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ClotAssist: A program to treat cancer-associated thrombosis in an outpatient pharmacy setting

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Abstract

Stable cancer patients diagnosed with a pulmonary embolus or deep vein thrombosis are commonly referred to the emergency department for management. This practice strains an already overburdened emergency department and is associated with long wait times and poor disease/injection education for patients. This pilot study sought to determine if stable cancer patients with newly diagnosed cancer-associated thrombosis could be effectively managed by community-based pharmacists who followed an evidence-based protocol to prescribe and initiate low-molecular weight heparin therapy. We hypothesized that this novel care pathway could provide faster patient care with more comprehensive disease education, self-injection training, and follow-up. Fifty-five patients with various cancers, including gastroesophageal, urogenital, breast, brain, and lung were enrolled into this pilot study. We observed that this alternative first-dose treatment pathway provided safe and effective treatment of venous thromboembolism combined with excellent patient satisfaction. Following their interaction with the pharmacist, patients felt confident about their ability to self-inject and about their venous thromboembolism management overall. No occurrences of bleeding or other side-effects were observed. This pilot study demonstrates that community-based pharmacists are capable of delivering complex care services in the outpatient environment, particularly in the management of venous thromboembolism.

Keywords

Low-molecular weight heparin, cancer-associated thrombosis, thrombosis, outpatient pharmacy

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Introduction

Compared with non-cancer patients, patients with cancer have a five- to- sevenfold increased risk for venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE).[1–3] Cancer-associated thrombosis (CAT) incidence rates are impacted by cancer type, stage, and time since diagnosis,[4] with clotting risk highest in the first three to six months after cancer diagnosis.[5] Administration of chemotherapy further increases the risk for VTE with incidence rates rising from 7.3% to 13.5% 12 months following therapy initiation.[6] Although the majority of identified blood clots are associated with symptoms, incidentally detected asymptomatic VTE also occur in patients with cancer and are associated with lower survival compared to matched controls (hazard ratio [HR]: 1.51; 95% confidence interval [CI]: 1.01–2.27; $p = 0.048$).[7]

Clinical data have demonstrated that cancer patients on active treatment who develop symptomatic or asymptomatic VTE should receive therapy using low-molecular weight heparin (LMWH), which more effectively prevents recurrent clots than warfarin.[8–11] Guidelines recommend

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that CAT be treated with LMWH for at least three to six months to decrease recurrence rates on treatment.[12–14] Clinical data further demonstrate that long-term anticoagulation with LMWH does not increase the rates of either major or nonmajor bleeding compared with long-term use of warfarin.[8,10]

Despite the risk of VTE, patients often receive little to no information to help them recognize symptoms associated with blood clots and the importance of seeking timely treatment. Also, patients with cancer as well as clinical staff may attribute symptoms of VTE to their malignancy or to chemotherapy, further complicating access to timely care.[15] While other cancer complications have clear treatment pathways, VTE does not appear to have been afforded the same priority.[15]

Treatment pathways for VTE differ depending on when it is identified and represent a care gap for patients with cancer. If a clot is suspected during outpatient clinic hours, patients may be sent for imaging (typically an ultrasound for a DVT or a CT scan for PE). Alternately, an unsuspected clot may be detected in a routine scan. Once a clot has been confirmed, the clinically stable patients may be sent to the pharmacy to pick up the prescribed LMWH and then must return to the cancer center to receive their injection and training. Other patients may simply be directed to the closest emergency department (ED) for diagnosis and initial treatment. Outside of clinic hours, patients typically present to the ED. Patients who present to an ED in Canada are generally faced with a wait of between 4 and 8 h before being diagnosed and treated.[16] Once diagnosed with VTE and prescribed an LMWH, patients may or may not receive adequate teaching on how to self-inject their LMWH and are often sent home until they can follow-up with a CAT clinic if available, or their oncologist. In general, the experience of patients with cancer who have been diagnosed with a clot is unsatisfactory, characterized by long wait times, poor education, and anxiety.[15,17] Evidence from the PELICAN study revealed that for many patients, the entire process of VTE diagnosis and treatment can be more anxiety provoking than the actual diagnosis of cancer.[15]

In Alberta, Canada, pharmacists can obtain broad prescribing privileges after undergoing a rigorous review that assesses knowledge, scope of practice, and clinical decision making. They also can review and order laboratory tests, as well as administer injections. Given the relatively easy access to community pharmacists (multiple locations, 24-h pharmacies), we hypothesized that community pharmacists within Alberta who have prescribing privileges could address the current care gap for cancer patients diagnosed with VTE.

