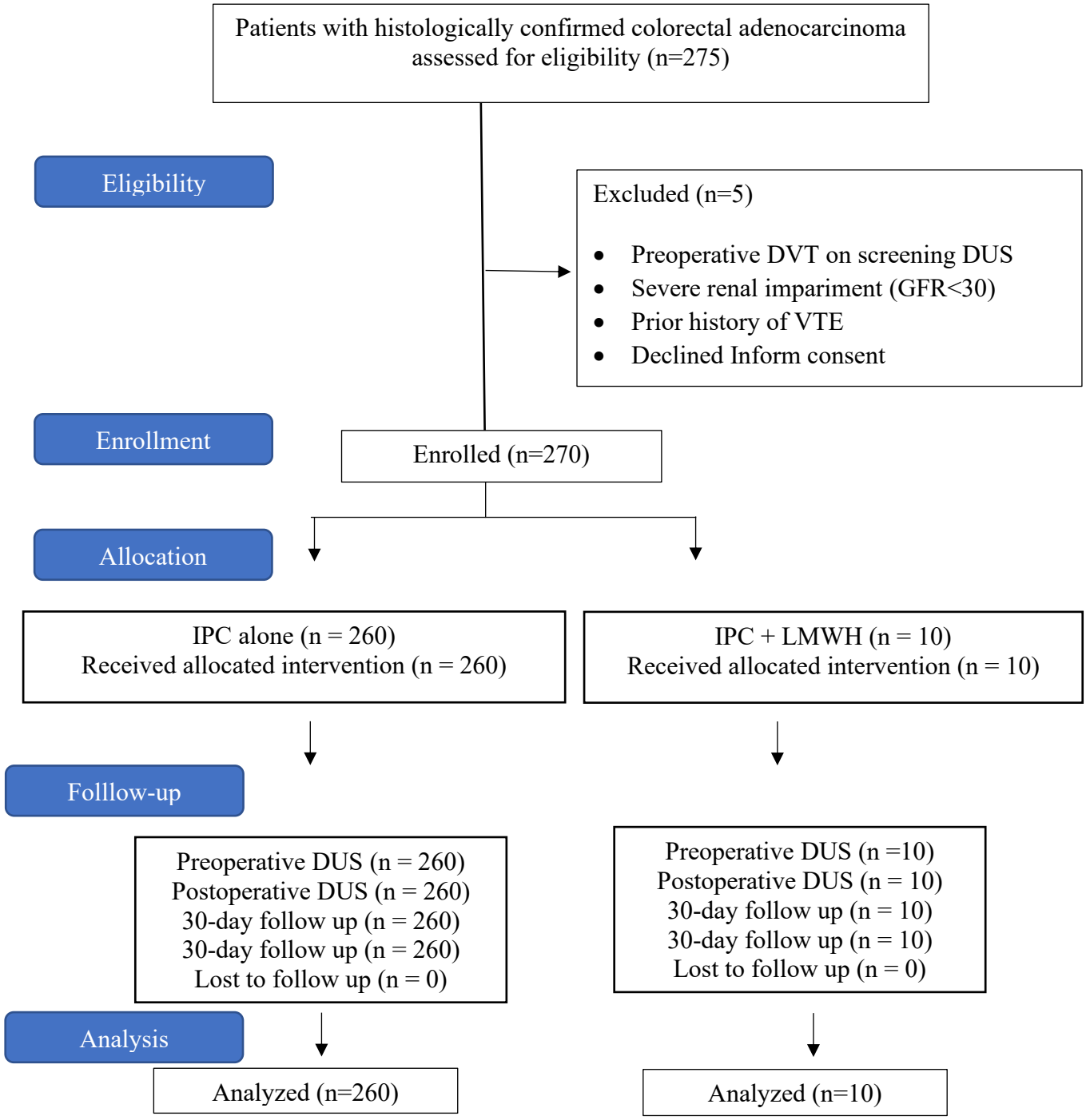
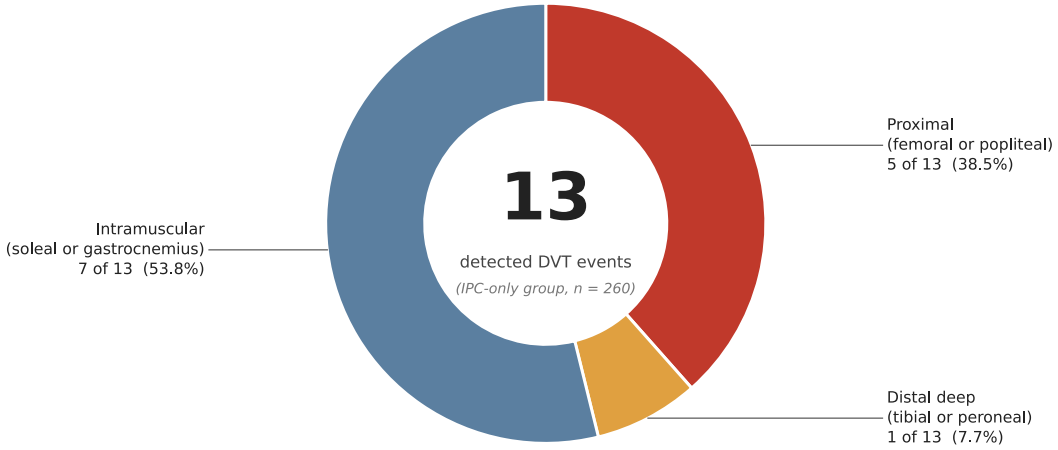
