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'Spot the CLOT': What cancer patients want to know

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INTRODUCTION

This article is the second in a dedicated series, entitled 'Spot the CLOT', designed to raise awareness of cancer-associated thrombosis (CAT), with the goal of improving patient education and patient outcomes. The initial article, 'The Significance of VTE in Cancer: Introduction of the *Spot the CLOT* Series', provided an overview of CAT and identified knowledge deficits in the cancer patient population (Sardo, Bayadinova, Jenkins, & Penton, 2021). It highlighted the fact that cancer patients received little to no information on the associated risk of venous thromboembolism (VTE). Strategies offered in this article are designed to raise awareness of VTE among cancer patients, offer approaches to assist with patient education on VTE and, ultimately, reduce the burden of CAT.

THE IMPORTANCE OF EDUCATION ON VTE IN CANCER

Cancer care is complex and newly diagnosed cancer patients are provided with extensive information on treatment and prognosis. Information on CAT is likely not considered a priority when managing the initial chaos of such a life-altering diagnosis. However, cancer is an independent and major risk factor for developing thrombosis, and VTE is the second leading cause of death in cancer patients, second only to the cancer itself (Khorana et al., 2007).

Presenting information on CAT to patients and caregivers early and throughout the various stages of cancer treatment is beneficial, as a significant proportion of cancer patients will develop CAT (Matsuyama et al., 2013). Understanding signs and symptoms of VTE can empower patients to be vigilant for red flags and, hence, less likely to confuse these symptoms with their cancer and/or cancer treatments. Furthermore, studies demonstrated they will be more likely to seek medical attention for symptoms in a timely fashion when they possess this awareness (Matsuyama et al., 2013).

CAT may result in serious complications if not managed quickly. It may cause a lengthy delay or, in severe cases, a complete cessation of cancer treatments. If left untreated, or in the case of a late diagnosis, the patient may be left with damage to the vessels. This may be irreversible and result in debilitating lifelong complications, such as post thrombotic syndrome, chronic thromboembolic pulmonary hypertension, or even death.

As outlined in the UK PELICAN and the subsequent PELICANADA study (Noble et al., 2015; 2019), CAT is a distressing experience for patients, further complicating the cancer trajectory. Patients felt the lack of forewarning regarding the risk of clots and possibility of death was a significant driver of distress. Interestingly, cancer patients prefer being aware of all side effects of cancer and its treatments, including those that are fatal, despite healthcare providers' reservations about sharing this information (Matsuyama et al., 2013). The conclusion from both PELICAN studies was that some of the distress associated with CAT could be ameliorated by information on CAT, early access to specialist services, and emotional support.

To summarize, here are three reasons why it is important to talk to patients about CAT:

1. It is NOT RARE! About 1 in 200 cancer patients will develop CAT. VTE is the second leading cause of death in patients with cancer, second only to disease progression.
2. Pulmonary embolism (PE) can be FATAL! Teaching about signs and symptoms of VTE can alert patients to seek medical care sooner, thereby improving patient outcomes.
3. CAT can be a very DISTRESSING experience, particularly if there is limited support or information. Cancer patients want to know!

STRATEGIES FOR PATIENT EDUCATION

Patient education is a foundational pillar of nursing practice for the improvement of health outcomes and quality of life. The importance of patient education is particularly relevant in the field of oncology care, where medical information is very complex (Truccolo

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et al., 2015). Its timing could be the determining factor in one's ability to understand and retain information. The acute hospitalization phase, whether in relation to cancer treatment or newly diagnosed VTE, may necessitate reinforcement of education once the stressful event has passed, or the patient is discharged home.

Considering Health Literacy in the Cancer Patient

Health literacy is defined as the degree to which individuals can obtain, process, understand, and communicate about health-related information needed to make informed healthcare decisions (Berkman et al., 2010). Incomplete understanding of health information may lead to poor health outcomes, including more emergency department visits, higher numbers of hospital admissions, and improper administration of medications (Berkman et al., 2011). The United States Department of Education (2006) estimated that $50 to $73 billion of annual healthcare costs may be attributed to poor health literacy.

