Abstract

Objectives: The purpose of this study was to describe the use of pharmacological and mechanical prophylaxis and clinical outcomes of patients undergoing diagnostic tests for suspected venous thromboembolism (VTE).

Methods: The medical records of 660 consecutive inpatients referred for suspected VTE at an academic medical center were retrospectively reviewed.

Results: Acute VTE was diagnosed in 138 (21%) of the 660 patients; the incidence of deep vein thrombosis and pulmonary embolism was 18–25%, respectively. Only 61% of eligible patients received pharmacological prophylaxis and 43% of patients received mechanical prophylaxis. The incidence of VTE was higher in patients who did not receive pharmacological prophylaxis (30%) compared with patients who did (16%, P value <0.001).

Conclusions: Preventive measures for VTE, including both pharmacological and mechanical prophylaxis, were underutilized in hospitalized patients undergoing diagnostic tests for suspected VTE.

Keywords: prophylaxis; venous thromboembolism

Introduction

Venous thromboembolism (VTE) consists of two related conditions: deep vein thrombosis (DVT) and pulmonary embolism (PE). VTE is one of the most common clinical conditions in hospitalized patients and PE is the most common preventable cause of hospital death in the United States.1 Approximately two-thirds of patients with symptomatic VTE manifest DVT alone, whereas one-third of patients manifest PE.1 The mortality rates associated with untreated PE range from 5%2 to 35%.3,4 PE is associated with 10% of deaths in hospitalized patients in the United States.5

Evidence-based recommendations for VTE prevention have been available during the last decade.6 Appropriate prophylactic regimens and treatment for specific patient groups have been recommended by a Consensus Panel of the American College of Chest Physicians (ACCP).7,8 Despite substantial evidence on the prevention and treatment of VTE, there have been errors from omission of prophylaxis, objective diagnostic testing and inadequate treatment that has resulted in significant harm to hospitalized patients.9–12

VTE is not a new clinical problem, but it is one that requires coordination of care across multiple locations by multiple providers. VTE continues to be a major patient safety problem in hospitalized patients and the Agency for Healthcare Research and Quality (AHRQ) lists VTE prevention in the top 10 patient safety problems.13 There is a plethora of evidence on VTE prevention and treatment, yet
200,000 patients die of PE each year in the United States. The Centres for Medicare and Medicaid Services (CMS) in partnership with the National Quality Forum and the Joint Commission have developed measures for reporting VTE prophylaxis in hospitalized patients. Financial incentives and disincentives are also being provided by CMS as a mechanism to improve the reporting of VTE prophylaxis. These changes will require hospitals and providers to adopt guidelines for assessing patients' risks for developing VTE and for implementing system-wide VTE prophylaxis measures. Moreover, in 2010 CMS will stop paying for VTE.

The academic medical centre where this study was carried out considered VTE prophylaxis to be a major patient safety issue. Data from three sources – (1) internal audits on the use of VTE prophylaxis, (2) benchmarking data on pharmacological prophylaxis through University Hospital Consortiums and (3) room audits to determine the use of mechanical prophylaxis – revealed that less than half of the eligible patients were being assessed for VTE risk and placed on pharmacological prophylaxis and less than 40% of patients who were given orders for mechanical prophylaxis were actually wearing the devices. The leadership team added VTE prophylaxis to the medical centre’s operation budget and plan for fiscal years 2004–2005. The purposes of this study were to describe the use of pharmacological and mechanical prophylaxis and clinical outcomes of patients undergoing diagnostic tests for suspected VTE.

Methods

This study was a descriptive study using retrospective medical chart reviews. During the period from 1 October 2005 to 31 March 2006, descriptive data on the use of VTE prophylaxis, the utilization of diagnostic tests for VTE and clinical outcomes for patients who underwent diagnostic tests for suspected VTE were collected.

The radiology electronic database was used to identify patients with suspected VTE who were referred for venous duplex scanning (VDS), ventilation and perfusion scanning (V/Q scan), or computed tomographic angiography (CTA) for suspected VTE. Retrospective reviews of medical records for 660 consecutive hospitalized patients referred to the vascular or radiology laboratories were conducted. All patients greater than 18 years of age who underwent lower extremity VDS or lung scanning (CTA or V/Q) for suspected VTE were included for the review.

