Clinical outcomes of implementing evidence-based practice on venous thromboembolism prevention for cancer patients in Qatar, a retrospective study
Shereen Elazzazy*
National Center for Cancer Care and Research (NCCCR), Hamad Medical Corporation, Doha, Qatar

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*For Correspondence: Dr. Shereen ElAzzazy, RPH, BSc Pharm, PharmD, CACP Asst. Director of Pharmacy - Clinical Services National Center of Cancer Care and Research NCCCR, Qatar.
E-mail: sheren_amin@yahoo.com

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Purpose: Venous Thrombo Embolism (VTE) disease is a serious condition; approximately 20% of all VTE cases occur in patients with cancer and it is a significant cause of morbidity and mortality in cancer patients. Plus, it is a significant predictor of increased mortality during the first year after diagnosis among all types and stages of cancer. Furthermore, VTE affects up to 20% of patients with cancer before death and has been reported in up to half of patients at the time of postmortem examination. Most hospitalized patients with cancer require thromboprophylaxis throughout hospitalization [3]. This study was performed in the National Centre for Cancer Care and Research (NCCCR); the only tertiary care cancer center in Qatar. NCCCR is 1out of 8 teaching hospitals in Hamad Medical Corporation (HMC) the main and largest healthcare organization in Qatar. An evidence based protocol for of VTE risk assessment and VTE prophylaxis was initiated in June 2011, piloted till December 2011, and then fully implemented in January 2012 to all cancer patients admitted to inpatients wards. This study focuses on the assessment of the clinical outcome in preventing VTE amongst cancer population in Qatar after implementation of evidence based thromboprophylaxis guidelines.

Primary outcome: to measure the incidence rate of DVT before and after implementation of
thromboprophylaxis protocol.

**Secondary outcome:** measuring physician compliance rate with the guidelines.

**Methods:** A retrospective study was conducted to evaluate the incidence of DVT by evaluating doppler ultrasound (US) database for 364 cases of inpatients and outpatients over 24 months (from January 2011 through December 2012) study period, all findings were retrospectively analyzed by a hematologist to identify patients who developed deep vein thrombosis (DVT) due to any current or previous admission (within 30 days before the doppler US). The relationship between the incidence of developing VTE over time and the compliance to VTE prevention protocol were established by correlation and regression analysis. Statistical analyses are done using excel and statistical packages SPSS 20.0.

**Findings:** The study showed that the overall compliance to VTE prophylaxis protocol introduced to inpatients population (n = 2595) increased from 61.5% to 84.6% with (p = 0.0297), the incidence of DVT decreased by 66.4% (P= 0.0145), which was correlated with a significant increase in the percentage of patients who received adequate VTE thromboprophylaxis. A percentage of 78% of patients developed DVT during admission in 2011 did not receive prophylaxis, compared to 29% in 2012. While this could be seen as a positive impact of thrombophylaxis, the number of patients who developed DVT despite receiving appropriate prophylaxis, increased from 22% in 2011 to 71% in 2012.

**Implications:** Appropriate Thrombophylaxis could considerably improve the incidence of DVT in cancer patients. The majority of VTE in cancer patients occurred due to inappropriate prophylaxis, however the minority was due to prophylaxis failure, which raised the importance of implementing evidence based practice for
INTRODUCTION

Venous thromboembolic (VTE) disease represents a spectrum of conditions that includes Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE). (DVT) is a blood clotting condition usually occurs in a vein of the deep system. DVTs can occur anywhere in the body, but most frequently are found in the deep veins of the legs, thighs, and pelvis. DVT may infrequently occur in the upper extremities due to trauma, or catheters [1]. A Pulmonary Embolism (PE), strikes when a blood clot in the leg breaks loose and passes into the pulmonary circulation, resulting in a sudden blockage in a lung artery. [1]. PE is a serious condition that can cause permanent damage to the affected lung and other organs due to low oxygen supply, and may lead to death, depending on the number and size of the clots [1].

The estimated annual incidence of VTE is 117 cases per 100,000 persons. The incidence rises markedly with age > 90 years and reaches up to 900 cases per 100,000 by the age of 85 years [2]. Risk factors for venous thromboembolic disease include elder age, prolonged immobility, surgery, trauma, malignancy, pregnancy, estrogenic medications and hormone therapy, chemotherapy, congestive heart failure, hyperhomocysteinemia, diseases that alter blood viscosity (e.g., polycythemia, sickle cell disease, multiple myeloma), and inherited thrombophilias. Studies show that, VTE is common amongst about 75% of patients with at least one established risk factor, and 50% of DVT cases occur in hospitalized patients or nursing home facilities [2].

