Prevention of Venous Thromboembolism in Adult Patients With Cancer in the Acute Care Setting

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Adult patients with cancer in the acute care setting face numerous potential complications related to malignancy. Risk for development of venous thromboembolism (VTE) is among the most critical of adverse outcomes for this patient population, ultimately leading to increased morbidity and mortality rates. Nurses must be familiar with the general pathophysiology of VTE and pathophysiology specific to oncology to prevent the occurrence of this complex hematologic process. Knowledge of pharmacologic prevention methods, such as low-dose unfractionated heparin, low-molecular weight heparin, and warfarin, as well as mechanical prophylaxis such as graduated compression stockings and intermittent pneumatic compression devices, is essential to preventing VTE. The ability to develop and implement an educational plan tailored to the specific learning needs of each patient also is a vital skill that must be incorporated into the practice of nurses caring for patients with cancer in the acute care setting to prevent the incidence of VTE in this population.

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Patients with cancer face a multitude of potential complications related to the disease process and treatment of cancer. Some complications will result regardless of measures taken to prevent them, whereas others can be avoided through the use of adequate screening techniques and effective interventions implemented in advance of their occurrence. One of the most prominent of these latter complications is venous thromboembolism (VTE).

Patients with cancer are four to seven times more likely to develop VTE than those in the general population (Lippi & Franchini, 2008). This increased risk can be attributed to several factors, including the prothrombotic nature of malignancy, administration of chemotherapy, suppression of fibrinolytic activity, use of vascular access devices, and surgical intervention used to treat cancer (Lee & Khorana, 2011). The location of the malignancy also plays a role in the patient’s risk for developing VTE. In addition, pancreatic, gastric, ovarian, renal, brain, and lung cancers are associated with increased incidence of VTE, along with hematologic malignancies, particularly leukemia and lymphoma (Lee & Khorana, 2011). Additional risk factors include advanced age, obesity, prechemotherapy thrombocytosis, leukocytosis, prolonged immobilization, infection, and hospitalization (National Comprehensive Cancer Network [NCCN], 2013).

VTE is the second leading cause of death in patients with cancer and is associated with a two-fold increase in mortality (Lee & Khorana, 2011). To decrease the risk of VTE and associated mortality among adult patients with cancer, nurses in the acute care setting must be familiar with the pathophysiology of thrombosis, particularly as it pertains to patients with cancer. Recognition of the broad range of acute care settings where these patients might be encountered also is essential to ensuring that patients are adequately screened and receive prophylaxis for VTE. Those include hospitals, outpatient clinics, long-term acute care facilities, transitional care facilities, medical homes, and home healthcare settings. Nurses must also be familiar with VTE prevention, including pharmacologic and nonpharmacologic therapy. In addition, nurses must be able to effectively communicate this knowledge to patients to ensure compliance with prescribed VTE prophylaxis.

Pathophysiology of Venous Thromboembolism

Knowledge of the basic pathophysiology of VTE is essential to the development of effective prevention strategies. The primary
factors that lead to thrombus formation are endothelial injury, stasis or turbulence of blood flow, and hypercoagulability of blood. The combination of these three factors is known as Virchow’s triad (Mitchell, 2010). Injury of the endothelium, or the cells that make up vessel walls, can be caused by physical injury or by dysfunction of the cells related to hypertension, infection, radiation, and metabolic abnormalities (Mitchell, 2010). Endothelial damage related to malignancy can occur when neoplastic cells penetrate the vessel walls and cause initiation of the clotting cascade (Viale, 2005), or when chemotherapeutic agents that physically damage the endothelial cells are administered (Deitcher & Rodgers, 2009). Placement of central venous catheters also causes endothelial damage and has been directly linked to increased incidence of VTE in patients with cancer (Viale, 2005).

