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Adequate timing of thromboembolic prophylaxis in colorectal cancer surgery

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Abstract

Background: Patients undergoing colorectal cancer surgery are at high risk of venous thromboembolism (VTE) due to malignancy, surgical trauma, and perioperative immobility. The optimal timing for initiation of pharmacological thromboprophylaxis remains controversial, particularly regarding balancing thrombotic prevention with bleeding risk.

Objective: To evaluate the adequacy and clinical impact of timing of thromboembolic prophylaxis in patients undergoing elective colorectal cancer surgery.

Methods: A prospective observational study was conducted on 100 consecutive patients undergoing elective colorectal cancer surgery at a tertiary care hospital. Patients were grouped based on timing of pharmacologic prophylaxis initiation: preoperative (≤2 hours before incision), early postoperative (6–12 hours after surgery), and delayed postoperative (>12–24 hours after surgery). All patients received low molecular weight heparin (LMWH) and mechanical prophylaxis unless contraindicated. Primary outcomes included incidence of symptomatic VTE within 30 days. Secondary outcomes included postoperative bleeding, transfusion requirement, reoperation, and length of hospital stay.

Results: Of 100 patients, 32 received preoperative prophylaxis, 46 early postoperative, and 22 delayed postoperative prophylaxis. Overall VTE incidence was 8%. VTE occurred in 3.1% of preoperative, 6.5% of early postoperative, and 18.2% of delayed postoperative groups (p=0.041). Major bleeding occurred in 12% overall, with no statistically significant difference between preoperative (15.6%), early postoperative (10.9%), and delayed groups (9.1%) (p=0.68). Delayed prophylaxis was independently associated with increased VTE risk (adjusted OR 3.9, 95% CI 1.1–13.8).

Conclusion: Delayed initiation of thromboprophylaxis (>12 hours postoperatively) is associated with significantly higher VTE incidence without reducing bleeding complications. Early initiation, either preoperatively or within 12 hours postoperatively, appears safe and effective in colorectal cancer surgery.

Keywords: colorectal cancer, venous thromboembolism, thromboprophylaxis, timing, low molecular weight heparin, postoperative bleeding

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Introduction

Venous thromboembolism (VTE), comprising deep vein thrombosis (DVT) and pulmonary embolism (PE), represents a significant cause of postoperative morbidity and mortality in patients undergoing major abdominal surgery[1]. Malignancy itself is a well-recognized hypercoagulable state, and colorectal cancer patients are particularly vulnerable due to advanced age, inflammatory response, prolonged operative time, and perioperative immobility.

The incidence of postoperative VTE in cancer surgery patients without prophylaxis may exceed 20%, with fatal pulmonary embolism reported in up to 1–2% of cases[2-3]. Although routine pharmacologic prophylaxis using low molecular weight heparin (LMWH) is widely recommended, the optimal timing of initiation remains controversial. Early administration may reduce thrombotic events but potentially increase bleeding complications, particularly in pelvic and colorectal surgery where anastomotic integrity is critical[4].

International guidelines recommend initiation either 2–12 hours before surgery or within 6–12 hours postoperatively; however, clinical practice varies considerably. Concerns regarding intraoperative bleeding, epidural catheter placement, and early postoperative hemostasis often result in delayed initiation[5-6].

The present study aimed to assess the adequacy of timing of thromboembolic prophylaxis in colorectal cancer surgery and evaluate its association with postoperative VTE and bleeding complications in a prospective cohort of 100 patients[7].

Materials and Methods

This prospective observational study was conducted at a Tertiary Care Teaching Hospital for 01 Year. Written informed consent was obtained from all participants.

Study Population

One hundred consecutive adult patients (≥18 years) undergoing elective colorectal cancer surgery were included.

Inclusion Criteria

- Histologically confirmed colorectal adenocarcinoma
- Elective curative or palliative resection
- ASA physical status I–III

Exclusion Criteria

- Emergency surgery
- Ongoing anticoagulation for other indications
- Known bleeding disorders
- Severe thrombocytopenia (<50,000/mm³)
- Refusal to participate

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Thromboprophylaxis Protocol

All patients received:

- Mechanical prophylaxis (graduated compression stockings ± intermittent pneumatic compression)
- Pharmacologic prophylaxis with LMWH (enoxaparin 40 mg subcutaneously once daily, adjusted for renal function)

Patients were categorized based on timing of first LMWH dose:

1. **Preoperative group:** ≤2 hours before skin incision
2. **Early postoperative group:** 6–12 hours after surgery
3. **Delayed postoperative group:** >12–24 hours after surgery

Prophylaxis continued for at least 7 days or until discharge. Extended prophylaxis beyond discharge was not routinely administered unless clinically indicated.

Data Collection

Demographic, clinical, and operative variables were recorded:

- Age, sex, BMI
- Comorbidities
- Tumor location and stage
- Type and duration of surgery
- Blood loss
- Need for transfusion

Outcomes

Primary Outcome

- Incidence of symptomatic VTE (DVT confirmed by duplex ultrasound; PE confirmed by CT pulmonary angiography) within 30 days postoperatively.

Statistical Analysis

Data were analyzed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation and compared using ANOVA. Categorical variables were compared using Chi-square test. Multivariate logistic regression was performed to identify independent predictors of VTE. A p-value <0.05 was considered statistically significant.