To this end, a novel pilot program was developed. Following the diagnosis of VTE, patients with cancer were referred to a specific community-based outpatient pharmacy where prescribing pharmacists trained in the LMWH treatment protocol provided treatment, education, and initial follow-up.

Methods

Development and implementation of the pilot study

This pilot study was developed collaboratively by medical oncologists, community pharmacists, and industry. Using the Canadian guidelines for the management of VTE in cancer patients as a template,[14] an evidence-based treatment algorithm (Appendix) was created to manage newly diagnosed blood clots in stable patients with cancer. During project planning, Anticoagulation Management Services (AMS) leaders were invited to information lectures and their advice was solicited. This pilot program was run in the province of Alberta, Canada from December 2015 to March 2017 in three cancer centers and three pharmacies. Industry support for this pilot study was provided by LEO Pharma Inc.

First-dose pilot program protocol

Once an oncologist was made aware of a confirmed clot in a clinically stable patient with cancer, a one-page document was completed and faxed to a specific community-based outpatient pharmacy staffed by prescribing pharmacists trained in the protocol. The faxed document contained patient demographics, clot location, current systemic therapy, current anticoagulant/anti-platelet treatments and a preferred LMWH (optional). The LMWH dose was not calculated by the referring oncologist.

At the pharmacy, the pharmacist weighed the patient, reconciled medications, and reviewed lab data to determine renal function and platelet count. The pharmacist prescribed a 14-day supply of LMWH, rounding up the dose to the nearest prefilled syringe. This is a standard accepted practice advocated in most VTE guidelines, including the Canadian consensus guidelines for VTE management in cancer patients.[14] Fourteen days were chosen as an appropriate time frame for the oncologist to review and renew the prescription and to see the patient in clinic. The pharmacist administered the first injection to the patient using a bruiseless subcutaneous injection technique and taught the patient or their caregiver how to administer subsequent doses. The pharmacist also followed up by telephone the next day (and more if needed) to assess the patient's comfort with self-injection.

In addition, the pharmacist screened the patient for heparin-induced thrombocytopenia (HIT), a possible side effect of LWMH. Following injection training, patients were provided with a lab requisition to have

their platelets evaluated 5–10 days after their first LMWH injection. A complete blood count requisition was to be completed after five days if their platelets were between 50,000 and 99,999, seven days if between 100,000 and 149,999, and 10 days if over 150,000. The pharmacist reviewed the bloodwork and, in the event of a platelet decrease, the oncologist was informed of the platelet decrease and requested to consider ordering an HIT assay.

As part of the algorithm, the pharmacist was instructed to contact the on-call oncologist with any concerns including lab data older than 14 days, CrCl under 20, platelets under 50,000, INR over 3, and identification of a bleeding or clotting disorder that had not been communicated by the oncologist to the pharmacist. Quality of service was tracked through anonymous patient questionnaires. The pharmacy then sent a notification form to the referring oncologist, with a copy to the patient's general practitioner (GP), listing patient lab results, dose, and education given and that the patient did receive follow up. All clinical and questionnaire data were collated by the pharmacist (AA) and reviewed by the physician (JE).

A financial review of costs incurred by this program was compared to costs using an ED. In this study, the pharmacist's time, including prescribing ($25) and injecting ($20), was paid by Alberta Health Services. We used publicly available information from Alberta health services and billing data from the community pharmacy to compare costs.

Table 1. Patient characteristics.