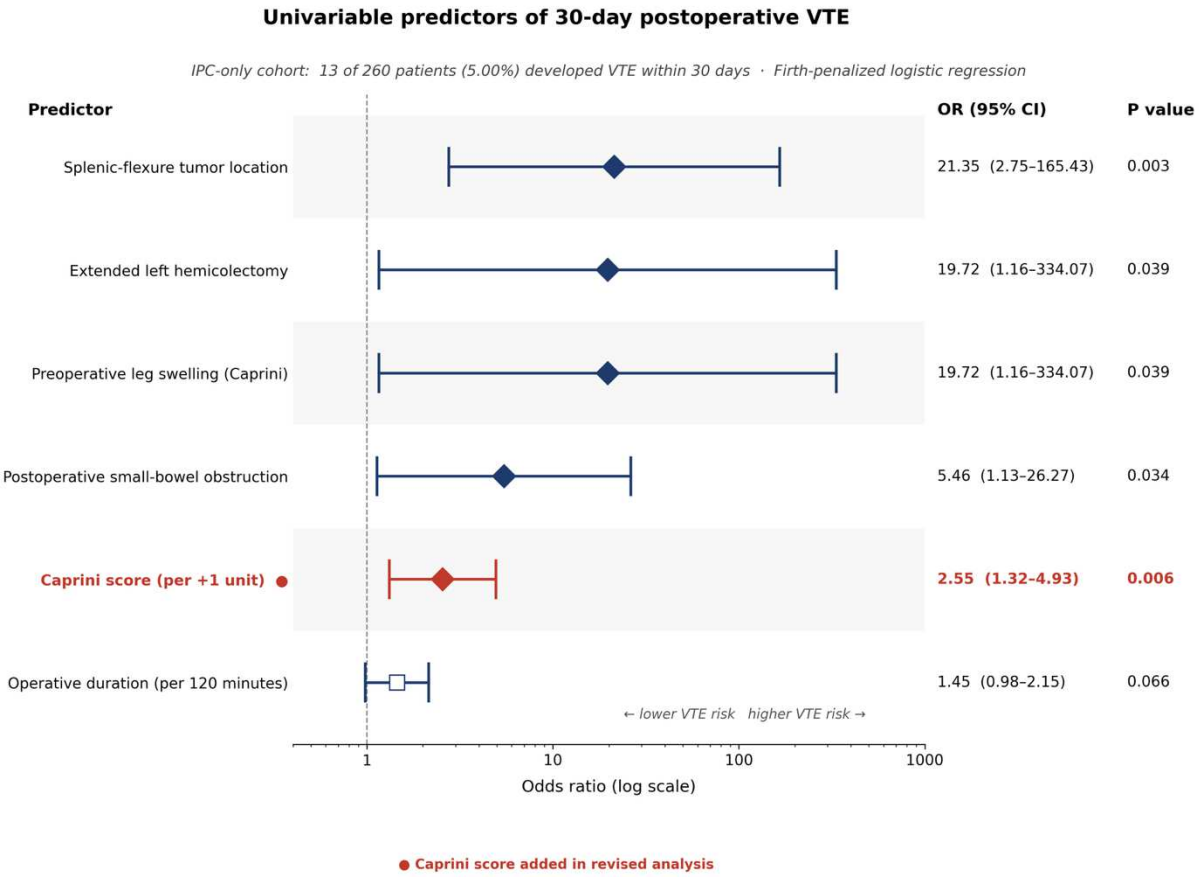