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Results

A total of 100 patients were included. The mean age was 62.4 ± 10.8 years, and 58% were male. Baseline characteristics were comparable among groups.

Table 1: Baseline Demographic and Clinical Characteristics

Variable	Preoperative (n=32)	Early Postoperative (n=46)	Delayed Postoperative (n=22)	p-value
Mean age (years)	61.8 ± 9.6	63.1 ± 11.2	62.7 ± 10.4	0.82
Male (%)	56.3	60.9	54.5	0.87
BMI (kg/m²)	26.4 ± 3.2	27.1 ± 4.0	26.8 ± 3.6	0.71
Diabetes (%)	25.0	28.3	27.3	0.94
Hypertension (%)	40.6	43.5	45.5	0.92
Stage III/IV (%)	46.9	50.0	54.5	0.81

No statistically significant differences were observed among groups in baseline characteristics.

The majority of procedures were open resections (62%), while 38% were laparoscopic. Mean operative time was 178 ± 34 minutes.

Table 2: Operative and Perioperative Variables

Variable	Preoperative	Early Postoperative	Delayed Postoperative	p-value
Open surgery (%)	59.4	63.0	63.6	0.93
Mean operative time (min)	172 ± 29	181 ± 36	179 ± 34	0.42
Blood loss (mL)	310 ± 90	325 ± 110	340 ± 120	0.51
Transfusion required (%)	12.5	15.2	18.2	0.78
Epidural analgesia (%)	40.6	43.5	36.4	0.84

Incidence of Venous Thromboembolism

Eight patients developed symptomatic VTE (8%). Six cases were DVT, and two were pulmonary embolism.

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Table 3: Postoperative VTE Incidence

Outcome	Preoperative (n=32)	Early Postoperative (n=46)	Delayed Postoperative (n=22)	p-value
DVT (%)	1 (3.1)	2 (4.3)	3 (13.6)	
PE (%)	0	1 (2.2)	1 (4.5)	
Total VTE (%)	1 (3.1)	3 (6.5)	4 (18.2)	0.041

Delayed initiation was associated with significantly higher VTE incidence (p=0.041).

Bleeding and Other Complications

Major bleeding occurred in 12 patients (12%). Minor bleeding occurred in 18%.

Table 4: Postoperative Bleeding and Clinical Outcomes

Outcome	Preoperative	Early Postoperative	Delayed Postoperative	p-value
Major bleeding (%)	5 (15.6)	5 (10.9)	2 (9.1)	0.68
Minor bleeding (%)	7 (21.9)	8 (17.4)	3 (13.6)	0.71
Reoperation (%)	2 (6.3)	2 (4.3)	1 (4.5)	0.91
Mean hospital stay (days)	9.2 ± 2.1	8.8 ± 1.9	10.6 ± 2.8	0.03
30-day mortality (%)	0	1 (2.2)	1 (4.5)	0.43

Delayed prophylaxis was associated with longer hospital stay (p=0.03).

Multivariate Analysis

After adjusting for age, BMI, operative time, stage, and surgical approach, delayed prophylaxis remained an independent predictor of VTE (adjusted OR 3.9; 95% CI 1.1–13.8; p=0.036). Preoperative and early postoperative groups showed no significant difference in bleeding risk.

Discussion

This prospective observational study demonstrates that delayed initiation of pharmacologic thromboprophylaxis (>12 hours postoperatively) significantly increases the incidence of VTE in patients undergoing colorectal cancer surgery without conferring a significant reduction in bleeding complications[8].

The overall VTE incidence of 8% in our cohort aligns with published literature reporting rates between 5–12% in colorectal cancer surgery despite prophylaxis. Notably, the delayed

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group exhibited nearly threefold higher VTE incidence compared to early initiation groups[9].

The hypercoagulable state in cancer patients is exacerbated by surgical trauma and inflammatory cytokine release. Coagulation activation begins intraoperatively and peaks within the first 24 hours postoperatively[10]. Delaying pharmacologic prophylaxis beyond this window may permit early thrombus formation.

Our findings support early administration of LMWH either shortly before incision or within 6–12 hours postoperatively. Importantly, preoperative initiation did not significantly increase major bleeding compared to postoperative groups[11]. Although slightly higher numerical bleeding rates were observed in the preoperative group, differences were not statistically significant.

Concerns regarding anastomotic bleeding and epidural catheter-related hematoma often prompt surgeons to delay prophylaxis. However, evidence suggests that appropriate timing and careful patient selection mitigate these risks[12].

Length of hospital stay was significantly longer in the delayed group, likely reflecting complications related to thromboembolic events. Extended hospitalization increases healthcare costs and morbidity.

Strengths of this study include prospective design and uniform prophylaxis regimen. Limitations include single-center setting, modest sample size, and absence of routine screening for asymptomatic DVT.

Future randomized controlled trials comparing preoperative versus early postoperative initiation with extended prophylaxis duration would further clarify optimal protocols.

Conclusion

Delayed initiation of thromboprophylaxis beyond 12 hours after colorectal cancer surgery significantly increases VTE risk without reducing major bleeding. Early administration either preoperatively or within 12 hours postoperatively appears safe and more effective in preventing thromboembolic events.

Standardized institutional protocols emphasizing timely prophylaxis may improve surgical outcomes in colorectal cancer patients.

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