	Number of patients
VTE diagnosis	
PE	19
Lower extremity DVT	18
Upper extremity DVT	6
Unusual site thrombosis	10
VTE prophylaxis	2
Type of cancer	
Gastroesophageal	12
Urogenital	12
Breast	7
Brain	6
Lung	6
Hematologic	3
Pancreas	3
Other	6
LMWH dosing[a]	
Tinzaparin	9000–20,000 IU sc daily
Dalteparin	10,000 IU sc daily
Dosing	
Duration of dosing	10–180 days

DVT: deep vein thrombosis; PE: pulmonary embolism; LMWH: low-molecular weight heparin; VTE: venous thromboembolism.
[a]No patient was given enoxaparin in this study.

Results

Fifty-five patients with cancer (57% males, 47% females) were enrolled in this pilot program. In total, 35% were diagnosed with PE, 44% with DVT (upper or lower extremity), and 18% with unusual site thrombosis (i.e., portal vein, cerebral vein). Two patients were treated prophylactically. Cancer types included gastroesophageal, urogenital, breast, and brain primary cancers. Ninety-eight percent of patients were prescribed the LMWH tinzaparin, supplied in a prefilled dose-specific syringe, for a minimum of 10 days with some patients receiving long-term anticoagulation of up to 180 days. This reflects local practice patterns although physicians and pharmacists could choose any LMWH. LMWH dosing was based on the patient weight with rounding up of the dose to the nearest prefilled syringe size (Table 1).

Blood work was available for all patients with most lab data being less than one week old at the time of the initial visit. The pharmacist ordered bloodwork for every patient to evaluate for thrombocytopenia and therefore a potential risk of HIT. Less than 10% of patients were observed to have a falling platelet count. In one case, the pharmacist attempted to call the oncologist, but the physician was not available. Thereafter, the protocol was modified so that a letter would be faxed to the referring oncologist's office asking them to consider ordering an HIT assay.

The bruiseless self-injection training was well received by the patients with fewer than 5% of patients being unable to self-inject for reasons varying between physical inability to personal discomfort with needles. In such cases, the pharmacist offered to provide daily injections at the pharmacy or arrangements were made with local pharmacy or home care services. No known occurrences of bleeding or other side effects were observed in the patients enrolled in the pilot study. Overall, satisfaction was high with the program as most patients felt well educated about their VTE diagnosis and confident in their ability to self-inject (Table 2).

A significant saving to the healthcare system was also realized by this program. The median cost for a visit to an ED in Alberta is $750, taking into account physician, nursing, allied healthcare time, and supplies. This does not include lab-testing costs or the costs to the patient, which include time waiting in the ED, parking, and other ancillary costs. The median cost to Alberta Health Services (for the pilot study was $45 initiation of therapy and injection administration) resulting in a remarkable 94% cost savings to the provincial health service for each patient ($750 vs. $45/patient).

Table 2. Anonymous patient care survey.

Comments	Score ($N = 45$)[a]
I have increased confidence in my ability to self-inject	Strongly agree ($n = 24$); agree ($n = 14$); neutral ($n = 3$)
The information I received regarding my VTE diagnosis and treatment from the pharmacist was satisfactory	Strongly agree ($n = 31$); agree ($n = 13$); neutral ($n = 1$)
How would you rate the quality of care you received in your diagnosis of VTE from the cancer center	Very satisfied ($n = 40$); somewhat satisfied ($n = 4$); neutral ($n = 1$)
How would you rate the quality of care you received in your diagnosis of VTE from the pharmacy/pharmacist	Very satisfied ($n = 40$); somewhat satisfied ($n = 4$); neutral ($n = 0$)

Comments
Everything was excellent. No suggestions for improving; everything was perfect. It was very useful and now I am able to inject myself with more confidence. The pharmacist was excellent in providing me with information and explaining the procedure.
Good class. Should send to class right after emergency. Helped lots. Was doing everything wrong. No suggestions for improving.
Would be nice if the medication was available in a self-dose pen-like insulin.
Excellent assistance.
Very efficient. The video helped and was useful before pharmacist consultation.
Very prompt and knowledgeable. Very convenient for me.
Offer same service at other Shoppers Drug Mart locations. Great empathy and care. Wonderful follow-up care.
Great team!
Pharmacist was very thorough and easy to understand. I was very pleased.