Clinical data included patient demographic information, risk factors for VTE, signs and symptoms at the time of the initial VDS, V/Q or CTA scanning, results of the objective studies, prophylaxis strategies including pharmacological and mechanical compression devices, VTE treatment strategies and clinical outcomes associated with VTE (propagation of DVT, bleeding events and mortality). Risk factors for VTE that were assessed included prior DVT/PE, cancer, major surgery, cardiac disease, immobilization, limb trauma, hormone therapy including either hormone replacement therapy or oral contraceptive, pregnancy or postpartum, morbid obesity, prolonged travel, inherited or acquired thrombophilias and a family history of VTE. We reviewed all records for any documentation on testing or consulting for thrombophilias. Inherited thrombophilia that we reviewed included antithrombin III deficiency, protein C deficiency, protein S deficiency, Factor V Leiden mutation, prothrombin gene mutation, hyperhomocystenaemia and excessive release of plasminogen activator inhibitor (PAI-1). Acquired thrombophilias that were reviewed included myeloproliferative disorders, heparin-induced thrombocytopenia, nephritic syndrome, disseminated intravascular coagulation, lupus anticoagulant, antcardioliopin antibody, paroxysmal nocturnal haemoglobinuria, Buerger’s disease and Behcet’s syndrome.

Clinical outcomes data included the incidence of VTE (DVT and PE), propagation of thrombus in legs within three months after the diagnosis of DVT, major bleeding episodes within three months after anticoagulation therapy and mortality within three months following the diagnosis of VTE. Sixteen of 138 patients diagnosed with VTE did not have any follow-up data available, but the remaining patients (122 patients or 88%) with VTE were followed for a minimum of three months.

VTE prophylaxis included pharmacological and mechanical prophylaxis. Pharmacological prophylaxis included low-dose unfractionated heparin (UFH), low-molecular-weight heparin (LMWH) or warfarin. Aspirin was not included for VTE prophylaxis as it was not recommended by the 8th ACCP Consensus Panel as a VTE prophylaxis measure. Mechanical prophylaxis included sequential compression devices (SCDs) or graduated compression stockings (GCSs). Daily documentation on the use of mechanical prophylaxis for all patients is required by the nursing staff at this medical centre. All patients undergoing surgery or prolonged bed rest have a standing...
order for SCDs and all patients receive compression stockings (8–10 mmHg). The nursing notes were reviewed to determine whether or not the patient was on mechanical prophylaxis. The nursing notes did not have detailed information on the duration/frequency of the SCDs or the levels of patient compliance. A previous audit of nursing documentation for the use of SCDs at this institution revealed that 40% of patients who had an order for SCDs did not have the SCDs on their legs at the time of the room audit (unpublished quality improvement project, 2002).

The criteria for VTE prophylaxis were based on the patients’ mobility and risk assessment for VTE on admission and included hospitalized patients without contraindications to pharmacological prophylaxis. Physician documentation on VTE risk assessment on admission, medication records on pharmacological prophylaxis and nursing notes on mechanical prophylaxis were used to determine the use of VTE prophylaxis. There was inconsistent and inadequate documentation (missing data) on VTE prophylaxis in the patients’ medical records.

Acute DVT was diagnosed by VDS, which is the standard objective test for the diagnosis of DVT.20 Acute DVT was diagnosed following a comprehensive VDS at a dedicated vascular laboratory accredited by the Intersocietal Commission for the Accreditation of Vascular Laboratories (ICAVL) using registered vascular technologists. The VDS has been the standard objective test for DVT diagnosis at this medical centre for the last 10 years. Venous duplex sonography was performed in all of the deep veins in the lower extremities from the inferior vena cava to the paired calf veins. The criteria used to diagnose acute DVT included incompressibility of the vein walls, presence of intraluminal thrombus, loss of spontaneous and phasic Doppler flow signals, abnormal blood flow augmentation with calf vein compression and valsalva manoeuvres.21,22 Proximal DVT was defined as a thrombus involving the vena cava and proximal veins, including external iliac veins, common femoral veins, profunda femoris veins, superficial femoral veins and the popliteal vein. Calf DVT was defined as a thrombus in the deep calf veins, including posterior tibial, peroneal, soleal or gastrocnemius veins. The standard reporting criteria for the University of Washington Medical Center Vascular Laboratory is to distinguish between proximal and calf DVT and to describe the location(s) of the DVT, thrombus characteristics, Doppler flow signals and valve function.

