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Selected Topics: Oncologic Emergencies

ONCOLOGIC EMERGENCIES: TOO MUCH CLOTTING—VENOUS THROMBOEMBOLISM IN MALIGNANCY

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☐ **Abstract—Background: Malignancy predisposes patients to higher risk of venous thromboembolism (VTE), which is the second leading cause of death in patients with cancer. Objective: This narrative review evaluates VTE in malignancy and the emergency medicine investigation and management of this patient population. Discussion: Patients with malignancy are at higher risk of VTE, including deep venous thrombosis (DVT) and pulmonary embolism (PE). Risk factors include the underlying cancer, other hematologic disorders, cancer therapies, and underlying comorbidities. While patients with malignancy and VTE can present similarly to those without malignancy, incidental VTE is more common in cancer patients. Existing scores such as the Wells and Revised Geneva score can assist in risk stratification in patients with malignancy. A negative D-dimer result in the appropriately risk-stratified patient can be used to exclude VTE, though D-dimer is more commonly elevated at baseline in patients with malignancy. Several scoring systems may be useful to predict recurrent risk of VTE, including the Khorana and Ottawa scores. Treatment includes anticoagulation with direct oral anticoagulants (DOACs) or low molecular weight heparin (LMWH). Outpatient therapy may be appropriate in select patients. Conclusions: This narrative review provides key updates in the assessment and management of cancer patients with VTE. Published by Elsevier Inc.**

☐ **Keywords—anticoagulation; cancer; deep venous thrombosis; malignancy; pulmonary embolism; venous thromboembolism**

CLINICAL SCENARIO 1

A 63-year-old man with a history of pancreatic cancer diagnosed 3 months ago presents with left-sided pleuritic chest pain and dyspnea. These symptoms have worsened over the last 2 days. He denies fevers, limb swelling, recent long trips, or back pain, and he endorses normal oral intake. His vital signs include an oral temperature of 36.8°C, heart rate of 102 beats/min, blood pressure of 123/72 mm Hg, respiratory rate of 22 breaths/min, and oxygen saturation of 90% on room air. Electrocardiography reveals new right bundle branch block and tachycardia. A chest radiograph is normal. A computed tomography scan of the chest with intravenous contrast reveals a left segmental pulmonary embolism.

CLINICAL SCENARIO 2

A 52-year-old female with a history of ovarian cancer and chronic tobacco use presents with left lower leg swelling and pain. Her symptoms started 3 days ago. She denies fevers, but believes the leg is also starting to redden. Her vital signs include an oral temperature of 37.1°C, heart rate 81 beats/min, blood pressure of 128/68 mm Hg, respiratory rate of 16 breaths/min, and oxygen

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saturation of 99% on room air. On physical examination, her left leg is markedly swollen compared with her right, with mild redness. Ultrasonography reveals deep venous thrombosis in the common femoral vein.

INTRODUCTION

Cancer is common in the U.S. and presents with a variety of complications, due to the malignancy itself, therapies, and other comorbidities (1–5). Venous thromboembolism (VTE), including pulmonary embolism (PE) and deep venous thrombosis (DVT), affects a variety of patient populations. Patients with malignancy are a unique population at higher risk than the general population for VTE, due to a variety of reasons.

METHODS

This narrative review is part of a series evaluating several classes of complications associated with malignancy and therapy. This is not a meta-analysis or systematic review, but rather a narrative review of the current literature which evaluates the diagnosis and management of VTE in patients with malignancy. To complete this review, authors conducted a literature search of PubMed, Google Scholar, and MEDLINE using search term "venous thromboembolism" OR "VTE" OR "pulmonary embolism" OR "deep venous thrombosis" AND "cancer" OR "malignancy". Authors included randomized controlled trials (RCTs), cohort/observational studies, narrative reviews, guidelines, and systematic reviews/meta-analyses. Studies were limited to English and adult patients. Initial literature search revealed 320 resources. Authors excluded studies not focusing on emergency medicine evaluation and management, resulting in inclusion of 86 resources.

Why Are Patients With Cancer at Such Greater Risk of VTE?

