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# Positive Quality Intervention: Prevention and Treatment of Cancer-Associated Venous Thromboembolic Disease

**Description:** The goal of this PQI is to prevent and manage cancer associated venous thromboembolism (VTE)

**Background:** One-third of all VTEs are cancer associated.[1] Approximately 6.6% of cancer patients will develop cancer associated VTE.[2] Cancer-associated VTE is the second leading cause of death in patients with cancer after progression. The incidence is increasing over time due to longer patient survival, more lines of anticancer therapies received, increased detection of incidental VTE during surveillance imaging, and wider use of central venous catheters.[3] Cancer site (e.g., pancreas, stomach), cancer stage (e.g., advanced disease), hospitalization, surgery, radiation, and particular anticancer agents (e.g., platinum-based agents, immunomodulatory agents, VEGF inhibitors, BCR-ABL RTKI, etc.) increase the risk of cancer associated VTE.[4] Anticoagulation therapy may reduce the risk of cancer related VTE up to 80%, depending on the indication, cancer type and anticoagulation agent.[5]

**PQI Process:**

- Assess each cancer patient risk for cancer associated VTE (*see Supplemental Section*) and need for prophylactic anticoagulant therapy;[6]
    - Use Khorana risk score for general cancer[7]
    - Use ThroLy score for lymphoma[8]
    - Use SAVED score for multiple myeloma[9]
    - Brain cancer VTE risk evaluation is still challenging; use pragmatic classification and if available *isocitrate dehydrogenase1 (IDH1)* mutation and podoplanin expression status[6,10]
- Check possible contraindications (e.g., thrombocytopenia, underlying bleeding, neuraxial anesthesia/lumbar puncture, etc.)[11] for initiation of anticoagulation therapy
- Assess the risk for bleeding using a pragmatic classification based on cancer type or CAT-BLEED score[12] (NOTE: not yet validated) (see *Supplemental Section*)
- Choose anticoagulant, dosing (see *Supplemental Section*) and duration of therapy based on guideline recommendations and individual patient characteristics;
    - Initiate prophylactic anticoagulant therapy during hospitalization in medically-treated patients with cancer who are hospitalized[3]
    - Prophylactic anticoagulant therapy to prevent postoperative VTE in patients with cancer should be started 2–12 hr preoperatively and continued for at least 7–10 days;
        - Extended prophylaxis (4 weeks) is recommended in patients with cancer after major abdominal or pelvic surgery (either laparotomy or laparoscopy) who do not have a high risk of bleeding[3]
    - Prophylactic anticoagulant therapy in ambulatory setting is given continuously in patients who are in the need for this therapy (see specific risk scores for cancer associated VTE and bleeding risk);[3] reassess the need for anticoagulant therapy during cancer patient follow-up.
    - Duration of anticoagulant therapy in established VTE is minimum 3-6 months; decision on continuation beyond 6 months should be based on individual evaluation of the benefit–risk ratio, tolerability, drug availability, patient preference, and cancer activity[3]

**Patient Centered Activities:**

- Consult patient on dosing, administration, and duration of an anticoagulation therapy
- Advise patient on possible side-effects and management
- In case of vitamin K antagonist (VKA), advise patient on possible food-drug interactions

## References:


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11. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology. Cancer-Associated Venous Thromboembolic Disease https://www.nccn.org/professionals/physician_gls/pdf/vte.pdf.
12. De Winter MA, Dorresteijn JAN, Ageno W, et al. Estimating bleeding risk in patients with cancer-associated thrombosis: evaluation of existing risk scores and development of a new risk score. Thromb Haemost. 2022;122(05):818-829.


## Supplemental information:

Khorana score[7]

| Patient characteristics | Points |
|---|---|
| Site of cancer | |
| Very high risk (stomach, pancreas) | 2 |
| High risk (lung, lymphoma, gynecologic, bladder, testicular) | 1 |
| Pre-chemotherapy platelet count ≥350x10⁹/L | 1 |
| Hemoglobin level <10 g/dL or using RBC growth factors | 1 |
| Pre-chemotherapy leukocyte count >11x10⁹/L | 1 |
| BMI ≥35 kg/m² | 1 |

*BMI (body mass index), RBC (red blood cell).*

Interpretation: High-risk ≥3, Intermediate-risk 1–2, Low-risk. Initiate thromboprophylaxis in outpatient cancer patients with an intermediate- to high-risk Khorana score of ≥2.