More than 65% of all cancers involve adults aged 65 and over—a population that faces increasingly complex management options, cognitive and sensory deficits, and intergenerational barriers. As a result of these and other factors, older cancer patients have among the lowest health literacy levels (Almaraj et al., 2009). Studies show that low health literacy in this population contributes to poor health outcomes and increased mortality (Berkman et al., 2011).

To ensure appropriate learning, teaching must be tailored to a patient's education level, language, and age. Materials should be written at or below the fifth-grade level to facilitate understanding, regardless of the patient's educational status (The Joint Commission, 2010). Providing the education in the patient's preferred language and use of visuals, such as diagrams or pictures, enhances comprehension (The Joint Commission, 2010).

Learning Theories

There is a paucity of evidence in relation to which theoretical framework is most effective for patients with thrombosis (Hews-Girard et al., 2017). However, key theories in adult learning developed by psychologists and neuroscientists exist. Gardner's multimodal learning theory posits that the use of more than one sense, including written, auditory, and visual, will help a patient learn by capturing their preferred style (Leshkovska & Spaseva, 2016). For this reason, connecting cancer patients with resources that make use of videos, pictures, and written handouts in combination may be of use.

Nursing educational theories focus on the nurse-patient relationship, setting mutually agreeable goals and ensuring that the patient has constant input. One-to-one nursing teaching visits can help set a therapeutic relationship and provide for individualized care based on the patient's self-described needs.

The Health Belief Model indicates patient behaviours are influenced by their perception of the severity of potential illness, their susceptibility to that illness, the benefits of taking preventative action, and the barriers to that action (Hews-Girard et al., 2017). This model highlights the importance of educating cancer patients about their risk of VTE, signs and symptoms to watch for, and how CAT could impact their quality of life.

Technology as an Educational Tool

Patient preferences vary between in-person educational visits versus virtual encounters. This can present challenges in the time of the COVID-19 pandemic, where reducing in-person clinical care has been an essential aspect of protecting patients, healthcare providers, and health system resources (Giuliani et al., 2020) and appointments have moved to a digital format in the majority of situations. A push toward using digital education tools can be useful for patients, as it facilitates around-the-clock access to different modes of learning online or via the use of smartphone applications. As mentioned earlier however, the majority of cancer patients are older, which may create a digital access divide. If patients experience these barriers, it is important for nurses to connect with family members and caregivers to assist in the use of these technologies.

VTE HEALTH EDUCATION TOPICS: WHAT CANCER PATIENTS NEED TO KNOW

Patients with cancer have a seven-fold increase in the risk of VTE (Blom et al., 2005). It is, therefore, both important and necessary to explain this risk to all newly diagnosed cancer patients. In order to facilitate better understanding, VTE should be defined and described. Educating patients about signs and symptoms of CAT is of critical importance given that patients may otherwise believe these are symptoms of cancer, or a side effect of therapy and, therefore, may avoid or delay seeking medical attention. Finally, risk factors for the development of CAT should be discussed, so patients are aware of the need to be more vigilant if any of the risk factors apply to them, especially during high-risk periods of their treatment. Appendix A provides a sample CAT brochure outlining main points for patient education in those newly diagnosed with cancer. The authors grant permission for use of this patient handout for education purposes. In addition, the Thrombosis Canada website has an animated patient-friendly video describing CAT, an excellent resource for visual learners (see video titled VTE and Cancer Whiteboard available in English and French on https://thrombosiscanada.ca/resourcepage/patient-family-information/).

What is CAT?

Although thrombosis may be arterial or venous, VTE is the more common phenomenon in cancer patients (Abdol Razak et al., 2018). It can occur at multiple sites, but the most common sites are deep vein thrombosis (DVT) in the lower or upper extremities and Pulmonary Embolism (PE).