Malignancy and VTE are closely associated. Patients with malignancy possess a 4–7 times increased risk of VTE compared to patients without malignancy, with an incidence that reaches 15% per year (1–3). VTE is the second leading cause of death in patients with active malignancy. This increased risk of VTE in cancer is due to several complex mechanisms, which stems from a hypercoagulable state with procoagulant production, as well as potential venous stasis and vascular endothelial injury (4,5). Platelets, inflammatory cytokines, and tissue factor play key roles in the pathophysiology (4,5). Gastric, lung, pancreatic, renal, uterine, bladder, and primary brain cancers, as well as cancers with metastases, demonstrate the highest rate of VTE. Pancreatic cancer is the solid tumor with the highest rate of VTE (3–6). A solid tumor with distant metastases also significantly increases the risk of VTE (7). Other risk factors can be divided into 4 categories (Table 1) (3–6).

DISCUSSION

How Do DVT and PE Present in Malignancy, and What About Testing?

DVT typically presents similarly in patients with or without active malignancy. The most common symptoms include extremity edema (80%), pain (75%), and erythema (26%) in patients with DVT (4,5,8). PE may present with a variety of symptoms including dyspnea, chest pain, and tachypnea. Specifically in patients with malignancy, the most common symptoms include dyspnea (85%), chest pain (40%), and tachypnea (29%) (4,5,8). The Wells criteria and Geneva score (and Revised Geneva score) are typically used in patients for risk stratification and determination of the need for further diagnostic evaluation in VTE (9–16). Cancer is a component of both scoring systems. Regarding the Wells criteria, 1 point is provided for malignancy, and regarding the Revised Geneva Score, 2 points are provided for active malignancy or if cure has occurred within 1 year (9–16). Studies evaluating these scores have incorporated patients with cancer, and data suggest these scores can safely be used to risk stratify patients with cancer (9–16).

D-dimer testing is also commonly utilized in patients for further risk stratification regarding VTE. However, coagulation effects from cancer can elevate D-dimer (1,5–21). Thus, some recommend against utilizing D-dimer testing in patients with cancer; however, literature suggests a

Table 1. Risk Factors for VTE (4)

Patient-related	Older age, comorbidities, immobilization, recent/recurrent hospitalization, prior VTE, hereditary thrombophilia, obesity, smoking
Cancer-related	Type of cancer (very high risk includes gastric, pancreatic, primary brain cancer; high risk includes lung, hematologic, gynecologic, renal, bladder), stage of cancer, histologic tumor grade, local tumor compression
Treatment-related	Chemotherapy (cisplatin-based, anti-angiogenesis agents), hormonal therapy, red blood cell transfusions, erythropoiesis-stimulating agents, surgery, radiotherapy, central venous access
Hematologic-related	Hemoglobin < 10 g/dL, WBC > 11 × 10(9)/L, platelets > 350 × 10(9)/L

VTE = venous thromboembolism; WBC = white blood cells.

negative D-dimer result can be used to safely exclude VTE in patients stratified as low to intermediate risk with Wells or Revised Geneva score (1,5,21). A negative D-dimer in a patient appropriately stratified significantly lowers the risk of VTE. Further testing in this setting is associated with increased harm and is not recommended (22). Age-adjusted D-dimer has been evaluated and validated in the general population for VTE investigation (17,18,22,23). This is calculated by age multiplied by 10 micrograms/L for fibrinogen equivalent units, or multiplied by 5 micrograms/L for D-dimer units, in patients older than 50 years. This can increase the PE exclusion rate by over 10% (17,18,22,23). In patients with cancer, age-adjusted D-dimer does not have as much robust data compared to the general population, but several studies have suggested increased efficiency in VTE evaluation and ability to exclude disease with age-adjusted D-dimer (19,21). A recent 2017 study that included 429 patients with cancer found use of an age-adjusted D-dimer doubled the number of patients (6.3% to 12.6%) who can be safely excluded without need for further imaging (21). No VTE events were found during 3 month follow-up (21). Utilizing age-adjusted D-dimer assays requires further study in patients with cancer; however, a negative D-dimer result in patients at otherwise low to intermediate risk can exclude the need for further imaging.

