8-20-2009

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Word Count: 2,490

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Funding source: none.

Conflicts of interest: none.

## Abstract

**Background:** Although venous thromboembolism is an important cause of morbidity and mortality within the hospital, a significant proportion of at-risk inpatients do not receive measures known to reduce the risk of deep vein thrombosis and pulmonary embolism.

**Objective:** To determine whether a pharmacy driven alert system would, compared to usual care, be associated with a higher rate of adequate VTE prevention measures among at-risk inpatients on a general internal medicine service.

**Design:** Prospective, controlled trial.

**Setting:** A university-based teaching hospital.

**Patients:** Adults admitted (Monday through Friday) to the general internal medicine inpatient service from 6/19/06-9/21/06.

**Intervention:** Pharmacist assessment of venous thromboembolism risk; pharmacist-driven alert to treating physician.

**Measurements:** Proportion of at-risk patients receiving adequate thromboprophylaxis within 36 hours of admission.

**Results:** Overall, 140 patients were at sufficient risk for VTE to be included. In the usual care group, prophylactic measures were ordered for 49 (61%) of the 80 patients at moderate to high risk. In the pharmacist-alert group, 44 (73%) of the 60 moderate to high VTE risk patients received adequate thromboprophylaxis ($p = 0.15$).

**Conclusions:** Although we did not observe a statistically significant difference between the experimental groups, our results are consistent with previous reports suggesting that alert systems (whether computerized or human) can increase the proportion of hospitalized patients who receive adequate measures to prevent VTE.

## Background

Venous thromboembolism (VTE) is a disease that encompasses all pathological thrombosis occurring on the venous side of the circulation. The most common manifestations are deep venous thrombosis (DVT) of the lower extremities and its potentially fatal complication, pulmonary embolism (PE). VTE accounts for more than

250,000 hospitalizations annually in the U.S. and causes of death in a substantial number of hospitalized patients (1). PE has a mortality rate of up to 17% (2), and approximately 25-30% of patients with proximal DVT will develop symptomatic PE (3). Among hospitalized patients who experience VTE, up to 5% will suffer a fatal PE (4). The often clinically elusive nature of this disease is highlighted by one published report in which only 3% of patients who had a DVT present at autopsy had been suspected or evaluated for DVT prior to death (5). Since sudden death can, in some cases, be the first clinically apparent manifestation of PE, significant attention has been dedicated to the primary prevention of VTE in patients at high risk. In the United States, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) and the National Quality Forum (NQF) have promoted efforts to create 'National Consensus Standards for the Prevention and Care of Deep Vein Thrombosis' (6).

Despite the significant risk for VTE among patients hospitalized for "medical" (i.e. non-surgical) diagnosis, the rate at which prophylaxis measures are used among at-risk subgroups has consistently been reported to be less than 50% (7). In one study of 2,726 patients who were diagnosed with a DVT while in the hospital, only 1,147 (42%) had received thromboprophylaxis within 30 days of the diagnosis (3). Another study demonstrated that only 33% of patients admitted to a medical intensive care unit received

VTE prophylaxis, despite the fact that over 50% of these patients had multiple risk factors for VTE (8). Taking the previous data into account, the low rate of thromboprophylaxis does not correlate with evidence documenting the efficacy of measures designed to reduce VTE risk. Numerous clinical trials have established that the use of pharmacologic or mechanical interventions can substantially reduce the risk of VTE among medical inpatients with risk factors; this evidence has been reviewed elsewhere (9).

Some authors have speculated that physicians fail to order thromboprophylaxis among medical inpatients because they are unaware of the substantial proportion of patients who are at moderate or high risk of venous thrombosis. Kucher et al demonstrated that adding electronic alerts for medium to high risk patients within a computerized-physician-order-entry system reduced the number of patients experiencing DVT or PE by 41% (10). Studies like this suggest that either a knowledge gap or lack of awareness may exist among practitioners. A study evaluating methods to improve VTE prophylaxis by implementing a pharmacy-driven staff education program focusing on the importance of using enoxaparin and heparin in medically ill patients was found to increase the use of appropriate prophylaxis from 43% in the preeducation groups to 58% in the posteducation groups (11). With these data in mind, we conducted a prospective, controlled study to

evaluate the hypothesis that a pharmacist-driven identification and notification system would increase the rate of appropriate thromboprophylaxis use among medical inpatients.

## Methods

### *Patients*

All patients admitted to the General Internal Medicine teams at the University of New Mexico Hospital between 6/19/06 through 9/21/06 were included. Patients admitted over the weekend were excluded from the study because pharmacist availability on weekends was inconsistent. Patients who were already receiving therapeutic doses of anticoagulants for other reasons were also excluded from the study. Four internal medicine teams admitted all the General Medicine inpatients (over a 24-hour period) rotating every four days. House officers rotated onto a particular team for 1 month at a time. Two of the teams were randomly assigned to be in the intervention group (the other 2 teams served as the control group) for the duration of the study. A list of all patients admitted to the internal medicine service was provided by the billing department to the pharmacists every morning, Monday through Friday.