Epidemiology

CAT is a significant contributor to mortality and morbidity in people diagnosed with cancer. Cancer increases the risk of development of VTE five- to seven-fold, the risk of recurrence of VTE

three-fold, and the risk of death ten-fold (Streiff et al., 2021). Various studies have demonstrated that between four to 20% of cancer patients develop CAT at some point in their cancer journey, with the first months after diagnosis representing the highest risk (Abdol Razak et al., 2018). It is estimated that 0.5% of cancer patients develop CAT on an annual basis (Abdol Razak et al., 2018). This risk is higher for upper extremity DVTs, with almost 1% of cancer patients developing this type of thrombosis (Poh et al., 2019). However, in cancer patients who have central venous catheters, the incidence of upper extremity DVTs has been reported to be as high as 66% (Verso & Agnelli, 2016). Up to 25% of patients with catheter-associated upper extremity DVT will develop PE (Verso & Agnelli, 2016).

Pathophysiology

Hemostasis is the normal response to bleeding. In pathologic thrombosis, however, the normal physiologic mechanism of hemostasis is altered, resulting in a complete or partial occlusion of a vessel. There are multiple mechanisms that contribute to the development of CAT, which can be explained by Virchow's triad (Mukai & Oka, 2018) (see Figure 1).

The first contributing factor is the development of a hypercoagulable state due to the presence of cancer and the activation of the clotting cascade by white blood cells and tumour cells. Endothelial injury typically occurs with many cancer treatments including surgery, central lines, and chemotherapy, particularly thalidomide, bevacizumab, and lenalidomide (Charalel & Vedantham, 2017). The final factor in the triad, venous stasis, can be exacerbated by tumour compression, presence of central lines, and immobility.

Symptoms

CAT may be asymptomatic or present with uncomfortable symptoms. (See Table 1 for a summary of symptoms of CAT.) Patients with PE often present with pleuritic chest pain, new onset or worsening of existing shortness of breath (SOB), syncope/presyncope, hemoptysis, and tachycardia (Chapuy & Connors, 2020). Common signs and symptoms of DVT in the legs include edema, erythema, warmth, and pain in

Figure 1

Virchow's Triad in CAT (Mukai & Oka, 2018)