Definitive diagnosis includes imaging, dependent on the clinical suspicion of DVT and PE (22–25) Clinicians must consider that diagnostic testing should be based on clinical suspicion of the disease, or the pretest probability (15,22–24). Extremity ultrasound is the primary diagnostic modality for DVT in non-cancer patients with high sensitivity, as well as in patients with malignancy (4,5,14). This test evaluates for the presence of thrombus and venous blood flow and is the imaging modality of choice in the ED. Magnetic resonance imaging or CT with contrast can be used as well, especially in the setting of pelvic vein, iliac vein, or vena cava thrombosis (22–24). Chest computed tomography (CT) with intravenous (IV) contrast is recommended for evaluation of the pulmonary vasculature in suspected PE and is readily available in the ED (4,5,22–24). However, literature suggests a negative CT in a patient with suspected PE and high pretest probability or high pretest prevalence of disease may not be able to definitively exclude PE (4,5,19–21). One meta-analysis suggests that patients with a likelihood of disease or pretest prevalence ≥ 40% for PE and negative CT experienced an 8.1% VTE rate at follow-up, which is similar to a prior meta-analysis (26,27). Patients with pretest prevalence < 40% and negative imaging had a VTE rate of approximately 1% during follow-up (26). Thus, patients with high likelihood or high prevalence of disease and negative imaging may require further testing (27).

Other imaging includes ventilation perfusion (V/Q) scan, which is affected by preexisting lung disease and test availability. In institutions where V/Q scan is available and chest x-ray is normal, V/Q scan may be an optimal test. However, in those with abnormal initial chest radiography or if V/Q scan is not easy to obtain, CT with IV contrast evaluating the pulmonary vasculature is recommended (22–24).

How Often Is Incidental VTE Found in Malignancy?

Incidental VTE is common in patients with cancer, especially subsegmental PEs (4,5). Over 50% of all PEs are diagnosed incidentally in patients with cancer, with a prevalence of incidental PE ranging from 1–15% (28,29). Improved CT technology has increased detection of smaller filling defects located within subsegmental pulmonary arteries (22). Subsegmental PE is most commonly diagnosed on CT imaging in cancer patients undergoing imaging to assess treatment response, during disease staging, or in routine follow-up (4,5,29,30). Despite the diagnosis of these PEs, studies evaluating prognosis in isolated subsegmental PE compared to those with proximal lesions demonstrate conflicting results (30,31). In the general population, treatment of an isolated incidental subsegmental PE treatment requires consideration of the risks and benefits of anticoagulation on a case-by-case basis (22–24,28). In patients with cancer and incidental VTE, anticoagulation should be strongly considered and is supported by several current clinical practice guidelines (32–36). In patients with subsegmental PE, no symptoms, hemodynamic stability, no concurrent DVT, and high risk of bleeding, anticoagulation may be withheld (22–24,28).

Is It Possible to Predict the Risk of VTE in Cancer Patients?

Several scores have been specifically designed for assessing the risk of VTE in patients with malignancy and need for prophylaxis (3–5,28,33–44). The Khorana score was developed to evaluate VTE risk in ambulatory outpatients with cancer receiving chemotherapy and contains 5 factors (Table 2) (28,37,38). However, this score should not be used in those with primary cancer of the brain or myelomas (28–30,32,33). Low risk is associated with a score of 0, which has a 2.5 month VTE rate of 0.3–0.8%. A score of 1–2 points is intermediate, with 2.5 month rate of VTE of 1.8–2.0%, while scores ≥ 3 are high risk and associated with a 2.5 month rate of VTE of 6.7–7.1% (37,38). Other scores include the PROTECHT score, which adds platinum and

gemcitabine therapy to the Khorana score, and the Ay Score, which adds D-dimer and p-selectin (3–5,7,28,33–35). However, these scores have been derived in ambulatory patients with good performance status and solid tumors receiving chemotherapy. The Vienna Cancer and Thrombosis Study (CATS) score utilizes tumor-site risk category and continuous D-dimer concentrations to predict cancer-associated VTE in patients with solid cancer who are ambulatory (39,40). The Ottawa score has also been developed for assessment of recurrent malignancy-associated VTE and demonstrates promise (Table 3) (41–43). An Ottawa score < 0 is associated with low risk for VTE, a score of 0 is intermediate risk, and scores ≥ 1 are high risk. The original derivation study found recurrence rates of 5.1%, 9.9%, and 15.8% for low-risk, intermediate-risk and high-risk patients, respectively, while a recent study found recurrence rates of 2.4%, 8.8% and 15.9% for low-risk, intermediate-risk, and high-risk patients, respectively (41,42), Another validation study from the RIETE registry with 11,123 patients found recurrence rates of 6.88 %, 11.8 %, and 21.3% in low-risk, intermediate-risk, and high-risk patients, respectively (43). Authors of this study state the Ottawa score does not accurately predict VTE recurrence in patients with malignancy (43). A 2017 study comparing the Khorana, Vienna CATS, PROTECHT, and CONKO scores found the Vienna CATS and PROTECHT scores are better able to differentiate low and high risk patients, but overall, scores performed poorly in predicting VTE in patients with cancer (44). The American Society of Clinical Oncology (ASCO) recommends the use of the Khorana score or another validated tool (32). The National Comprehensive Cancer Network (NCCN), the National Institute of Health and Care Excellence (NICE) guidelines, and European Society of Medical Oncology (ESMO) support use of the Khorana score, though the American College of Chest Physicians and European Society of Cardiology do not incorporate these models (22–24,32–36).