Figure 2. Anatomical distribution of screening-detected DVT events



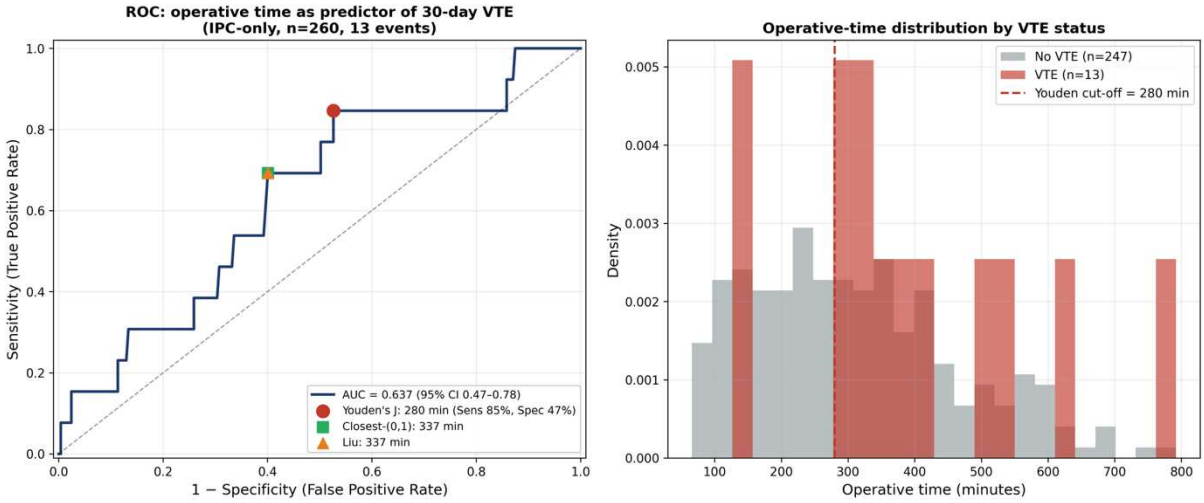
Anatomical distribution of screening-detected deep vein thrombosis events within 30 days of colorectal cancer surgery. Lower-extremity venous segments are categorized as proximal (femoral or popliteal) or distal (calf or intramuscular).

Figure 3. Forest plot of univariable predictors of 30-day VTE in the IPC-only cohort, with odds ratios and 95% confidence intervals.



Univariable predictors of 30-day postoperative venous thromboembolism in the IPC-only cohort (n = 260; 13 events). Filled diamonds denote predictors with 95% confidence intervals excluding the null value of 1; horizontal bars represent 95% confidence intervals. Operative duration is rescaled per 120-minute (2-hour) increment; the Caprini score is presented per 1-unit increment. CI, confidence interval; OR, odds ratio.

Figure 4: Discrimination of operative duration as a sole predictor of 30-day postoperative venous thromboembolism.



Discrimination of operative duration as a sole predictor of 30-day postoperative venous thromboembolism. (A) Receiver-operating-characteristic curve with bootstrap-derived 95% confidence interval for the area under the curve (AUC = 0.64; 95% CI 0.47–0.78). The Youden-optimal threshold of 280 minutes (filled red circle) yielded a sensitivity of 85% and specificity of 47%, with three convergent cut-off methods (Youden's J, closest-to-(0,1), and Liu's index) shown for sensitivity analysis. (B) Density distribution of operative time stratified by VTE status, illustrating substantial overlap between groups (median 363 min in events vs 294 min in non-events; Mann–Whitney p = 0.097). The dashed vertical line marks the Youden cut-off. AUC, area under the curve; CI, confidence interval; VTE, venous thromboembolism.

Supplementary Table S1. Prespecified subgroup analyses of 30-day postoperative venous thromboembolism in the IPC-only cohort (n = 260; 13 events).

Firth's penalized maximum-likelihood logistic regression for each prespecified subgroup.

Bold values indicate $p < 0.05$.

Subgroup	VTE events / n (%) Exposed	VTE events / n (%) Unexposed	OR (95% CI)	P value
Demographics				
Age ≥70 years	8/90 (8.9)	5/170 (2.9)	**3.10 (1.02–9.40)**	**0.046**
Male sex	8/164 (4.9)	5/96 (5.2)	0.90 (0.30–2.74)	0.858
Anthropometric				
BMI ≥25 kg/m²	4/73 (5.5)	9/187 (4.8)	1.22 (0.38–3.89)	0.741
BMI ≥30 kg/m²	1/10 (10.0)	12/250 (4.8)	3.01 (0.45–20.02)	0.254
Comorbidity and lifestyle				
ASA physical status ≥3	5/80 (6.2)	8/180 (4.4)	1.48 (0.49–4.49)	0.491
Current or former smoker	0/10 (0.0)	13/250 (5.2)	0.84 (0.04–17.27)	0.909
Surgical approach and tumor characteristics				
Laparoscopic (vs open)	5/73 (6.8)	8/187 (4.3)	1.70 (0.56–5.17)	0.353
Rectal cancer (vs colonic)	5/124 (4.0)	8/136 (5.9)	0.70 (0.23–2.10)	0.520

Operative complexity				
Operative duration ≥4 hours	11/164 (6.7)	2/96 (2.1)	2.83 (0.70–11.46)	0.145
Operative duration ≥6 hours	7/91 (7.7)	6/169 (3.6)	2.23 (0.75–6.62)	0.148
Caprini risk strata				
Caprini score ≥7	6/51 (11.8)	7/209 (3.3)	**3.86 (1.28–11.65)**	**0.017**
Caprini score ≥8	2/9 (22.2)	11/251 (4.4)	**6.97 (1.38–35.26)**	**0.019**

Footnote.