Alteration in normal blood flow, such as stasis or turbulence, is the second component of Virchow’s triad that leads to VTE. Normal blood flow occurs in a laminar pattern, which means that the blood flows through the center of the vessel and is separated from the endothelium by a thin layer of plasma. When stasis or turbulence of blood flow occurs, laminar flow is disrupted and endothelial activation occurs that leads to procoagulant activity and adhesion of blood components to the vessel wall (Mitchell, 2010). Venous thrombosis caused by stasis also can be attributed to the anatomic structure of venous valves, which results in retrograde currents that cause the formation of pockets of stasis in the vessel (Deitcher & Rodgers, 2011). Venous stasis and turbulence of blood flow specific to patients with cancer may occur from decreased activity level resulting from fatigue caused by chemotherapy administration, anemia, radiation therapy, or by direct impingement of the vessels by tumors (Viale, 2005).

The third component of Virchow’s triad, hypercoagulability (thrombophilia), is the alteration of coagulation pathways that increases the risk of developing VTE. Primary (genetic) and secondary (acquired) coagulation disorders are the cause of these alterations (Mitchell, 2010). Deitcher and Rodgers (2009) also cite situational risk factors, such as surgery, prolonged immobilization, oral contraception, hormone replacement therapy, pregnancy, chemotherapy, and heparin-induced thrombocytopenia as major contributors to incidence of VTE. Situational risk factors differ from secondary risk factors in that they are the result of an adverse reaction to a therapeutic intervention rather than the result of an abnormality in hemostasis or irreversible hematologic disorder (Deitcher & Rodgers, 2009).

Pathophysiology of Venous Thromboembolism Specific to Oncology

As previously mentioned, malignancy is, in itself, a prothrombotic state, so the increased risk for developing VTE in this patient population may be inevitable. Nurses in the acute care setting must approach management of patients with this awareness in mind, and develop an understanding of the pathophysiology of VTE specific to oncology to best provide effective prevention and treatment.

One of the primary causes of hypercoagulability in malignancy is the production of procoagulants by tumor cells. Tissue factor (TF), the chief culprit of cancer-related hypercoagulability, is a transmembrane glycoprotein receptor that is found on the surface of endothelial cells, monocytes, macrophages, and most malignant cells (Viale, 2005). When the plasma membrane of cells containing TF is disrupted, the procoagulant activity of the cell is increased. Disruption of the plasma membrane of cancer cells is most often caused by cell apoptosis (death) as a result of treatment, such as chemotherapy or radiation therapy (Lechner & Welterman, 2008). Once TF is released, it activates coagulation factors VII and X, which leads to thrombin generation, platelet activation, development of insoluble fibrin networks, and, ultimately, clot formation. This high expression of TF translates to a poor prognosis because of the high likelihood of metastasis and an increased risk of VTE, which also may increase mortality (Lee & Khorana, 2011).

The release of vascular endothelial growth factor (VEGF) also contributes to hypercoagulability associated with malignancy and is directly related to production of TF. Neoplastic cells release VEGF as a means of promoting angiogenesis and metastasis of tumors. The production of VEGF promotes the procoagulant activity of TF and, in turn, TF increases the transcription of VEGF. This interaction between procoagulants and growth factors contributes to the increased incidence of VTE in patients with metastatic disease (Viale, 2005).

<table>
<thead>
<tr>
<th>TABLE 1. Normal Laboratory Values and Indications</th>
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<tr>
<td>Test</td>
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DIC—disseminated intravascular coagulation; INR—internationalized ratio; PE—pleural effusion; PT—protime; PTT—partial thromboplastin time; VTE—venous thromboembolism

Note: Based on information from Daniels, 2010.
Implications for Practice

- Increase awareness of risk for venous thromboembolism (VTE) in adult patients with cancer in the acute care setting.
- Improve patient education regarding VTE prophylaxis to help increase adherence to treatment.
- Provide nurses with a concise summary of VTE pathophysiology, prevention measures, and patient education.