Table 2. Khorana Score

Factor	Points
Primary Tumor Site	
Very high risk: stomach, pancreas	2
High risk: lung, lymphoma, gynecologic, bladder, testicular	1
All other sites	0
Prechemotherapy platelet count ≥ 350 × 10(9)/L	1
Hemoglobin < 10 g/dL or use of RBC growth factors	1
Prechemotherapy WBC > 11 × 10(9)/L	1
Body mass index ≥ 35 kg/m(2)	1
Score Interpretation	
Low Risk = 0.3–0.8% rate of VTE at 2.5 months	0
Intermediate Risk = 1.8–2.0% rate of VTE at 2.5 months	1–2
High Risk = 6.7–7.1% rate of VTE at 2.5 months	≥ 3

VTE = venous thromboembolism; RBC = red blood cells; WBC = white blood cells.

What Treatment Is Recommended?

Management includes anticoagulation for those with diagnosed VTE. If patients with DVT do not receive anticoagulation, 50% of these will progress to PE, and of patients with PE who do not receive anticoagulation, mortality rates can reach 30% (3–5,22–24,32–36). Anticoagulation reduces the risk of recurrent VTE from 13.2 events per 100 patient years to 2.0 events per 100 patient years (22–24,45–47). Treatment requires balance between the acute risk of worsening VTE and recurrent VTE and risk of bleeding from anticoagulation (22–25,28). Risks of bleeding in those with malignancy include metastases (odds ratio (OR) 1.6, 95% CI 1.1–2.3), recent hemorrhage (OR 2.4, 95% CI 1.1–5.1), creatinine clearance < 30 mL/min (OR 2.2, 95% CI 1.5–3.4), and immobilization (OR 1.8, 95% CI 1.2–2.7) (48,49). Gastrointestinal cancers (esophageal, hepatobiliary, colorectal, and pancreatic) also significantly increase the rate of major bleeding. The incidence of major bleeding ranges from 6.5–18% in these patients (28,46,50–52). The presence of comorbid conditions in patients with malignancy can make management also difficult, as many medications interact with anticoagulant therapies (3–5,22,28,52,53). Absolute contraindications to anticoagulation include intracranial hemorrhage; severe active bleeding; and recent brain, eye, or spinal surgery. Relative contraindications to anticoagulation include platelet count below 50,000/microL, recent major surgery, and recent cerebrovascular event (24,25). If absolute contraindications to anticoagulation are present, an inferior vena cava filter (IVCF) may be necessary, but this decision should occur in conjunction with hematology/oncology and interventional radiology (28,54). IVCF may also be needed in those who are not compliant with anticoagulation, have a free-floating IVC thrombus, and possess limited cardiopulmonary reserve (54).

Table 3. Ottawa Score for Recurrent VTE Risk

Factor	Points
Female	1
Lung cancer	1
Breast cancer	−1
TNM stage 1 and 2 solid tumors (localized cancer with no metastasis)	−1
Previous VTE	1
Interpretation	
Low risk: Score < 0	
Intermediate risk: Score = 0	
High risk: Score ≥ 1	

VTE = venous thromboembolism.