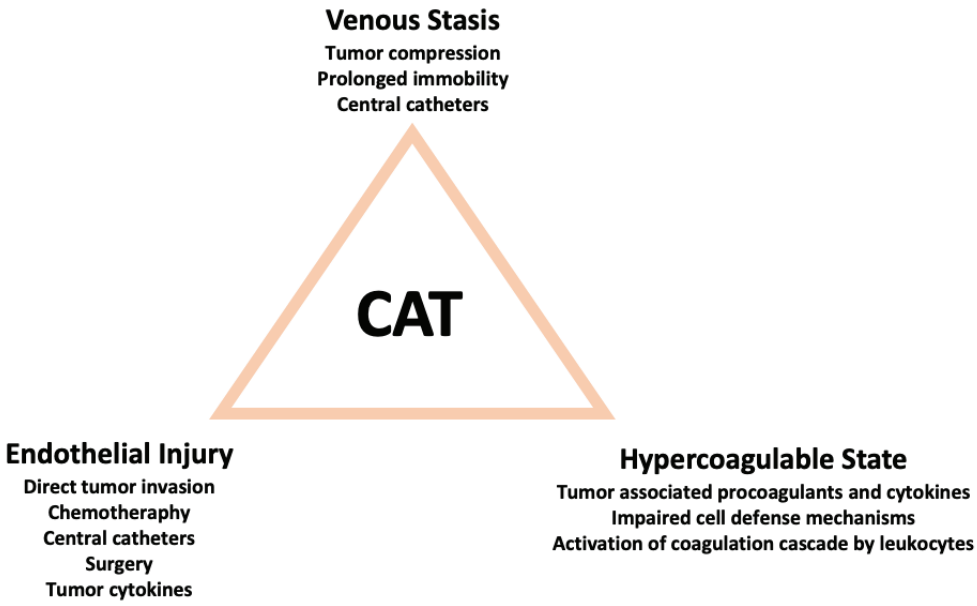

Table 1

Symptoms of CAT

PE	Lower Extremity DVT (confined to affected extremity)	Upper Extremity DVT (confined to the affected extremity)
• Dyspnea/Worsening of baseline SOB • Pleuritic chest pain • Hemoptysis • Tachycardia/tachypnea • Syncope/presyncope	• Whole leg edema • Erythema or warmth • Pain along the deep venous system (proximal medial aspect of calf, popliteal fossa, medial thigh) • Dilated superficial veins of thigh • Palpable venous cords	• Arm or neck edema • Erythema or warmth • Pain along the deep venous system (medial aspect upper arm) • Dilated superficial veins upper arm or anterior chest wall • Palpable venous cords • Malfunctioning central line

the affected extremity, as well as dilation of superficial veins or the presence of a palpable cord-like clotted vein (Ramzi & Leeper, 2004). Upper extremity DVT is often asymptomatic, especially in patients with central venous catheters (Verso & Agnelli, 2016). In symptomatic patients, the most common symptoms include arm or neck swelling, arm pain, erythema, distended superficial veins (due to deep venous occlusion), or a malfunctioning central line (Verso & Agnelli, 2016). Because a large proportion of patients have asymptomatic upper extremity DVTs, their first symptoms may, unfortunately, present as PE (Verso & Agnelli, 2016).

Diagnosis and Treatment

Contrast venography is the gold standard for the diagnosis of DVT but, because of its invasive nature, diagnosis is typically made by compression ultrasound (Chapuy & Connors, 2020). Diagnosis of PE is typically made by a ventilation/perfusion scan (V/Q scan), or a computed tomography pulmonary angiogram (CTPA) (Chapuy & Connors, 2020).

CAT is typically treated with anticoagulants, which may come in the form of tablets or injections. Duration of treatment is generally a minimum of three months, though it is longer if cancer remains active (Lyman et al., 2021). Individual patient characteristics and risk factors for both thrombosis and bleeding determine the treatment trajectory. A detailed overview of treatment recommendations will be provided in an upcoming article in this series. Despite common misconceptions, in upper extremity DVT associated with central lines, the removal of the central catheter is not necessary, unless it is not functional, no longer needed, or infection is present (Rajasekhar & Streiff, 2019).

Risk Factors for VTE

Age above 65 has consistently been shown to be a risk factor in the development of VTE in cancer patients (Abdol Razak et al., 2018). Immobility, especially bedrest with a duration of at least three days, also significantly increases the risk of VTE (Abdol Razak et al., 2018). Multiple comorbid conditions further contribute to the risk, including renal failure, coronary artery disease, obesity, and respiratory infections (Abdol Razak et al., 2018). In addition, multiple cancer-specific factors have been identified, including the type and stage of cancer, and cancer treatment. The primary cancers with the highest rates of VTE include those of the pancreas, uterus, lung, stomach, kidneys, and brain (Abdol Razak et al., 2018). Advanced cancer stage and cancer with distant metastases also pose a higher risk for VTE (Abdol Razak et al, 2018). The initial three to six months after cancer diagnosis represent the highest risk period (Abdol Razak et al., 2018). Finally, cancer treatments such as chemotherapy, radiation therapy, and surgery, especially ones that requiring hospitalization, all compound the risk of VTE (Abdol Razak et al., 2018). Patients at highest risk for CAT may be offered preventative treatment in the form of blood thinners to reduce their risk of VTE. Recent trials demonstrating benefit of anticoagulation for the primary prevention of VTE in cancer patients will be discussed in an upcoming article in this series.