PE was diagnosed by either CTA or V/Q lung scanning in patients with symptoms suggestive of PE. If the CTA results were non-diagnostic, then V/Q and/or VDS were performed and vice versa. If the V/Q results were non-diagnostic for PE, then a CTA and/or VDS were obtained. Pulmonary angiography was only performed for the therapeutic purpose of pulmonary thromboendarterectomy or for the evaluation of chronic pulmonary hypertension in this institution. There were no patients who underwent pulmonary angiography to rule out PE in this study.

Patients with DVT having at least one follow-up scan within three months after the initial objective testing were included in the evaluation for clinical outcomes. Medical charts of the patients with PE were also reviewed three months after the initial lung scanning to record clinical outcome measures.

Data were analysed using SPSS 15 for Windows. Descriptive statistical methods were used to describe patient demographic characteristics, signs and symptoms of VTE, risk factors for VTE, and VTE prophylaxis measures and treatment strategies. The chi-square (χ²) test or the Fisher’s exact tests were performed to analyse categorical variables and Student’s t-tests were performed for continuous variables. Multivariate logistic regression analyses were performed to evaluate significant risk factors associated with the development of VTE controlling for other covariates. The institutional review board approved the study.

Results

Acute VTE was diagnosed in 138 (21%) of 660 consecutive hospitalized patients undergoing objective diagnostic evaluation to rule out either DVT or PE. The incidence of DVT was 18% (83 of 469) in those who underwent VDS and the incidence of PE was 25% (83 of 332) in those who underwent lung scanning; 28 patients were diagnosed with both DVT and PE. Baseline patient data including VTE risk factors are shown in Table 1. The mean age was 56 ± 17 years, ranging from 18 to 99. Fifty-two percent of patients were women. The majority of hospitalized patients were Caucasian (80.2%, P = 0.020). The mean length of hospital stay prior to receiving an objective diagnostic test for suspected VTE was six days, ranging from 0 to 100 days. Significant VTE risk factors in this patient population were prior VTE and cancer (respectively, P < 0.001, P = 0.002). The mean number of VTE risk factors was 1.5 ± 1 (P = 0.049).

The types of VTE prophylaxis used in hospitalized patients with suspected VTE are presented in Table 2. Pharmacological prophylaxis was used in 57% of the patients while mechanical compressions...
including GCSs and/or SCDs were applied in 43% of the patients prior to the diagnosis of VTE.

Approximately 31% (205 of 660) of the patients in this study did not receive any form of prophylaxis (mechanical or pharmacological). Approximately 7% (48 of 660) of hospitalized patients were not eligible to receive pharmacological prophylaxis due to contraindications. Among those who were ineligible for pharmacological prophylaxis, 44% (21 of 48) received mechanical compression as a prophylaxis measure and more than half of the patients (56%, 27 of 48) had no mechanical prophylaxis measures used. Approximately 61% (374 among 612 eligible patients) received pharmacological prophylaxis measures to prevent VTE. The incidence of VTE was higher (30%, 71 of 238) in patients who did not receive pharmacological prophylaxis compared with those who had pharmacological prophylaxis (16%, 61 of 374) (P<0.001).