Similar options for anticoagulation exist for cancer and those without cancer. Current guidelines include direct oral anticoagulants (DOACs), low molecular weight heparin (LMWH), unfractionated heparin, fondaparinux, and warfarin (22–25). Patients with cancer and acute VTE are typically treated with LMWH, based on the CLOT and CATCH trials (55,56). The CLOT trial suggested greater efficacy of LMWH compared to warfarin in reducing VTE risk of recurrence but similar bleeding risk, while the CATCH trial found similar rates of recurrent VTE but decreased recurrent bleeding with LMWH (56). A meta-analysis in 2018 found a relative risk (RR) of 0.66 for recurrent VTE with LMWH compared to UFH, without increased risk of bleeding. However, this is dependent on normal renal function (57). While LMWH is associated with reduced rates of recurrent VTE compared to warfarin, it does not improve mortality (58,59). Warfarin can be utilized in patients with renal dysfunction or for those who refuse subcutaneous injections (22–25). In patients with renal disease, UFH can be utilized, and for patients with history of heparin-induced thrombocytopenia, fondaparinux is recommended (22–24,28,32–36). Fondaparinux demonstrates similar rates of recurrent VTE or bleeding in cancer patients with VTE when compared to LMWH (60).

What About Direct Oral Anticoagulants?

Direct oral anticoagulants (DOACs) include dabigatran, apixaban, edoxaban, and rivaroxaban, with the first studies evaluating these medications excluding patients with malignancy (52,53,61–66). These studies found DOAC therapy to be comparable to, if not more efficacious than, standard therapy (22,52,53,61–66). DOACs offer several advantages including fixed doses, no requirement for routine laboratory monitoring, and obtaining therapeutic efficacy in 1–4 hours (22,52,53,61–71).

Recent literature has evaluated DOAC efficacy and adverse events in patients with cancer and VTE. A pooled analysis of cancer patients with DVT treated with rivaroxaban found similar rates of VTE recurrence compared with warfarin, and another pooled analysis with dabigatran found similar results (65,66). A subgroup analysis of the AMPLIFY trial evaluating apixaban versus enoxaparin followed by warfarin in cancer patients with VTE found similar recurrent VTE and bleeding rates (67). A study published in 2018 found edoxaban reduced the risk of recurrent DVT, while rates of recurrent PE were similar when compared with LMWH (50). Overall risk of recurrence was decreased with edoxaban, but risk of major bleeding was increased (6.9% vs. 4%) (50). Most of these major bleeding episodes occurred in patients with malignancy of the upper gastrointestinal (GI) tract (50). A pilot study, the SELECT-D trial, included 406 patients comparing rivaroxaban with dalteparin (68). Rates of major bleeding were similar, but rivaroxaban was associated with reduced 6-month rate of recurrence (4% versus 11%) (68). Finally, a prospective study of 200 patients found rivaroxaban was associated with a VTE recurrence rate of 4%, major bleeding rate of 2%, and all-cause mortality rate of 18%, similar to those without cancer (69).

Several meta-analyses have also evaluated DOACs versus standard therapies in patients with cancer and acute VTE. A meta-analysis of 5 studies with 982 patients found DOAC therapy reduced the rate of recurrent VTE compared to warfarin, with a RR of 0.66, but no change in mortality or major bleeding (59). Another meta-analysis of 6 studies and 1132 patients found similar rates of VTE recurrence and major bleeding in those with DOACs versus conventional therapy with heparin and warfarin (64). A third meta-analysis published in 2019 evaluating 14 studies and 4,661 patients found DOACs were superior to LMWH in preventing VTE recurrence (hazard ratio (HR) 0.63, 95% CI 0.42–0.96); however, DOACs were associated with higher bleeding risk (HR 1.78, 95% CI 1.11–2.87) (70). The most recent meta-analysis from 2019 evaluated 2 RCTs and 9 observational studies (51). This registered meta-analysis found DOACs, specifically rivaroxaban, significantly reduced the risk of recurrent VTE, with an absolute risk reduction of 2.4% compared to LMWH, or number needed to treat of 41 for DOACs to prevent 1 recurrent VTE. DOACs were associated with higher risk of bleeding with a pooled RR of 1.78 for RCTs, but this was not seen in observational studies. On subgroup analysis, rivaroxaban was not associated with increased bleeding (51).

What Do Guidelines Recommend?