VTE: venous thromboembolism.
[a]Reflects total number of patients who completed patient care survey, patients did not answer all questions

Discussion

CAT is a common occurrence that significantly impacts a patient's cancer journey. Unfortunately, many patients are unaware of the signs and symptoms of a blood clot and may not understand the importance of seeking timely treatment. Most other cancer complications have clear treatment pathways; however, thrombosis has not been afforded the same priority, likely related to the low awareness of its occurrence and related morbidity/mortality.[7,13,15,18]

Many cancer patients with VTE will seek care from the local ED either because they have been sent by their oncologist or they have developed symptoms after hours. Many of these patients will wait for several hours before being diagnosed and given appropriate treatment. After diagnosis in the ED, most patients are given a single injection of LMWH and then provided with a prescription for further doses of LMWH. However, self-injection training is often brief and may be limited by the time, staff, and space available. This leaves the patient to self-learn how to inject from the product information if the pharmacist is unable to provide injection training.

Our study allowed us to test a specific hypothesis that community-based outpatient pharmacists following an algorithm based on the Canadian Guidelines for VTE Management in cancer patients could provide comprehensive and timely care for cancer patients with thromboses. In Alberta, some patients have access to an AMS to help manage anticoagulation, however, these clinics are primarily for warfarin management, and already have significant patient loads with wait times of 24–48 h. None of the pilot centers had the availability of a CAT clinic, with the one Alberta center that does currently offer a CAT clinic, having a wait time of two weeks. With this management gap in mind, this pilot was designed to complement, not compete with, these services.

Cancer patients are often diagnosed in the evening or weekend and rapid access to thrombosis services is essential, not only for initiation of treatment but also for patient peace of mind. This pilot study was run in 24-h or extended-hour outpatient pharmacies, allowing patients to access anticoagulation care after regular working hours, often within 1 h of being diagnosed.

Several lessons were learned through this pilot study. First, this pilot program revealed the lack of standardized management and follow-up (i.e., identifying falling platelet levels suggestive of HIT) protocols for CAT among oncologists and ED physicians. We established that pharmacists with prescribing privileges trained in an evidence-based treatment protocol are able to safely prescribe and inject an LMWH, as well as provide consistent patient teaching and follow-up including monitoring laboratory tests. Second, patients highly rated this program indicating confidence in the teaching they received and appreciation for the service provided by the pharmacist. Third, we demonstrated that patient data could be seamlessly collected, collated, and shared between cancer centers and outpatient pharmacies. Finally, this project supports that patient care for VTE can be provided outside the cancer clinic and the ED with significant savings to the patient (time and anxiety) and to the healthcare system (cost and less patients in the ED).

At a larger clinical level, the data also clearly demonstrate that outpatient pharmacists are capable of more than their traditional role of dispensing medications and counselling patients. Instead, our data support an expanded role for community pharmacists in the outpatient environment. Pharmacists can serve a critical role as part of an expanded team that manages complex medical issues, including CAT.

The program has now expanded to include other cities within the province of Alberta and is now in the process of being initiated in other Canadian provinces. In addition, we are in the process of expanding pharmacist involvement to include VTE prophylaxis of postoperative patients and high-risk pregnancy patients. Finally, we are now looking to use this service to provide injections that are traditionally given in the cancer center (e.g., Luteinizing hormone-releasing hormone agonists for prostate cancer, denosumab for patients with bone metastases).

Our study was a collaborative program developed to improve care for cancer patients diagnosed with VTE. The program provided patients with rapid access to a trained pharmacist who could initiate LMWH therapy and supported patients with VTE education, injection training, and follow-up. This pilot program demonstrated that stable patients with diagnosed CAT can be managed in a community-based local pharmacy with no need to visit the ED, overall affording the patient excellent care at a lower cost to the healthcare system.

