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Implementation and validation of a risk stratification method at The Ottawa Hospital to guide thromboprophylaxis in ambulatory cancer patients at intermediate-high risk for venous thrombosis

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ABSTRACT

Background: Cancer patients have a significantly higher risk of developing a venous thromboembolism (VTE) compared to non-cancer patients and yet studies suggest VTE risk among ambulatory cancer patients varies widely. Recently, predictive models capable of risk-stratifying a broad range of ambulatory cancer outpatients have been developed. Using the Khorana model a score of 2 was intermediate-high risk for VTE as reported by Ay and colleagues. However, validation in a broader population and methods to implement this model seamlessly into clinical practice are lacking.
Objective: To create and assess the feasibility of an innovative computerized Care Process Management System (CPMS) that would automatically access electronic medical records to calculate in real-time the risk of VTE in patients with active cancer using an established VTE risk scoring system.
Methods: A prospective observational study of all newly referred cancer patients at the Ottawa Regional Cancer Center, the sole cancer care provider for 1.2 million inhabitants, was conducted.
Results: 699 new referrals were determined to have a cancer diagnosis for the first time as identified by the computer software and qualified for our study and 580 were eligible. In total 25% had intermediate-high risk for VTE and during the 3-month follow up period, 16 of the 143 (11%) developed a VTE which further validates the Khorana model for identifying intermediate-high risk patients. Of the 437 patients in the low risk group 19 (4%) developed a VTE.
Conclusion: Newly diagnosed cancer patients can be readily stratified into intermediate-high and low risk of VTE using our novel CPMS system. This innovative tool can be used to facilitate customized management decisions regarding VTE prophylaxis for intermediate-high risk patients based their individual risk factors.

1. Introduction

Cancer patients have a 7–28 fold higher risk of developing deep vein thrombosis (DVT) and pulmonary embolism (PE), collectively described as venous thromboembolism (VTE), compared to non-cancer patients [1,2]. Pharmacological prophylaxis of VTE is the recommended approach for decreasing disease burden. However, establishing a unique solution of thromboprophylaxis for preventing VTE in all cancer patients is challenging because not all cancer patients have the same risk for first and recurrent VTE [1,2]. Given the cost and concomitant bleeding risk associated with anticoagulants, administration of VTE prophylaxis in cancer patients is currently not standard of care. Recently, Khorana and colleagues developed a predictive model to risk-stratify a broad range of ambulatory cancer outpatients potentially allowing for a more favourable risk-to-benefit ratio to be calculated when thromboprophylaxis is being considered [3]. This was validated by Ay et al. [5], indeed a score of 2 was associated with a rate of VTE of 9.6%. However, methods to implement it into clinical practice have not been developed. The purpose of this study was to create and assess the feasibility of an innovative computerized Care Process Management System (CPMS) that would calculate in real-time the risk of VTE in patients with active cancer. Clinical information and laboratory tests contained in patient electronic records were used to populate the predictive model allowing us to identify, educate and follow patients at intermediate-high risk of developing a VTE. This innovative approach to health care delivery will ideally lead to sustainable changes in the management guidelines of VTE risk in cancer patients in the future.

Abbreviations: VTE, Venous Thromboembolism; DVT, Deep Vein Thrombosis; PE, Pulmonary Embolism; CPMS, Care Process Management System.

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2. Materials and Methods

With Institutional Research Ethics Board approval we conducted a prospective observational study of all newly referred cancer patients at the Ottawa Regional Cancer Center, the sole provider of cancer care for a region of 1.2 million inhabitants, from November 2012 to August 2013. Patient eligibility was determined after a cancer diagnosis was confirmed histologically and within 3 weeks prior to the initiation of anticancer treatment. Inclusion into the study required a diagnosis of specific "high risk" cancers including: brain (high grade glioma), bladder, lung, testicular, gynecological, pancreatic and lymphomas or progression of the malignant disease after complete or partial remission. Patients were excluded if: (1) they were to be followed up with or treated at a facility other than The Ottawa Hospital; 2) they had a confirmed VTE/arterial embolism (stroke or peripheral arterial embolism) within the 3 months prior to diagnosis; 3) they were receiving continuous anticoagulation treatment; 4) they had previously been treated for cancer; 5) they had received chemotherapy or radiotherapy in the prior three months; 6) major surgery occurred in the prior 2 weeks. A novel computerized care process management system was created that incorporated clinical information and laboratory tests contained in the patients electronic record. The Khorana predictive model for chemotherapy-associated VTE [3] was utilized to assess the risk of developing a VTE i.e. using the following five predictive variables: (1) type of cancer (2) platelet count ≥350 x 10^9/L, (3) hemoglobin <10 g/dL and/or use of erythropoiesis-stimulating agents, (4) leukocyte count >11 x 10^9/L, and (5) body mass index (BMI) ≥35 kg/m^2, and assigns one point for each (Table 1). Brain cancer was not originally included in the Khorana model but is a malignancy known to be strongly associated with a very high VTE risk and was included in the "very high risk cancer site" [5].