LMWH was the first-line recommended therapy for cancer patients with acute VTE based on prior literature. While more recent guidelines pertaining to patients with cancer and VTE incorporate DOACs, these guidelines differ in their specific recommendations (22–25,32–37,71). The American Society of Clinical Oncology recommends using LMWH for patients with cancer and acute VTE, but does not recommend DOACs (32). Despite this, the National Comprehensive Cancer Network (NCCN) and International Society on Thrombosis and Haemostasis provide a level 1 recommendation for edoxaban and level 2 recommendation for rivaroxaban regarding anticoagulation for cancer-associated VTE (33,71).

What Should You Use in the Cancer Patient With Acute VTE?

DOACs, especially rivaroxaban, may be an acceptable alternative therapy in cancer patients with VTE (28,51,71). The

Table 4. PESI and sPESI Scores

Original and Simplified Pulmonary Embolism Severity Index (PESI)		
	Score	
Variable	Original PESI	Simplified PESI
Age	Age in years	Age > 80 = 1
Male sex	+10	
History of cancer	+30	1
History of heart failure*	+10	1*
History of chronic lung disease*	+10	1*
Pulse ≥ 110 beats/min	+20	1
Systolic blood pressure < 100 mm Hg	+30	1
Respiratory rate ≥ 30 breaths/min	+20	
Temperature < 36°C	+20	
Altered mental status	+60	
Oxygenation saturation < 90%	+20	1

PESI Score		
Score	Class	30 day mortality
<65	I	0%–1.6%
66–85	II	1.7%–3.5%
86–105	III	3.2%–7.1%
106–125	IV	4.0%–11.4%
>125	V	10.0%–24.5%

SPESI – ≥ 1 point warrants consideration of inpatient therapy
* The combination of heart failure and chronic lung disease defines cardiopulmonary disease

risks of major bleeding must be discussed with the patient, as DOACs are associated with higher risk of bleeding in those with GI cancers (28,51,58–71). This increased risk may be due to the combination of local GI tract inflammation from chemotherapy, direct tumor effects, and higher GI tract DOAC concentrations (28,51–53,58–71).

Patient preferences should be considered in the context of age, prior bleeding, blood disorders such as anemia, medications, and renal function (28,71). Tablets may be more convenient, but interactions with other medications should be discussed with the oncologist and patient. Inhibitors and inducers of the p-glycoprotein and cytochrome p450 CYP3A4 systems affect the metabolism of DOACs. If the patient is taking these medications, LMWH is recommended over DOACs (22–25,28,52,53). The International Society on Thrombosis and Haemostasis states shared decision making with the patient is needed, and rivaroxaban or edoxaban may be appropriate in patients who possess a low risk of bleeding and no significant drug interactions (71,72). However, those with thrombocytopenia, high risk of bleeding, GI cancers, and medication interactions should likely receive LMWH (71,72).

Additional Nuances of Therapy

Anticoagulation is recommended for 3–6 months in patients with VTE (22–25,32–36,71,73). However, this may need to be extended beyond 6 months in patients with active cancer, as these patients are at elevated risk for recurrent VTE (22–25,28,71,73). Patients with recurrent VTE while on LMWH may require dose escalation; these patients should be discussed with the hematology/oncology specialist. In cancer patients with recurrent VTE despite standard, weight-based dosing of LMWH or vitamin K antagonists (VKA), dose escalation by 20–25% for at least 4 weeks can be effective and safe (28,74).

Table 5. Hestia Criteria

Hestia Criteria
1. Hemodynamically unstable? 2. Thrombolysis or embolectomy necessary? 3. Active bleeding or high risk of bleeding? 4. Oxygen supply needed to maintain oxygen > 90% > 24 hr? 5. Pulmonary embolism diagnosed during anticoagulant treatment? 6. Intravenous pain medication > 24 hr? 7. Medical or social reason for treatment in hospital > 24 hr? 8. Creatinine clearance less than 30 mL/min? 9. Severe liver impairment? 10. Pregnant? 11. Documented history of heparin-induced thrombocytopenia?
• If any of the above are answered "yes," the patient should NOT be treated as outpatient
• An answer of "no" to all of the above meets criteria for outpatient therapy

Can These Patients Be Treated at Home?