ThroLy score[8]

| ThroLy predictors | Points |
|---|---|
| Previous VTE/AMI/stroke | 2 |
| Reduced mobility (ECOG 2-4) | 1 |
| Obesity (BMI >30 kg/m²) | 2 |
| Extranodal localization | 1 |
| Mediastinal involvement | 2 |
| Neutrophils <1 × $10^9$/L | 1 |
| Hemoglobin <100 g/L | 1 |

*AMI (acute myocardial infarction), BMI (body mass index), VTE (venous thromboembolism).*

Interpretation: High-risk >3, Intermediate-risk 2-3, Low-risk 0-1. Intermediate and high-risk scores are considered at risk.

SAVED score[9]

| Variables | Points |
|---|---|
| Surgery (within 90 days) | +2 |
| Asian race | -3 |
| VTE history | +3 |
| Eighty (age ≥80 y) | +1 |
| Dexamethasone dose | |
| Standard dose (120–160 mg) | +1 |
| High dose (>160 mg) | +2 |

*VTE (venous thromboembolism).*

Interpretation: High-risk ≥2, Low-risk ≤1. Initiate thromboprophylaxis in high risk group.

Anticoagulant therapy dosing for cancer associated VTE[3,11]

| Anticoagulant agent | Standard dosing | Dosing in special populations |
|---|---|---|
| **DOAC** | | |
| **Apixaban** | Cancer surgery (*alternative*): UFH 5000 units SUBQ 30 minutes prior to surgery and tid through postoperative day 1, then apixaban 2.5 mg PO BID | Avoid if CrCl is ≤30 mL/min |
| | | Avoid if weight <40 kg |
| | | Adjust/avoid with strong dual inhibitors/inducers of CYP3A4 and P-gp |
| | Prophylaxis ambulatory (*preferred*): 2.5 mg PO BID | Avoid if platelet count <50,000/µL |
| | Established VTE (*preferred in non gastric or gastroesophageal lesions*): 10 mg PO BID for 7 days followed by 5 mg PO BID. | Avoid if ALT/AST >3x ULN, total bilirubin >2 x ULN |
| **Dabigatran** | Established VTE (*alternative in non gastric or gastroesophageal lesions*): LMWH or UFH for at least 5 days, then dabigatran 150 mg PO BID | Avoid if CrCl <30 mL/min, caution if CrCl 30–49 mL/min |
| | | Avoid with strong dual inhibitors/inducers of P-gp |
| | | Avoid if ALT/AST >2x ULN |
| | | Caution if platelet count <50,000/µL |
| **Edoxaban** | Established VTE (*preferred in non gastric or gastroesophageal lesions*): LMWH or UFH for at least 5 days, then edoxaban 60 mg PO daily | Avoid if CrCl is ≤30 mL/min, if CrCl 30–50 mL/min consider 30 mg PO qd |
| | | If weight <60 kg consider 30 mg PO daily |
| | | If concomitant potent P-gp inhibitors consider 30 mg PO daily |
| | | Avoid if ALT/AST >3x ULN, total bilirubin >2 x ULN |
| **Rivaroxaban** | Prophylaxis ambulatory (*preferred*): 10 mg PO daily | Avoid if CrCl is ≤30 mL/min |
| | Established VTE (*preferred in non gastric or gastroesophageal lesions*): 15 mg PO bid first 21 days followed by 20 mg daily | Adjust/avoid with strong dual inhibitors/inducers of CYP3A4 and P-gp |
| | | Avoid if ALT/AST >3x ULN |
| | | Avoid if platelet count <50,000/µL |
| **Factor Xa Inhibitor** | | |
| **Fondaparinux** | Prophylaxis hospitalized (*preferred*): 2.5 mg SUBQ daily | Avoid if CrCl <30 mL/min, caution if CrCl 30–49 mL/min |
| | Cancer surgery (*alternative*): 2.5 mg SUBQ daily (start no earlier than 6–8 hours postoperative) | Caution if weight <50 kg and >75 years |
| | Established VTE (*alternative for the first 5–10 days*): 5 mg SUBQ qd (<50 kg), 7.5 mg SUBQ qd (50–100 kg), 10 mg SUBQ daily (>100 kg) | If BMI ≥40 kg/m$^2$ consider 5 mg SUBQ qd (*prophylaxis hospitalized and cancer surgery*) |
| | | Avoid if platelet count <50,000/µL |
| **LMWH** | | |
| **Dalteparin** | Prophylaxis hospitalized (*preferred*): 5000 units SUBQ qd | Avoid if CrCl <30 mL/min |
| | Cancer surgery (*preferred*): 5000 units SUBQ the evening prior to surgery, then 5000 units SUBQ qd OR 2500 units SUBQ 1–2 hours prior to surgery and 2500 units SUBQ 12 hours | If BMI ≥40 kg/m$^2$ consider 7500 units SUBQ qd OR 5000 units SUBQ bid OR 40–75 units/kg SUBQ qd (*prophylaxis hospitalized and cancer surgery*) |
| | | Avoid if weight <40 kg |