CONCLUSION

CAT is a common and serious complication of cancer, which increases rates of mortality and morbidity. Cancer patients have expressed a desire and need to know about its associated risks, symptoms, and management before the diagnosis is made. This knowledge empowers patients to seek medical attention in a timely manner, which can prevent delays in diagnosis and treatment, both of which are important prognostic considerations.

Patient education should be tailored to the learning needs and health literacy level of the individual patient. This article offers topics that are important for discussion and review in the newly diagnosed cancer population. A sample patient education handout and video resource are provided to assist in the development of educational programs to increase awareness of CAT, with the ultimate goal of improved patient outcomes. The remaining articles in the 'Spot the CLOT' series will focus on treatment of CAT and optimization of healthcare provider awareness of this important, yet understated complication.

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APPENDIX A—SAMPLE PATIENT HANDOUT ON CAT

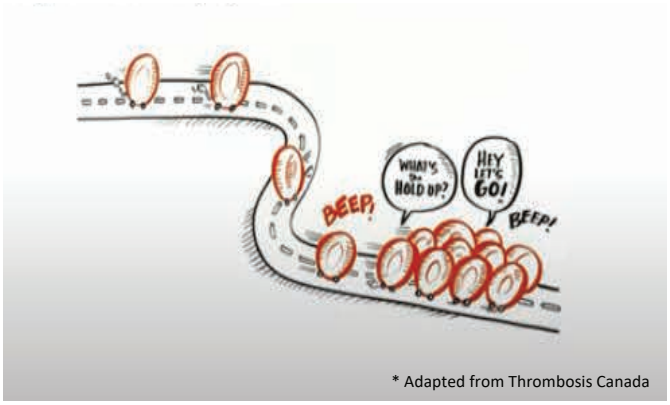
Please find an educational handout to give to patients. The authors grant permission for use and reproduction of this brochure for the purpose of patient education, but not for commercial use. If you would like to discuss other uses, please contact the authors.

CANCER AND BLOOD CLOTS

• When diagnosed with cancer, you are at risk of developing a blood clot. It is important to be aware of signs and symptoms of blood clots so you don't delay getting medical attention.
• These blood clots are known as cancer-associated thrombosis (CAT). The risk of developing a blood clot is higher because of your cancer and any treatments you may receive.
• The risk of developing a blood clot in a healthy person is 1 in 1000. This risk is increased to 1 in 200 with cancer, and 1 in 20 with intensive cancer treatment.
• Only 13% of Canadians know that cancer is a risk factor for blood clots. Reading this pamphlet will help you understand this topic better!

WHAT IS A BLOOD CLOT?

- Blood clotting is a normal part of the healing process, but sometimes blood clots form that are not needed
- Cancer patients are at risk for blood clots in the deep veins (in the legs or arms) as well as blood clots in the lungs. These blood clots are called deep vein thrombosis 'DVT' or pulmonary embolism 'PE'
- These blood clots can cause a blockage or 'traffic jam' in your veins causing the symptoms described in the pictures below:



* Adapted from Thrombosis Canada

SIGNS OF BLOOD CLOTS


Leg or arm swelling


Redness or warmth


Shortness of Breath


Dizziness


Chest Pain

WHY ARE CANCER PATIENTS AT AN INCREASED RISK OF BLOOD CLOTS?

Cancer-Related Risk Factors	Other Risk Factors
• Cancer creates an environment where blood is more likely to clot • Type & stage of cancer (pancreas, stomach, uterus, lung, kidney/bladder & brain or metastatic cancer have higher risk) • Chemotherapy, surgery, radiation • PICC lines, ports or central lines	• Older age • Bedrest or limited mobility • Obesity

WHAT YOU NEED TO KNOW

- Cancer patients are at risk for blood clots. This risk increases if you are getting cancer treatment, have a central line or have surgery
- It is important to watch for signs and symptoms of blood clots
- Get medical attention if you have any signs of blood clots. Blood clots are treatable!