Another issue associated with hypercoagulability in cancer is inhibition of the fibrinolytic system. This process occurs through the release of proteins by neoplastic cells, such as urokinase-type plasminogen activator and tissue-type plasminogen activator (tPA), which regulate the fibrinolytic system and initiate the clotting cascade. Plasminogen, another component of the fibrinolytic system, is deactivated by plasminogen activator inhibitor type 1 (PAI-1) that is released by malignant cells. This process results in a decrease in fibrinolysis and continuation of coagulation, ultimately leading to angiogenesis, tumor growth, and increased risk for VTE (Viale, 2005).

Production of cytokines, low-molecular weight polypeptides that control inflammation, also is a contributing factor to hypercoagulability related to malignancy. Neoplastic cells release cytokines (tumor necrosis factor-alpha and interleukin-1), which cause the endothelial cells to become prothrombotic (Viale, 2005). Adding to the complication, chemotherapy causes damage to the endothelium, which makes it even more susceptible to activation by cytokines released from neoplastic cells. This “double-whammy” of cytokine release and endothelial damage predisposes patients with cancer to VTE (Viale, 2005, p. 15).

Pharmacologic and Mechanical Prevention

After gaining an understanding of the general pathophysiology of thrombosis and pathophysiology specific to malignancy, nurses caring for patients with cancer in the acute care setting must develop knowledge of effective VTE prevention methods. Although nurses will not be making the decisions regarding which type of prophylaxis will be used, developing an understanding of different prevention methods to ensure patient safety is imperative.

Pharmacologic prevention of VTE in the acute care setting is managed through the use of antithrombotic agents that directly inhibit thrombin and fibrin generation (Deitcher & Rodgers, 2009). Medications most commonly administered include anticoagulants such as IV or subcutaneous low-dose unfractionated heparin, subcutaneous low-molecular weight heparin, and oral warfarin.

Heparin prevents or slows the formation of blood clots by binding with antithrombin III at two sites. This prevents the conversion of prothrombin to thrombin, a key element in the production of fibrin, which is the primary component of a thrombus (Yeo, 2009). Several important considerations exist regarding the pharmacokinetics of heparin: an immediate onset of action takes place with IV administration, elimination of the effect of heparin occurs within hours of discontinuation of the drug, and metabolism of the drug takes place primarily in the liver and kidneys (Yeo, 2009).

Warfarin prevents formation of thrombi by blocking vitamin K-binding sites and inhibits the synthesis of clotting factors and anticoagulant proteins. The onset and duration of warfarin on each of the clotting factors differs, which means close monitoring is required to achieve and maintain a safe, therapeutic level for VTE prophylaxis. Warfarin is the main cause of adverse drug effects in the acute care setting, often from a lack of understanding regarding onset of action, drug-food interactions, and inadequate monitoring of laboratory values, such as internationalized ratio (INR) (Yeo, 2009). Important considerations regarding pharmacokinetics of warfarin include onset of action 24 hours after administration, duration of action of two to five days, primary metabolism by the liver, and multiple interactions with other drugs (Yeo, 2009). Newer drugs that can be used for prophylaxis include factor Xa inhibitors such as fondaparinux, rivaroxaban, and apixaban. An advantage of these medications is oral administration (rivaroxaban and apixaban) without the need for stringent monitoring of INR associated with oral warfarin therapy (NCCN, 2013). NCCN (2013) recommends conducting an initial workup prior to initiating VTE prophylaxis, which should include a thorough history and physical, collection of complete blood count, protime, aPTT/INR, and serum creatinine levels to determine the best prophylactic method for that patient.

According to the NCCN (2013), the use of mechanical VTE prophylaxis has not been extensively studied in patients with cancer. Much of the data collected has come from studies conducted in surgical patient populations. These studies did not address issues specific to patients with cancer, such as severe thrombocytopenia (platelet count less than 20,000 mcl), presence of a hematoma or large tumor, and chemotherapy-induced neuropathy, all of which would be contraindications for use of mechanical prophylaxis. However, some form of prophylaxis is preferable to a complete lack of VTE prevention in this high-risk population. According to the NCCN (2013), hospitalized patients with an active cancer diagnosis are considered to be at high risk for VTE and should have some sort of prophylaxis ordered aside from ambulation. This recommendation is based on the assumption that ambulation within the acute care setting is not sufficient to prevent VTE in this patient population (NCCN, 2013).