Permission to perform this study was granted by the Institutional Review Board at the University of New Mexico Health Sciences Center.

*Intervention Group*

The pharmacist used the history and physical exam available in the hospital chart to determine the patient's VTE risk score. The VTE risk scores were determined by a standardized risk-assessment template (Table 1) (10). Patients were risk-stratified and classified as medium or high risk (determined by a score of greater than 4). A score of 4 or above on the risk assessment scale was chosen because this level VTE risk justifies the cost and small risk of hemorrhage associated with prophylactic therapy. Once identified, the pharmacist determined if the moderate to high risk patients had a documented order for VTE prophylaxis. For each such patient, the pharmacist notified the physician about the patient's VTE risk. The physician caring for the patient was then left to decide: 1) whether to institute DVT prophylaxis, and 2) if pharmacological prophylaxis was not contraindicated, which evidence-based therapy would be used. If a patient had an increased risk of bleeding contraindicating pharmacologic prophylaxis, sequential compression devices (SCD) were recommended.

*Control Group*

For the patients admitted to the two teams designated as the "control" groups, a record of names and medical record numbers was collected by the pharmacists (using the same

method as described above), but no attempt was made to alter the usual care received by these patients.

**Outcome Measures**

At the conclusion of the study, the hospital records of all patients involved in the study were reviewed to assess for time and type of VTE prophylaxis administered. For each patient, the primary outcome measure was whether adequate VTE prophylaxis was ordered within 36 hours of admission to the hospital. VTE prophylaxis was considered adequate if one of the following management strategies, available at UNM hospital, was initiated within 36 hours of hospital admission: heparin 5000 units subcutaneously (SC) every eight hours, enoxaparin 40 mg SC every day, fondaparinux 2.5 mg SC daily, or sequential compression devices. In addition to the primary outcome, other data were recorded: admitting team, time of admission, age, gender, VTE risk score, contraindications, treatment given, time treatment was ordered and time administered.

**Statistical Analysis**

We estimated that 300 patients would be needed to have power of 90% (two-sided alpha of 5%) to detect an increase in appropriate VTE prophylaxis from 40% in the control

group to 60% in the intervention group. Our assumption that 40% of the control patients would receive appropriate VTE prophylaxis was based upon internal data gathered in prior years for quality improvement purposes. Our comparison between intervention and control groups was done by the t-test for continuous outcomes, and by the Fisher exact test for binary/categorical variables.

**Results**

Over a 12 week period, 376 patients were admitted to the internal medicine inpatient service between 7am Sunday and 7am Friday. One hundred sixty patients were admitted to the teams assigned to receive the intervention, while 216 patients were admitted to the control teams. The characteristics of the included patients are shown in Table 2. Overall, 43% were women. The average age of patients in both groups was 51 years; 140 (37%) patients had a VTE risk score of greater than 4. In the control group, prophylactic measures were ordered for 49 (61%) of the 80 patients at moderate to high risk. In the experimental group, 44 (73%) of the 60 moderate to high VTE risk patients received adequate thromboprophylaxis. The difference between rates of adequate prophylaxis use in the 2 groups was not statistically significant ($p = 0.15$). The most commonly prescribed pharmacologic agents were “low-dose unfractionated heparin,” used in 56% of all at risk

patients, and “prophylactic dose” enoxaparin, used in 11%. Sequential compression devices (SCD) were used commonly for at-risk patients in both the intervention (64%) and the control (50%) groups; SCD were commonly ordered along with (rather than in place of) pharmacologic strategies.

**Discussion**

Our study demonstrates that a pharmacist-driven risk stratification system is associated with a high rate of VTE prophylaxis. Although our study did not find a statistically significant difference, the trend we observed is consistent with the hypothesis that a pharmacist driven system can increase VTE prophylaxis use among at-risk individuals. It is probable that our study did not achieve statistical significance because VTE prophylaxis use in the control group was substantially higher than we had anticipated. Based on previous internal surveys, we estimated that 30-40% of the at-risk patients in the control group would receive VTE prophylaxis. Since the observed rate of adequate VTE prophylaxis in the control group exceeded 60%, our sample size, determined *a priori,* was not large enough to demonstrate a statistically significant difference. There are several possible reasons the observed rate of adequate VTE prophylaxis within the control group was higher than our pre-study assumptions. First, the internal data on which we based our power calculation was obtained four years prior to this study and it is likely that

physicians' consciousness of venous thromboembolism risk among hospitalized patients had increased since that time. Thus, the "baseline" rate of appropriate VTE prophylaxis at the University of New Mexico Hospital may also have increased. Second, our study design did not prevent or discourage the possibility of cross-talk between the control and interventional groups. It is likely that physicians treating patients in the control group became aware that their practice was being monitored and may have, simply based on this heightened awareness, and increased the frequency with which they used thromboprophylaxis (12). Finally, we under-estimated the proportion of patients admitted to the medical service whose VTE risk score would be 4 or greater. Thus, although we screened 376 patients for inclusion, only 140 were at sufficiently high risk for VTE to include in our comparison.