Table 3 describes VTE incidence and pharmacological prophylaxis utilization by each VTE risk category for patients eligible to receive prophylactic anticoagulants. The proportion of patients receiving pharmacological prophylaxis significantly increased with the number of risk factors for VTE (no risks – 46.3%, 1–2 risk factors – 60.3%, ≥3 risk factors – 80.5%, P<0.001). Patients without pharmacological prophylaxis had a significantly higher incidence rate of VTE compared with patients with pharmacological prophylaxis for all groups (P<0.001) in patients with

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**Table 1** Patient baseline characteristics

| Characteristics | Total (%) | With VTE (%) | Without VTE (%) | P value |
|-----------------|-----------|--------------|-----------------|---------|
| Patients N (%)  | 660       | 138 (20.9)   | 522 (79.1)      | 0.620   |
| Age in years (mean ± SD, range) | 56.3 (+17, 18–99) | 55 (+16) | 56 (+18) | 0.185 |
| Age group       |           |              |                 |         |
| 18–39           | 118 (17.9)| 22 (18.6)    | 96 (81.4)       |         |
| 40–64           | 332 (50.3)| 80 (24.1)    | 252 (75.9)      |         |
| 65–74           | 109 (16.5)| 21 (19.3)    | 88 (80.7)       |         |
| >75             | 101 (15.3)| 15 (14.9)    | 86 (85.1)       |         |
| Gender (males)  |           |              |                 |         |
|                | 315 (47.7)| 78 (24.6)    | 237 (75.4)      | 0.020   |
| Race (Caucasian)|           |              |                 |         |
|                | 529 (80.2)| 122 (23.1)   | 407 (76.9)      | 0.016   |
| Length of hospital stay (mean day ± SD, range) | 5.9 (+11, 0–100) | 5.7 (+11) | 5.9 (+11) | 0.860 |
| Body mass index (BMI)† (mean ± SD, range) | 29.4 (+8.4, 14–64) | 30.3 (+7.1) | 29.1 (+8.7) | 0.260 |

**Table 2** Type of prophylaxis in patients with suspected VTE

| Type of VTE prophylaxis | Frequency (%) | VTE (%) |
|-------------------------|---------------|---------|
| Both anticoagulation and mechanical compressions§ | 205 (31.1) | 25 (12.2) |
| Anticoagulation only | 171 (25.9) | 36 (21.1) |
| Mechanical compressions only | 79 (12.0) | 11 (13.9) |
| None** | 205 (31.0) | 66 (32.2) |

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VTE, venous thromboembolism

*P < 0.001: Type of VTE prophylaxis versus VTE incidence

†Percentage of patients with VTE within each type of VTE prophylaxis

‡Anticoagulation for VTE prophylaxis included low dose unfractionated heparin, low molecular weight heparin and warfarin. Aspirin was not included for VTE prophylaxis

§Mechanical compressions included graduated compression stockings and intermittent pneumatic compression devices

**Non-prophylaxis included the patient cases with insufficient medication information due to retrospective chart reviews
The location of PE was identified in patients with a CT scan.

Patients with suspected DVT and PE were symptomatic and they presented with shortness of breath, tachycardia and pleuritic chest pain. Approximately 30% of patients with acute DVT had thrombus isolated to their calf veins. More than half of the pulmonary thrombi were located in the lobar and segmental levels of the lungs. Approximately 15% of patients with acute PE had thrombi in sub-segmental levels of the lungs. Dyspnea and tachycardia were statistically significant in patients who developed PE (respectively, \( P = 0.036, 0.010 \)).

Ninety-four percent of patients (130 of 138) who were diagnosed with VTE were treated with anticoagulation therapy. Eight patients had contraindications to standard anticoagulation treatment for VTE; three patients had inferior vena cava filter placements; one patient was assigned to hospice care for terminal conditions due to liver and renal failure; and the remaining four patients did not receive any treatment or subsequent measures to prevent propagation of their thrombi.

Three-month follow-up data on bleeding or mortality were not available in 11.6% (16 of 138) of patients with VTE diagnosis. Complications such as gastrointestinal bleeding or heparin-induced thrombocytopenia within three months after therapeutic anticoagulation were reported in 4.3% (5 of 115) of patients with VTE. One patient developed heparin-induced thrombocytopenia following anticoagulation therapy. The mortality rate within three months after VTE diagnosis for those who had three-month follow-up medical records available was 12.5% (15 of 122) and eight patients among the 15 patients who died had a diagnosis of cancer.