Cancer patients are 5 times more likely to develop VTE, which is a common life threatening condition, than the general population [3]. A retrospective study showed that 2.7% to 12.1% of cancer patients, depending on the type of malignancy, experienced VTE during their first hospitalization [4]. VTE is the most frequent complication of cancer and the second leading cause of death in hospitalized cancer patients (second only to cancer itself) [3-6]. The occurrence of VTE increases the mortality rate by 6 folds amongst cancer patients [4]. Despite the increased risk, and the presence of evidence-based guidelines, cancer patients are less likely to receive prophylaxis compared to patients without cancer [3,5,7]. Admission for cancer management has even been associated with a lower likelihood of proper VTE prophylaxis [8,9]. Previous studies showed that the overall rate of any level of VTE prophylaxis was 53.6%; however, the rate of appropriate thromboprophylaxis (according to the 7th ACCP guidelines) was 27.0%. The most common reason for inappropriate prophylaxis (46.0% of all discharges) was “no prophylaxis received”, despite having no contraindication to anticoagulation [3].

Prophylaxis is preferred to treatment, as VTE can be hard to diagnose and in case of PE; there is often no warning that the patient is at risk. Death due to PE is often immediate or within 1 to 2 hours of onset. There is overwhelming evidence from randomized studies to support the positive impact of adequate prophylactic anticoagulation on reducing the incidence of thromboembolic diseases, [10–11]. Reputable organizations as the American Society of Clinical Oncology (ASCO) [12] and the National Comprehensive Cancer Network (NCCN) [7], recommend that; “all hospitalized cancer patients should be considered for VTE prophylaxis with anticoagulants in the absence of bleeding or other contraindications”
In high-risk groups including cancer patients, it is more cost effective to protect against DVT and PE than to treat these conditions when they occur [2]. Considering risk assessment and proper VTE prophylaxis to those who are at risk should be a routine practice in every hospital admission. A fact that underpins the need for the development of practice guidelines to ensure that more cancer patients receive appropriate thromboprophylaxis [3] however, the keys to preventing VTE are in identifying patients who are at risk, and applying the appropriate measures [2].

This study was performed at National Center for Cancer Care and Research (NCCCR) Doha –Qatar, A Joint Commission International (JCI)-accredited Academic Health Center. In our institute a baseline assessment was performed by the clinical pathway and guideline (CPG) committee in early 2011, it revealed that only 31% of cancer patients admitted to NCCCR receive adequate thromboprophylaxis. This could be attributed primarily to the absence of local clinical practice guidelines for the management of thromboprophylaxis in NCCCR [8,9]. Therefore, Quality Improvement (QI) project was started. In our QI project we implemented different QI tools such as a multidisciplinary approach, provider education, and standardization of risk assessment and management by using a combined risk assessment (based on Padua risk scoring) / order sets (with standardized medications orders) form. The formulated multidisciplinary team was sponsored by pharmacy, and was created to overview the development and implementation of the clinical guideline. The team consisted of; clinical leaders (physician and pharmacist), a representative of nursing department, and two pharmacists for monitoring, data collection and documentation.

Problem statement
To the authors knowledge; this is the first study on VTE prophylaxis outcome in Qatar. Our aim was to assess the clinical outcome in preventing DVT amongst cancer patients after applying evidence based thromboprophylaxis guidelines.

Primary outcome (clinical outcome) was to measure the incidence rate of DVT before and after implementation of VTE prophylaxis guidelines (by measuring the ration of the number of hospitalized or ambulatory cancer patients who developed DVT during admission or 30 days after admission to the total number of cancer patients admitted to NCCCR).

Secondary outcome (process measures) was to measure physician compliance to VTE prophylaxis guidelines (by measuring the ration of the number of hospitalized cancer patients who have been assessed for the risk of VTE and received appropriate thromboprophylaxis, to the total number of cancer patients admitted to NCCCR).

METHODS

Study Design
A retrospective patients’ charts review was performed to evaluate the incidence of DVT before and after the introduction of thromboprophylaxis guidelines in the cancer center during the study period of 24 month; from January 2011 (before VTE prophylaxis guidelines implementation in June 2011) up to December 2012 (after VTE prophylaxis guidelines implementation).

Our postulation was; at least 70% of hospitalized cancer patients will be assessed for the risk of VTE, and receive adequate thromboprophylaxis within 24 hours of admission by June 2012, and 85% by December 2012. Based on that; there should be a 50% decrease in the incidence of DVT events among hospitalized cancer patients by December 2012.

Population and sampling
To assess the level of compliance to guidelines all admitted cancer patients during the study period were included in the study to evaluate the risk assessment and prophylaxis introduced based on risk level. To assess admission related DVTs
before and after VTE prophylaxis guidelines implementation in the cancer center; all patients referred to NCCCR radiology department with suspicious of DVT were with either a solid or hematological cancer, at any stage of the disease.