| | | |
|---|---|---|
| | later, then 5000 units SUBQ qd beginning postoperative day 1 | |
| | Prophylaxis ambulatory (*preferred*) and established VTE (*preferred in gastric or gastroesophageal lesions*): 200 units/kg SUBQ qd x 1 month, then 150 units/kg SUBQ qd | Avoid if platelet count <50,000/μL |
| **Enoxaparin** | Prophylaxis hospitalized (*preferred*): 40 mg SUBQ qd | Avoid if CrCl <30 mL/min, if CrCl <30 mL/min 30 mg SUBQ qd (*cancer surgery*) |
| | Cancer surgery (*preferred)*: 40 mg SUBQ 10–12 hours prior to surgery, then 40 mg SUBQ qd or 40 mg SUBQ qd with first dose 6–12 hours postoperative | If BMI ≥40 kg/m$^2$ consider 40 mg SUBQ bid OR 0.5 mg/kg SUBQ qd (*prophylaxis hospitalized and cancer surgery*) |
| | Prophylaxis ambulatory (*preferred*): 1 mg/kg SUBQ daily x 3 months, then 40 mg SUBQ qd | Avoid if platelet count <50,000/μL, 0.5 mg/kg SUBQ qd if platelet count 50,000–75,000/μL |
| | Established VTE (*preferred in gastric or gastroesophageal lesions*): 1 mg/kg SUBQ bid, consider 1.5 mg/kg SUBQ qd after 1 month | |
| **UFH** | Prophylaxis hospitalized (*preferred*): 5000 units SUBQ bid-tid | If BMI ≥40 kg/m$^2$ consider 7500 units SUBQ tid (*prophylaxis hospitalized and cancer surgery*) |
| | Cancer surgery (*preferred)*: 5000 units SUBQ 2–4 hours prior to surgery, then 5000 units SUBQ tid through postoperative day 1 | |
| | Established VTE (*alternative for the first 5–10 days*): IV 80 units/kg bolus, followed by 18 units/kg/h adjusted to target aPTT of 2–2.5 X control or per hospital SOPs, followed by SUBQ 250 units/kg bid; OR SUBQ 333 units/kg load, followed by 250 units/kg bid | |
| **VKA** | Established VTE: (*alternative, option in special populations*): start warfarin concurrently with LMWH, fondaparinux, or UFH, 5 mg daily adjusted to INR 2–3 | Adjust if needed in a case of CYP1A2, CYP2C9 or CYP3A4 inhibitors/inducers, score INR 2.5 |
| | | Adjust in CYP2C9 and VKORC1 genetic variations |
| | | Adjust if change in diet containing vitamin K |

*ALT (alanine aminotransferase), aPTT (activated partial thromboplastin time), AST (aspartate aminotransferase), bid (twice daily), BMI (body mass index), CrCl (estimated creatinine clearance), DOAC (direct oral anticoagulants), LMWH (low-molecular-weight heparins), qd (once daily), P-gp (P-glycoprotein), PO (by mouth), SUBQ (subcutaneous), SOP (standard operating procedure), tid (three times daily), UFH (unfractionated heparin), ULN (upper limit of normal), VKA (vitamin K antagonists).*