Table 5 describes the significant factors that were associated with VTE in hospitalized patients with suspected VTE using a multivariate logistic regression analysis. The cut-off point for the \( P \) value for significance was 0.05. Caucasians were more likely to have VTE than other ethnic groups.
Patients who had a prior history of VTE or active cancer were more likely to have VTE (all odds ratios [OR] > 1, P < 0.05). Patients who received pharmacological prophylaxis were less likely to have VTE (OR = 0.397, P < 0.001). Female gender was a marginally significant factor for VTE (P = 0.056), while controlling for other covariates in this study.

### Discussion

The incidence of VTE was higher in hospitalized patients with suspected VTE who did not receive prophylaxis in this study, yet the overall incidence was similar to the literature, ranging from 11%5 to 28%. The overall incidence of VTE was 21%: DVT – 18%, PE – 25%, which might be due to the fact that more than a quarter of patients in this study had a diagnosis of cancer. There were no standard protocols or reporting systems for documenting baseline VTE risk assessment in hospitalized patients on admission or discharge. Approximately 40% of hospitalized patients at risk for VTE who underwent diagnostic studies for suspected VTE did not receive pharmacological prophylaxis to prevent VTE. We had unpublished data on VTE prevention in randomly selected 100 surgical and 100 medical inpatients and monthly audits of specialty providers’ use of pharmacological prophylaxis in high-risk patients. These data demonstrated that only half (51%) of the eligible surgical inpatients and 46% of eligible medical inpatients received pharmacological prophylaxis. According to the 2008 ACCP guidelines,7 pharmacological prophylaxis should be used in all hospitalized patients unless they are ineligible due to contraindications to anticoagulation. Those patients ineligible for pharmacological prophylaxis should be placed on mechanical prophylaxis to prevent VTE.

Mechanical prophylaxis using GCSs and SCDs can be applied to patients who are at risk for VTE to prevent venous stasis in the lower extremities. According to the 8th ACCP guidelines, mechanical prophylaxis is recommended primarily in patients at high risk for bleeding or possibly as an adjunct to pharmacological prophylaxis, and the proper use of and optimal patients’ adherence with these methods should be carefully ensured.7

A recent blinded randomized controlled trial23 showed that the rates of VTE and proximal DVT were significantly lower with pharmacological prophylaxis (fondaparinux) plus mechanical prophylaxis (intermittent pneumatic compression) than with mechanical prophylaxis alone in 1309 patients who had major abdominal surgery (1.7% versus 5.3%, P = 0.004). In this study, 43% of patients who were suspected of VTE received mechanical compressions, and among those approximately 30% received mechanical prophylaxis without pharmacological prophylaxis. The VTE rates were significantly different and varied by the types of VTE prophylaxis utilized (shown in Table 2), and the VTE rates were lower in those with both pharmacological and mechanical prophylaxis than with mechanical prophylaxis alone without adjusting co-variates (12.2% versus 13.9%, P < 0.001).

In addition, mechanical prophylaxis should be used to prevent propagation of DVT for patients who have a contraindication to pharmacological prophylaxis due to bleeding or allergies.7 However, mechanical prophylaxis was used in only 40% of those patients with contraindications in this study. Documentation for the use of mechanical prophylaxis was inadequate due to missing data on the placement and compliance of SCDs. The nursing staff were responsible for documenting the use of mechanical prophylaxis (SCDs and GCSs). Unpublished data from a previous room audit of patients with orders to wear mechanical compression devices for VTE prevention at this medical centre demonstrated that 40% of the SCDs were not applied to the patient at the time of the audit. In the current review of records, 43% of patients were documented as having mechanical prophylaxis, but the actual percentage of patients who utilized the devices might be less based on the results of a previous audit. The data about proper use of mechanical devices and patients’
adherence with the devices were difficult to collect due to poor documentation and missing data.

The results from this study confirmed underutilization of pharmacological prophylaxis in patients at risk for VTE. For example, cancer with/without chemotherapy and a prior history of VTE are independent risk factors for developing VTE, yet underuse of pharmacological prophylaxis for patients with these risks was documented in our patient population; only 53% of eligible patients with cancer and 72% of eligible patients with prior VTE received pharmacological prophylaxis in this study. Inherited or acquired thrombophilias (hypercoagulable state) are also significant risk factors for VTE. In this study, only 60% of patients with known hypercoagulable states received pharmacological prophylaxis.