**Inclusion criteria:** All cancer patients who were admitted to NCCCR hospital and developed DVT during the period of admission or within 30 days after previous admission.

**Exclusion criteria:** All patients who developed DVT with no previous history of admission within the previous 30 days of the DVT diagnosis, patients who developed DVT before admission, patients admitted to NCCCR with length of stay < 2 days and patients who were admitted to other hospitals, shows patients' characteristics.

**Data collection:** We retrospectively revised all admitted patients’ medical records to evaluate the risk assessment (based on Padua scoring) and prophylaxis introduced based on risk level. VTE prophylaxis order sets and medications history and details of all medications related details were extracted from Pharmacy Management System (PMS) and electronic Medical Record (e-MR) viewer to confirm previous admission date and thromboprophylaxis received. Data on Doppler US with suspicious DVT were collected from radiology department records to identify positive Doppler Ultrasonography test results. Data were collected on an excel sheet then validated by a hematologist and a clinical pharmacy specialist to confirm positive DVT cases and VTE prophylaxis appropriateness.

**Ethics:** This study was approved by the Medical Research Centre at HMC.

**Analysis**

Descriptive statistical analysis was applied to sum up patient’s demographics. Categorical and continuous values were introduced as frequency (percentage) and mean ± standard deviation (SD). Student t-test for two independent means was used to assess the significance of improvement in the mean percentage of patients who received adequate thromboprophylaxis before and after the guidelines implementation. Correlation analysis and Pearson correlation coefficient calculator were used to further confirmed the existence of a positive correlation, between filling order sets by physicians and the percentage of patients receiving appropriate thromboprophylaxis, and to assess the correlation between appropriate prophylaxis and the incidence of DVT. A p-value < 0.05 was considered as statistically significant. Statistical analyses were done using excel and statistical packages SPSS 20.0

**RESULTS**

The percentage of patients who received adequate thromboprophylaxis as baseline before implementing the guidelines was 31%. This percentage increased to 61.5% after guidelines implementation, then 70% by June 2012 exceeding the initial prediction, and eventually reached an average of 84.6% by December 2012, almost touching the predicted target of 85%. The overall improvement was found to be statistically significant (P= 0.0297). shows the percentage of patients admitted to NCCCR who received appropriate thromboprophylaxis during the study period.

On the other hand, physician’s adherence to the order set showed an initial improvement until April 2012, and then physicians started complaining about the complexity of the order set; therefore, the order set was modified. Although, the order set was reviewed and simplified, the indicator kept declining and eventually ended up at a level lower than the starting point with an overall performance of 43% in the first quarter 2012 and, overall performance of 43.2% for the remaining three quarters of the year.

Although, the compliance to filling VTE order sets was not high, we noticed positive linear correlation (r=0.2101) between filling order sets by physicians and the percentage of patients receiving appropriate thromboprophylaxis (p-value is 0.000313, statistically significant) presents the percentage of compliance to completing risk assessment and ordering
anticoagulants using the order set and the percentage of patients who received appropriate thromboprophylaxis within 24 hours after admission during the study period.

With increased compliance to guidelines; there was 66.4% reduction in the average rate of DVT incidents - confirmed by Doppler ultrasonography - from 1.117% (95% CI= 0.448 to 1.785) incident/month at the beginning of the program, to 0.375% (95% CI= 0.108 to 0.642) incident/month with statistically significant p-value < 0.05 (p-value= 0.004443) and negative correlation (r= -0.4641). shows the linear correlation between appropriate prophylaxis and DVT incidents.

Of those patients who developed DVT during admission in 2011, 78% of patients did not receive prophylaxis compared to 29% in 2012. While this could be seen as a positive impact of thrombophylaxis, the number of patients who developed DVT despite receiving appropriate prophylaxis, increased from 22% in 2011 to 71% in 2012. An in-depth investigation is required to identify potential link between VTE risk level and type of risk factors, at the time of admission and the likelihood of developing DVT despite of thrombophylaxis, and assess the need for an additional protective measure (Intermittent pneumatic compression), for this category of patients. Moreover, 50% of cancer cases developed DVT were breast cancer patients (n=24), 92% of them were outpatients.