Computer-based identification of high risk patients and alerting of physicians in a hospital setting appears to prevent thromboembolic events (10). Although the difference we observed was not statistically significant, our findings suggest that a method relying on person-to-person communication may be an effective alternative, especially in institutions where computerized order-entry is not yet available. In order for a pharmacy-driven identification and notification system to be effective, the pharmacist must have the time

and access necessary both to determine each patient's VTE risk as well as to contact the treating physician in a timely manner. Additional studies are needed to establish best practice models for pharmacist-driven thromboprophylaxis.

## Table 1. DVT Screening and Prophylaxis Sheet

**Date and Time:** _____ (circle points that apply)

| Medical Condition | Points | Medical Condition | Points | Medical Condition | Points |
|---|---|---|---|---|---|
| Stroke (with paresis) | 5 | Previous DVT/PE | 4 | Antithrombin III Deficiency | 3 |
| Acute MI | 3 | Age > 70 | 2 | Protein C/S Deficiency | 3 |
| Heart Failure | | Age 61-70 | 1 | Activated Protein C Resistance | 3 |
| Class IV | 3 | Age 41-60 | 0.5 | (Factor V Leiden) | |
| Class I-III | 1 | Anticipate confinement 72 hrs | 1 | Prothrombin Gene Mutation | 3 |
| Cancer | 3 | Obese (>20% IBW) | 1 | Homocysteinaemia | 3 |
| Acute Infection | 3 | Hormone Replacement | 1 | Lupus Anticoagulant | 3 |
| Acute Respiratory Disease | 1 | Therapy/Oral Contraceptive | | Anticardiolipin Antibodies | 3 |
| Inflammatory Bowel Disease | 1 | | | Nephrotic Syndrome | 3 |
| Acute Rheumatoid Arthritis | 1 | | | Myeloproliferative Disease | 3 |

**Total Score: (sum of points):** _____

### Contraindications to Medical Prophylaxis:

- Active major bleeding
- History of heparin induced thrombocytopenia
- History of hypersensitivity to enoxaparin sodium, heparin, or pork products
- Prosthetic heart valves
- Caution with spinal tap or epidural anesthesia within 24 hours (dosing interval adjustments needed)
- Caution with creatinine clearance < 30 ml/minute and uncontrolled hypertension
- Caution with conditions associated with increased risk of hemorrhage; bacterial endocarditis, congenital or acquired bleeding disorders, active ulcerative and angiodysplastic gastrointestinal disease, hemorrhagic stroke, or shortly after brain, spinal or opthalmological surgery, or in patients treated concomitantly with platelet inhibitors

### Contraindications to Mechanical Prophylaxis:

- Ischemic vascular disease
- Patient unable to wear due to size or injury

**Risk Category and Method Prophylaxis:** (check appropriate methods to order)

| Low Risk (1-3 points) | Moderate Risk (4-5 points) | High Risk (6 or more points) |
|---|---|---|
| No recommendations<br>Early mobilization | Heparin 5000 units SQ every 8 hours<br>Heparin 5000 units SQ every 12 hours (elderly or decreased renal function)<br>Enoxaparin 40 mg SQ daily<br>Enoxaparin 30 mg SQ daily (creatinine clearance < 30)<br>TED Hose<br>Sequential compression devices<br>Plexipulses | Heparin 5000 units SQ every 8 hours<br>Heparin 5000 units SQ every 12 hours (elderly or decreased renal function)<br>Enoxaparin 40 mg SQ daily<br>Enoxaparin 30 mg SQ daily (creatinine clearance < 30)<br>TED Hose<br>Sequential compression devices<br>Plexipulses |

**Patient label here**

**Physician Signature:** _____

**Physician Printed Name:**_____

**Table 2. Characteristics of patients and prophylactic measures against VTE**

| | Experimental n=160 | Control n=216 | P-Values |
|---|---|---|---|
| Females (%) | 64 (40%) | 96 (44%) | NS |
| Males | 96 (60%) | 120 (56%) | NS |
| Age | | | |
| Mean (Range) | 51 (18-97) | 51 (18-95) | NS |
| VTE score >4 | 60 (37.5%) | 80 (37.0%) | NS |
| VTE score avg | 3.4 | 3 | |
| Proportion of patients with VTE risk >4 who received prophylaxis | 44 (73%)<br>41.8-46.2 | 49 (61%)<br>46.55-51.45 | 0.15 |
| Heparin | 37 (62%) | 41 (51%) | 0.23 |
| LMWH | 10 (17%) | 6 (7.5%) | 0.11 |
| SCD's | 30 (50%) | 51 (64%) | 0.001 |

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