The gap between research and practice on the treatment of VTE has been reported. Caprini et al. reported that a lower than expected use of LMWH, inappropriate bridging from LMWH or UFH to oral anticoagulants were all problems, which resulted in a one-month mortality rate of 6% for DVT and 12% for PE. In this study, most of the patients diagnosed with VTE were treated using either anticoagulants or venous filter placement, but four patients with VTE did not receive any treatment. The three-month mortality rate based on the 88% of patients who had three-month follow-up medical records available was 12.5% for DVT and 13.5% for PE.

Several professional groups and consensus panels have recommended pharmacological prophylaxis for all hospitalized patients without contraindications to anticoagulation. However, the dissemination of evidence in the form of clinical guidelines into daily clinical practice is slow or non-existent. Low compliance with prophylaxis guidelines for VTE and underuse of VTE prophylaxis strategies have been reported. In this study, we found that only 61% of patients who were eligible to receive pharmacological prophylaxis did so, which is similar to the literature. In other words, approximately 40% of patients who were eligible to receive prophylaxis to prevent VTE did not receive any form of prophylaxis.

Inadequate documentation on whether patients were assessed for VTE risk or whether they received prophylactic measures because of their VTE risk was apparent in this study. Individual units within the medical centre had their own admission forms and not all of them required the assessment of VTE risk; therefore there was inadequate documentation across the institution. Chart audits revealed inconsistencies in reporting VTE risks and subsequent prophylaxis orders. A systems approach to improving documentation about VTE risk assessment and prophylaxis orders for all hospitalized patients is underway. The hospital is currently adopting an electronic medical record (EMR) that will require the provider to document whether a patient was assessed for VTE risk upon admission, and then the provider will be required to document plans for pharmacological and mechanical prophylaxis. If there are no contraindications to pharmacological prophylaxis, an EMR alert will force the provider to choose a prophylaxis strategy.

This study was part of a larger Partners in Patient Safety study funded by the AHRQ. The parent study was designed to evaluate the effectiveness of the two interventions on improving the prevention and management of VTE. The interventions included a VTE Safety Toolkit and an on-line provider training module on VTE prophylaxis. The VTE Safety Toolkit consists of clinical algorithms for the prevention, diagnosis and management of acute DVT and PE. The tools were developed by a multidisciplinary team based on evidence from the 7th ACCP guidelines and recent studies on PE diagnosis. The goal of the parent study was to evaluate the effectiveness of the tools and products of a systems-supported VTE Safety Toolkit on improving clinical and system outcomes for patients at risk for or diagnosed with VTE. The VTE Safety Toolkit has been disseminated nationally via AHRQ’s patient safety website (http://www.ahrq.gov/quality/pips/grants.htm). The VTE Safety Toolkit can also be found at the following website (http://vte.washington.edu).

This study has limitations due to the descriptive-observational study design at a single institution which provides the lowest methodological quality. There are inherent problems associated with secondary analyses using data abstracted from retrospective medical chart reviews, such as incomplete or inaccurate data, misinterpretation or lack of understanding of documentation. However, this study was conducted to provide baseline data on the use of pharmacological and mechanical prophylaxis strategies and the clinical outcomes of patients who underwent diagnostic studies for suspected VTE.

In summary, this study shows that the incidence of VTE and mortality in hospitalized patients referred for VTE diagnosis was high. The data from this study showed underutilization of pharmacologic prophylaxis for VTE prevention, which may have resulted in the high incidence of VTE. Health-care providers in multiple disciplines, including physicians,
nurse practitioners, pharmacists and nurses, are involved in the care of patients who are at risk for VTE. An effort to decrease the incidence of VTE by increasing the use of pharmacological prophylaxis through the use of a systems-supported VTE Safety Toolkit and web-based provider education is ongoing. Future audits of VTE management will be conducted to determine if the educational interventions had an effect on practice.

Acknowledgement

We would like to acknowledge Ann K Wittkowsky (PharmD) for the review of this manuscript.

Source of Funding: This project was supported by the Agency for Healthcare Research and Quality; Partnerships in Patient Safety grant number 1 U18 HS015898 (Principal Investigator: Brenda K Zierler, PhD).

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