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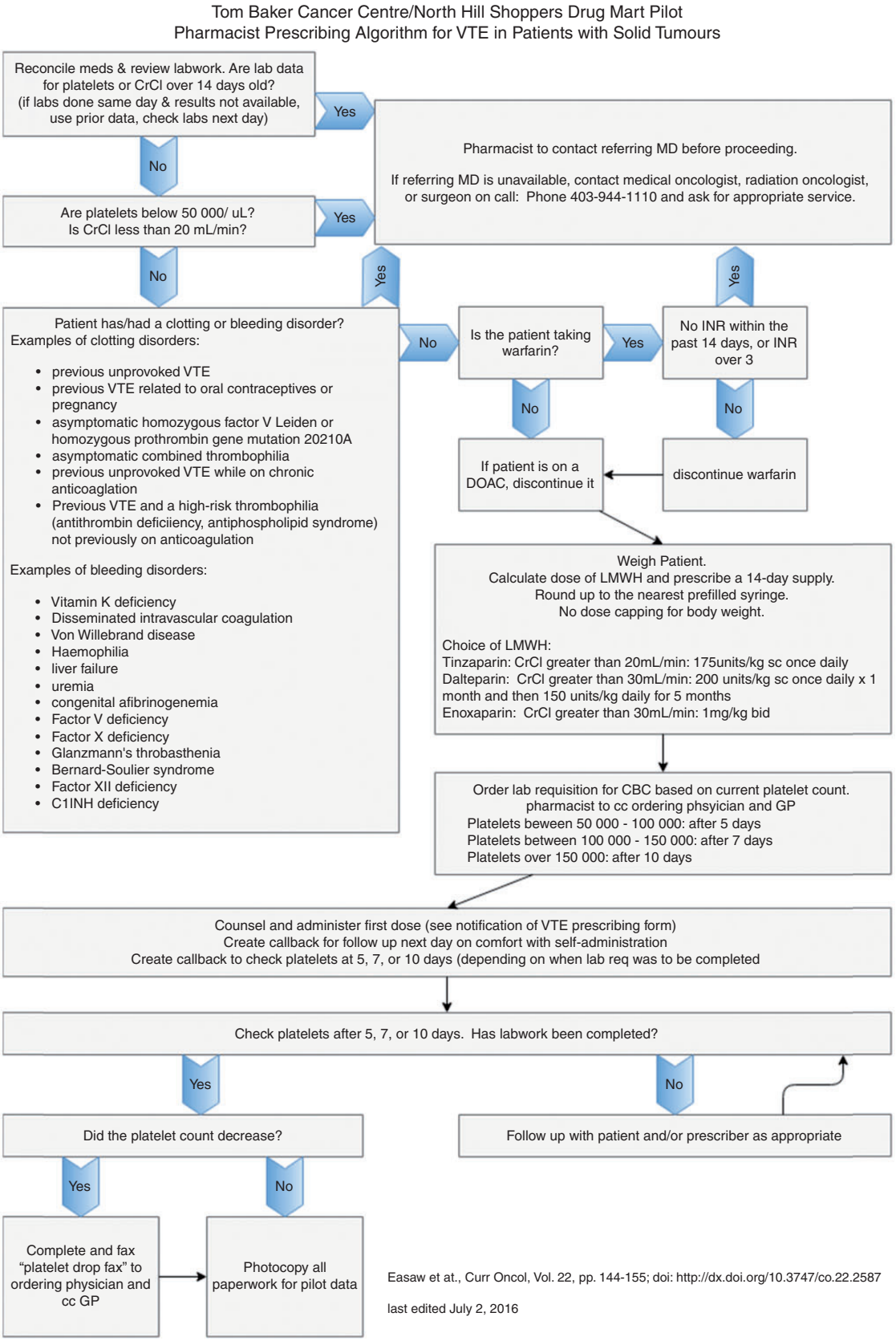
Appendix



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