**DISCUSSION**

Different international bodies like the American College of Chest Physicians (ACCP)\[12\], American Society of Clinical Oncology (ASCO)\[13,14\], National Comprehensive Cancer Network (NCCN)\[7,8,15\], and European Society for Medical Oncology (ESMO)\[16\] recommend pharmacologic anticoagulation prophylaxis during hospitalization for all cancer patients (if no contraindication to pharmacologic anticoagulants) to prevent VTE or mechanical prophylaxis (if contraindication to pharmacologic anticoagulants present). Data from previous surveillance studies show that only 5-37% of cancer patients receive VTE prophylaxis \[17-19\]. We can attribute this to different factors like; increased risk of bleeding with anticoagulants especially in cancer patients with chemotherapy induced thrombocytopenia, absence of local guidelines to control, standardize and enforce evidence based practice, and the complexity of applying the best practice due to unavailability of simple tools like simple and clear risk assessment forms and medications order sets with standardized medications orders. Thrombophylaxis was adopted by the NCCCR pharmacy and medical as a Key Performance Indicator (KPI) to be reported the hospital Quality and Patient Safety (QPS) as a patient safety indicator and subsequently as a component of the NCCCR library of measures in July 2011. Since then, the indicator consensus is presented to the QPS team on quarterly basis. Data is also shared with clinical teams during the morning reports to discuss findings and explore improvement strategies.

The order set was reviewed and simplified in April 2012 following complaints from prescribers about the complexity of the order set. Nevertheless, the number of order sets filled would not improve which indicates the need for firm management support to enforce the order set as a requirement for patient admission.

Our study data showed a linear correlation between the number of order sets filled and the number of patients assessed and received adequate prophylaxis which suggests that improving physician adherence to the order set would eventually increase the number of patients receiving adequate prophylaxis. Moreover, the implementation of the thromboprophylaxis protocol considerably reduced the incidence of DVT in hospitalized cancer patients; however, further efforts are required to
boost physician adherence to the standard guidelines including soliciting management support to enforce VTE risk assessment and prophylaxis as a requirement for patient admission.

Taking into consideration the study finding that the number of patients who developed DVT while receiving prophylaxis increased from 22% in 2011 to 71% in 2012, and after the revision of literature and international guidelines; we have found that although there have been few studies evaluating the benefits of combined mechanical and pharmacological prophylaxis in medical populations, the NCCN guidelines recommend that mechanical prophylaxis with Intermittent Pneumatic Compression (IPC) devices should be applied to all hospitalized patients with cancer, in combination with pharmacological prophylaxis if there are no contraindications \(^{15,20}\), therefore the increased number of patients who developed DVT while receiving prophylaxis in 2012 can be related to different factors and one of those factors is the usage of pharmacological prophylaxis only (as single prophylaxis) for very high risk patients, this point is an area of improvement in our next stage. Multifaceted strategies to raise awareness, and ensure implementation, of these guidelines are required to enhance awareness on the risk for VTE encountered by cancer patients, and promote adequate VTE prophylaxis for hospitalized patients with cancer.

Starting February 2013; Corporate VTE prevention program in Hamad Medical Corporation (HMC) - the main and largest healthcare organization in Qatar - was launched, since that date we are actively sharing with the group helped in shaping and developing a corporate model. Based on HMC executive management committee newsletter dated April 2013; Venous Thromboembolism Prevention has become a priority for HMC in 2013/14 and the objective is to ensure that every patient is risk assessed and receives appropriate VTE prophylaxis by the end of 2014. Currently, VTE prevention presents significant contribution towards the delivery of HMC Best Care Always campaign with the Institute for Healthcare Improvement (IHI) to reduce patient harm \(^{21}\).

Keeping into consideration that 50% of DVT cases were breast cancer and 92% of them were outpatients, this rises the need for further studies to identify potential link between VTE risk level in both inpatient and ambulatory settings and type of risk factors, the likelihood of developing DVT despite of thromboprophylaxis, and assess the need for an additional protective measure like Intermittent Pneumatic Compression.

**Strengths**

This is the first study of its kind in Qatar. It identifies different areas of improvement in preventing admission related VTE events. Additionally, this study can be conducted in other hospitals.

**Limitations**

The main limitation of our study was the inability to collect data on PE events to be included in our clinical outcomes assessment.

**CONCLUSIONS**

Cancer patients are at high risk for developing thrombosis and recurrent VTE complications, so that effective thromboprophylaxis will greatly reduce the risk for VTE and improves clinical outcomes. Cancer patients might develop DVT in spite of thromboprophylaxis being given which raise the need for more investigation about the efficacy of using pharmacological prophylaxis versus combined regimen (pharmacological prophylaxis + mechanical prophylaxis). Breast
cancer patients are very high risk for DVT, which raises the importance for future studies to assess VTE risk and role of thromboprophylaxis amongst cancer patients in ambulatory care sittings.

CONFLICTS OF INTEREST

The author(s) declare that they have no conflicts of interests.

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