Subgroup analyses were performed using Firth's penalized maximum-likelihood logistic regression [42,43] to mitigate small-sample bias and quasi-complete separation arising from rare exposures. Each row represents an independent univariable analysis comparing patients fulfilling the subgroup criterion ("Exposed") to those not fulfilling it ("Unexposed"). Effect estimates and confidence intervals from this approach differ from those produced by standard (unpenalized) maximum-likelihood logistic regression, which tends to overestimate odds ratios and underestimate standard errors when one or more cells contain few or no events.

Three subgroups showed statistically significant associations with 30-day VTE: age ≥70 years (OR 3.10; 95% CI 1.02–9.40; p = 0.046), Caprini score ≥7 (OR 3.86; 95% CI 1.28–11.65; p = 0.017), and Caprini score ≥8 (OR 6.97; 95% CI 1.38–35.26; p = 0.019). These findings should be interpreted as hypothesis-generating given the small number of events (n = 13) and the

limited number of patients in some exposure strata (n = 9 patients with Caprini score ≥8; n = 10 patients with BMI ≥30 kg/m²; n = 10 current or former smokers). Wide confidence intervals reflect this small-sample limitation.

All other prespecified subgroups (surgical approach, tumor location, operative duration thresholds, body mass index, sex, smoking, and ASA physical status) showed no statistically significant association with 30-day VTE.

ASA, American Society of Anesthesiologists; BMI, body mass index; CI, confidence interval; IPC, intermittent pneumatic compression; OR, odds ratio; VTE, venous thromboembolism.

Supplementary Table 2. Caprini-anchored composite VTE risk score — Firth-penalized multivariable model coefficients, integer-point clinical scoring system, and model performance.

IPC-only cohort (n = 260, 13 events). Firth's penalized maximum-likelihood logistic regression was used to mitigate small-sample bias and quasi-complete separation given the low number of events.

A. Multivariable model coefficients (Firth-penalized logistic regression)

Predictor	*β*	SE	Adjusted OR	95% CI	Wald z	P value
Caprini score (per +1 unit)	+1.119	0.369	**3.06**	1.49–6.31	3.03	**0.002**
Splenic-flexure tumor location	+2.813	1.164	**16.66**	1.70–163.03	2.42	**0.016**
Operative duration (per +120 min above 4 h)	+0.476	0.214	**1.61**	1.06–2.45	2.22	**0.027**
Extended left hemicolectomy	+0.821	1.759	2.27	0.07–71.32	0.47	0.641
Constant	−3.744	0.473	0.024	0.009–0.060	−7.91	<0.001

Operative duration centered at 240 minutes (4 hours) and reported per 120-minute (2-hour) increment. Caprini score modeled continuously per +1 unit. Bold values indicate $p < 0.05$.

B. Integer-point clinical scoring system (modified Caprini-plus)

Risk factor	Points	Frequency, n (%)	VTE event rate
Caprini score, per +1 unit above baseline (≥5)	**+2**	Continuous	OR 3.06 per +1
Splenic-flexure tumor	**+6**	4 (1.5)	2/4 (50.0%)
Extended left hemicolectomy	**+2**	2 (0.8)	1/2 (50.0%)
Operative time, per +60 min above 4 h	**+1**	Continuous	OR 1.27 per +60 min

Integer points derived by rounding Firth coefficients to nearest 0.5-unit log-odds increment (each integer ≈ OR 1.65). Score AUC = 0.769 with negligible discrimination loss vs continuous model. Optimal Youden cut-off ≥ 6 points yields sensitivity 62%, specificity 80%.

C. Discrimination, calibration, and clinical performance

Performance metric	Estimate	95% CI / interpretation
Discrimination		
AUC (area under ROC curve)	**0.784**	0.633–0.920 (bootstrap)
ΔAUC vs Caprini score alone	+0.091	DeLong p = 0.047
Calibration		
Brier score	0.040	Lower is better (range 0–1)

Brier skill score	0.157	16% improvement vs null model
Calibration intercept	+0.00	Ideal = 0.00
Calibration slope	1.05	Ideal = 1.00

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Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- STROBEchecklistv4combinedPlosMedicine2.docx