Although prophylaxis with anticoagulation therapy may be suitable for VTE prevention in many patients with cancer in the acute care setting, others are at high risk for bleeding because of their disease process, chemotherapy-induced thrombocytopenia (platelet count less than 100,000 mcl but greater than 20,000 mcl), or other hematologic abnormalities. In these patients, pharmacologic prophylaxis is contraindicated and alternate means must be used to prevent VTE. Mechanical prophylaxis, such as graduated compression stockings (GCS) or intermittent pneumatic compression (IPC) devices may be used as a temporary solution until the patient returns to a more stable hemodynamic status (NCCN, 2013).

GCS inhibits venous stasis and endothelial damage, two of the elements of Virchow’s triad that result in VTE. When venous stasis occurs, veins become distended and small tears develop in the endothelium, which are a prime location for platelet aggregation and subsequent thrombus formation.
GCS promotes sustained regressive pressure, which decreases the surface area of the venous circulation in the extremity, increases velocity of blood flow, and prevents venous stasis (Autar, 2009).

To be effective for prevention of VTE, GCS must be applied correctly to ensure that appropriate amounts of compression are delivered to each section of the lower extremity. This graduated distribution prevents the tourniquet effect that would be caused by applying stockings that distribute equal compression over the entire extremity (Autar, 2009).

IPC devices function in a similar manner to GCS in that they deliver varying amounts of compression to the ankles, calves, and thighs to prevent venous stasis. The amount of pressure delivered, the duration of inflation, and the intervals between inflation sequences vary between different devices (NCCN, 2013). IPC devices can be applied and removed more easily than GCS, but they also present a fall hazard for patients who are confused, impulsive, or rise from bed frequently for toileting as the hoses must be disconnected from the sleeves prior to ambulation. The decision regarding which method of graduated compression to use should be made on a patient-to-patient basis. Regardless of whether GCS or an IPC device is used, compliance with use of the prophylactic method is essential to preventing VTE in hospitalized patients with cancer.

In some cases, the ideal means of providing VTE prophylaxis may involve dual use of pharmacologic and mechanical prophylaxis. Einstein et al. (2008) found that using a protocol involving dual prophylaxis was associated with a significant decrease (70%) in VTE among hospitalized patients with gynecologic cancers without increasing complications related to bleeding.

**Implications for Nursing**

Because the risk for VTE among patients with cancer has been well established, the use of a protocol can be an effective means of ensuring that the proper VTE prophylaxis is used for each patient. According to Maynard and Stein (2010), a successful protocol for VTE prophylaxis includes a standardized risk assessment...
The following resources are available for teaching patients about venous thromboembolism (VTE) risk and prevention.

**Centers for Disease Control and Prevention**
Deep vein thrombosis and pulmonary embolism
www.cdc.gov/nchdddv/dvt/facts.html

**Cleveland Clinic**
Deep vein thrombosis
http://my.clevelandclinic.org/disorders/blood_clots/hic_deep_vein_thrombosis_dvt.aspx

**Mayo Clinic**
Deep vein thrombosis
www.mayoclinic.com/health/deep-vein-thrombosis/DS01005

**University of Washington Medical Center**
VTE signs and symptoms and prevention methods
http://vte.washington.edu/SubCategoryList.asp?SCID=6

**Up To Date Patient Information**
Deep vein thrombosis
www.uptodate.com/contents/deep-vein-thrombosis-dvt-beyond-the-basics

FIGURE 2. Patient Education Resources

As soon as a patient is determined to be at high risk for VTE and is clinically stable, education about prevention should be given (U.S. Department of Health and Human Services, 2010) (see Figure 2). Early identification of the patient’s education level to meet the literary capabilities of the majority of patients with contraindication to pharmacologic prophylaxis is paramount to early detection. The warning signs should also be communicated with patients to make them active participants in early detection of VTE. According to Lyman et al. (2013), patients with cancer are “woefully” unaware of their risk for VTE and associated signs and symptoms (p. 2201). A survey of hospitalized patients receiving VTE prophylaxis revealed that patients heard more about VTE from friends, family, or the media than from their healthcare providers (Lyman et al., 2013).