As per the data reported by Ay et al. (2010) we selected a score of ≥2 as intermediate-high risk for VTE, and patients who scored 2 or above were followed for three months. An overview of the CPMS and study process algorithm is shown in Fig. 2. Patients with a very high risk tumour site did not require incorporation of the other variables and were automatically flagged by the system. Those with other tumour sites had the predictive variables calculated through the CPMS. In all cases the clinic nurse was notified electronically of patients at intermediate-high risk prior to the clinic appointment. Patients' demographics, medical history, malignancy characteristics, diagnostic laboratory features, imaging information, BMI and plan of anti-cancer treatment were documented prior to initiation of cancer treatment. Educational material was provided by a nurse to intermediate-high risk patients regarding the signs and symptoms of VTE and their risk for VTE with the hope that such knowledge may prevent delayed diagnosis. Patients were followed-up with at 3 months (±7 days) following the initial consultation to determine if they were diagnosed with VTE. Diagnosis of DVT required confirmatory ultrasound. PE were confirmed by computed tomographic pulmonary angiography, or ventilation perfusion (V/Q) lung scanning, with a high probability result or a non-normal result that coincided with objectively confirmed DVT. (See Fig. 1.)

Table 1
Predictive Risk Stratification Scoring System For Developing a VTE.

Predictive Variable	Description	Score Value
Malignancy Type	**Type of Malignancy**	
Very High Risk Cancer Site	Brain (High Grade Glioma), Stomach or Pancreas	**2**
High Risk Cancer Site	Lung, Lymphoma, Gynecologic, Bladder or Testicular	**1**
Pre-Chemotherapy Blood Work	**Diagnostic Laboratory Criteria**	
Platelet Count	≥350 x 10^9/L	**1**
Hemoglobin	<10 g/dL or use of erythropoiesis-stimulating agent	**1**
Leukocyte Count	>11 x 10^9/L	**1**
Body Mass Index (BMI)	≥35 kg/m^2	**1**

3. Results

The computer software identified 699 newly diagnosed cancer patients during the 9 month study period. 580 were eligible to have the model applied and 119 met one or more of the exclusion criteria. On the basis of very high risk tumour site alone, 71 patients were initially deemed at intermediate-high risk of developing a VTE (score ≥2) (Fig. 2). Among the initial cohort of patients at low risk, 72 were elevated to intermediate-high risk based on BMI and/or pre-chemotherapy blood work. In total 143 patients (25%) were deemed to be at intermediate-high risk for VTE and during the 3-month follow up period, 16 of the 143 (11%) developed symptomatic VTE (7 had proximal DVT, 8 had PE, and 1 had both). Of the 437 patients in the low risk group 19 (4%) developed a VTE within the follow up period which validates the modified Khorana model for identifying cancer patients at intermediate-high risk for VTE and is in concordance with the results published by Ay et al. [5] who reported a 9.6% risk of VTE with a score of 2 or more (intermediate-high risk) and 3.8% in those with a score of 1.

4. Discussion

Determining whether thromboprophylaxis therapy should be initiated in individual cancer patients is challenging since not all cancer patients have the same risk for developing a VTE. From a clinical stand point, stratifying patients into high- or low-VTE risk is an ideal strategy since it would permit patients who are at a lower risk, and for whom thromboprophylaxis may not be of benefit, to be excluded. As a result, treatment would only be initiated in high risk patients, therefore minimizing the exposure of those at low risk to the side effects of anticoagulation. Currently, the most effective strategy to categorize the VTE risk of ambulatory cancer patients remains to be determined. In recent years, Khorana et al. developed a simple model capable of stratifying a broad range of cancer outpatients into distinct risk groups for VTE, however methods to easily incorporate this model into clinical practice have yet to be established and validation of this tool is still lacking in a broader population.

In this study, we have developed and demonstrated the feasibility of a novel computerized (CPMS) system at The Ottawa Hospital that accurately calculates, in real-time, the risk of VTE using, and concurrently validating, an accepted prediction model for ambulatory cancer patients. The strength of the CPMS resides in its ability to automatically gather clinical information and laboratory results contained in patients' electronic medical records in real-time; thus enabling the physician to quickly identify patients whom may benefit from early education and thromboprophylaxis regiments prior to initiating other cancer treatments. We acknowledge that the EMR and IT systems of hospitals can be very different and our system may not be easily applied in all hospitals. However, the concept has been proven and we have achieved similar results as published by Ay et al. in that patients with a score of 2 or above had an 11% risk of VTE in the first three months. This is a substantial risk. Early risk assessment of VTE is extremely important because most cancer patients will develop a DVT or PE within the first 3 months following their diagnosis [4].

5. Conclusion

In summary`, newly diagnosed cancer patients can be readily stratified into intermediate-high and low risk of VTE using our novel CPMS system. The implementation of an automated predictive method on the risk of VTE at our institution represents an innovative approach toward the decision making process for these patients as it would lead