Though studies evaluating outpatient management of DVT and PE have included few cancer patients, outpatient therapy may be possible in non-toxic, hemodynamically stable patients in conjunction with oncology consultation and follow-up (22–25,28). A variety of risk tools are available in determining the safety of outpatient therapy, including the pulmonary embolism severity index (PESI) score, the simplified PESI (sPESI) score, the Hestia Criteria, and others (Tables 4 and 5) (22,74–80). Based on the PESI score, patients with malignancy and PE may still be appropriate for outpatient therapy, based on low risk categorization (74,75). However, the sPESI score stratifies all patients with a history of malignancy as high risk, and the score suggests admission (Table 4) (76,77). The Hestia criteria have been prospectively evaluated and demonstrate safety in predicting those patients with acute PE appropriate for outpatient management (78–80). These criteria do not list cancer as an exclusion to outpatient therapy (Table 5). Ultimately, patient disposition depends upon several factors. With shared decision making, a well-appearing patient who meets all of the Hestia criteria or who is low risk for adverse outcome based on the PESI score may be appropriate for discharge if discussed with hematology/oncology and follow-up is obtained (22,74,75,78–80). Patients with active malignancy and DVT can also be discharged if reliable follow-up can be obtained (4,5,28).

How Should You Treat the Patient With Catheter-Related Thrombosis?

Central-venous catheters (CVC), most commonly those in the upper extremity, may be used for chemotherapy or parenteral nutrition in patients with cancer (28).Unfortunately, patients with these devices may experience catheter-related thrombosis (CRT), which results in symptomatic upper extremity thrombosis in 1–5% of patients (81,82). However, data are limited regarding the management of CRT, including the need for anticoagulation and catheter removal, and practice varies significantly (83). Most current guidelines recommend utilizing LMWH over VKA for patients with cancer and upper extremity CRT, (25,28,36,84) though rivaroxaban has been evaluated in a prospective pilot study (85). This study found that all patients receiving rivaroxaban maintained functional catheters with 1.43% risk of recurrent VTE, but bleeding occurred in 12.85% of patients (85). Further study is required regarding DOAC use in patients with CRT. If the patient requires the catheter and it remains functional, the catheter should be kept in place (28,36,84,86). However, if the catheter is not appropriately positioned, not functional, or infected, it should be removed, with 3–5 days of anticoagulation before removal if possible. Anticoagulation is recommended for at least 3 months whether or not the catheter is removed (28,36,84,86).

CLINICAL BOTTOM LINE

- Patients with malignancy possess a 4–7 fold increased risk of VTE compared to other patient populations, and VTE is the second leading cause of death in patients with malignancy.
- Patients with malignancy and VTE typically present in a similar fashion to patients without malignancy.
- The Wells criteria and Revised Geneva score are often used to assess likelihood of VTE, and these systems can be applied in cancer patients.
- A negative D-dimer result can safely rule out VTE in low to intermediate risk patients; however, it is more commonly elevated at baseline in patients with cancer.
- Incidental PEs are common and account for 50% of all PEs diagnosed in this patient population.
- Several tools such as the Khorana and Ottawa scores can predict the risk of VTE and need for thromboprophylaxis.
- Treatment includes anticoagulation with LMWH or DOAC. DOACs may reduce risk of recurrent VTE but can increase risk of bleeding in those with GI cancers.
- Catheter-associated thrombosis is also common. Anticoagulation is needed in these patients. If the catheter is not functional, is not appropriately positioned, or infected, it should be removed.

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ARTICLE SUMMARY

1) Why is this topic important? Patients with malignancy are at higher risk of VTE, which is the second leading cause of death in malignancy.

2) What does this review attempt to show? This review evaluates VTE in malignancy and the emergency medicine assessment and management of this patient population.

3) What are the key findings? VTE affects patients with malignancy at significantly higher rates than otherwise normal patients. Risk factors include those related to the patient, cancer, and treatment. Most patients with malignancy and DVT or PE will present in a similar manner to those without malignancy. Risk scores such as the Wells criteria and Revised Geneva score can be utilized. A negative D-dimer result in the appropriately risk-stratified patient is helpful to exclude VTE. Unfortunately, incidental VTE is common, accounting for 50% of all PEs diagnosed in this patient population. Several scoring systems may be useful to predict recurrent risk of VTE. Treatment requires anticoagulation with DOACS or LMWH. Outpatient therapy may be appropriate in select patients.

4) How is patient care impacted? This review provides key considerations in the assessment and management of patients with malignancy and VTE.