The ability to communicate accurate information regarding the purpose of VTE prophylaxis to patients provides rationale for nurses to build knowledge of pathophysiology and prevention methods. The key to successful implementation of nursing interventions and patient adherence with recommendations is adequate education. Patients and their families are far more likely to adhere with prescribed therapy if they understand the rationale behind it.

As soon as a patient is determined to be at high risk for VTE and is clinically stable, education about prevention should begin (U.S. Department of Health and Human Services, 2010) (see Figure 2). Early identification of the patient’s education level and learning style should be incorporated into the development of an educational program. Some patients may possess just one learning style, whereas others learn using a combination of the different styles (Inott & Kennedy, 2011).

Recognition of barriers to education, such as fear, anxiety, grief, and anger, is vital to providing effective education. Patients and their families should be allowed time to process the abrupt change that has taken place with a new cancer diagnosis. Patients often have an overwhelming amount of information to sift through, emotions are running high, and plans for the immediate future must be arranged; none of which will allow for long-term retention of education.

Ethnic and racial disparities must be considered in the development and delivery of education. “Minority racial/ethnic patients with cancer suffer disproportionately from comorbidities, experience more substantial obstacles to receiving care, are more likely to be uninsured, and are at greater risk of receiving care of poor quality than other Americans” (Lyman et al., 2013, p. 2201). Nurses in the acute healthcare setting are ideally placed to identify these patients and provide them with education regarding VTE risk and prevention tailored specifically to their cultural practices and beliefs.

Illiteracy also is a common barrier to patient education. Written materials should be presented at a fifth grade reading level to meet the literary capabilities of the majority of patients. Avoiding medical jargon and explaining concepts in plain language also is essential to the retention of information by patients and their families. Patient education should be presented in terms that can be easily understood by those without medical backgrounds (Inott & Kennedy, 2011).

Emphasizing the importance of the education being delivered is crucial to retention of the information by the patient. According to Inott and Kennedy (2011),

> Adults enter into learning for the purpose of change in skills, behavior, knowledge, or attitudes; therefore, this motivation is a key factor in initiating education. Awareness by the patient of the importance of what is being learned is essential because adults are motivated by their personal need to know the information. The individual must view the personal application of what is being taught within the context that it is occurring (p. 313).

Focusing the development of an educational plan around individual patient needs will ensure that knowledge is delivered and retained, which will ultimately lead to improved patient outcomes. Studies regarding patient teaching outcomes demonstrate cost effectiveness of successful education, increased patient satisfaction, improved quality of life, and decreased hospital readmissions, all of which coincide with nationwide goals for the future of health care in the United States (Inott & Kennedy, 2011).

**Conclusion**

Risk for development of VTE is among the most critical of adverse outcomes for patients with cancer, ultimately leading to increased morbidity and mortality rates. Nurses caring for these patients must be familiar with the general pathophysiology of VTE and pathophysiology specific to oncology to prevent the occurrence of this complex hematologic process. Knowledge of pharmacologic prevention methods and mechanical prophylaxis is essential to preventing VTE. Thorough physical assessment and adherence to a VTE prophylaxis protocol are essential to ensuring that all patients are screened for VTE risk and receive adequate prophylaxis. The ability to develop and implement an educational plan tailored to the specific learning needs of each patient also is a vital skill that
must be incorporated into the practice of nurses caring for patients with cancer in the acute care setting to prevent the incidence of VTE.

References


