

Physician Alerts to Prevent Venous Thromboembolism

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Objectives:

- To establish the importance of venous thromboembolism (VTE) prevention in the vulnerable medical patient population during hospitalization and after discharge
- To highlight the role of alert-based computerized decision support systems in the prevention of VTE among high-risk patients
- To emphasize the importance of improving adherence to physician-ordered prophylaxis among at-risk hospitalized patients.
- To describe the impact of “human” alerting strategies on prophylaxis utilization and the prevention of symptomatic VTE among high-risk patients

VTE, including deep vein thrombosis (DVT) and pulmonary embolism (PE), is an often preventable complication of medical illness associated with substantial healthcare costs [1,2]. DVT and PE may result in debilitating long-term complications of post-thrombotic syndrome [3] and chronic thromboembolic pulmonary hypertension [4], respectively. Common conditions among hospitalized medical patients, such as heart failure, chronic obstructive pulmonary disease, acute infection, atherosclerotic vascular disease, and malignancy, increase the risk of VTE [5]. Recent hospitalization has been implicated in the development of VTE in the outpatient setting [6].

Based on such observations, we designed and conducted our first Quality Improvement Initiative, the Electronic Alert Trial, at Brigham and Women’s Hospital [7]. Electronic Alert was a single-center randomized controlled trial designed to test the hypothesis that the use of an electronic alert program to encourage prophylaxis would reduce the frequency of VTE among high-risk hospitalized patients. First, we devised a risk scoring system to identify hospitalized patients at increased risk for VTE:

Major (High) Risk Factors (3 POINTS each):

- Cancer (active)
- Prior VTE
- Hypercoagulability

Intermediate Risk Factor (2 POINTS each):

- Major Surgery (> 60 minutes, during this admission)

Minor (Low) Risk Factors (1 POINT each):

- Advanced Age (> 70 years of age)
- Obesity (BMI > 29, or the presence of the word “obesity” in admission exam notes)
- Bed rest / Immobility (not related to surgery)
- Female Hormone Replacement Therapy or Oral Contraceptives

Patients with point scores of 4 or greater were designated as “high-risk” for VTE.

We then developed a computer program linked to the patient database to identify consecutive hospitalized patients at risk for VTE in the absence of prophylaxis. 1255 eligible patients were randomized to the intervention group, in which the responsible physician was alerted to the patient’s risk of VTE, and 1251 patients were randomized to a control group, in which no alert was issued. More than 80% of patients in both study groups were admitted to the Medical Service. The physician was required to acknowledge the alert and could then withhold or order prophylaxis, including mechanical or pharmacological modalities. The primary end point was clinically diagnosed, objectively confirmed DVT or PE at 90 days. More patients in the intervention group than in the control group received mechanical prophylaxis (10.0% vs. 1.5%, $p<0.001$) or pharmacologic prophylaxis (23.6% vs. 13.0%, $p<0.001$). The electronic alert reduced the risk of symptomatic DVT or PE at 90 days by 41% ($p=0.001$). There was no increase in the rate of major or minor hemorrhage at 30 days in the intervention group.

As we planned a multicenter randomized trial applying the electronic alert strategy to a broad array of hospitals across the U.S., we learned that replication of our electronic alert was not feasible. Therefore, we crafted a strategy that employed a “human” rather than electronic alerting system. The Physician Alert Quality Improvement Initiative was a multi-center randomized controlled trial to evaluate the impact of a direct page from a hospital staff member to the Attending Physician on prophylaxis utilization and symptomatic VTE among hospitalized patients [8]. The primary end point was reduction in symptomatic VTE within 90 days of randomization. 2,493 patients (82% on Medical Services) from 25 study sites were randomized to the intervention group ($n=1,238$) versus the control group ($n=1,255$). Patients whose physicians were alerted were more than twice as likely to receive VTE prophylaxis as controls (46.0% versus 20.6%, $p<0.0001$). The symptomatic VTE rate was lower in the intervention group (2.7% versus 3.4%; hazard ratio, 0.79; 95% confidence interval, 0.50 to 1.25), but the difference did not achieve statistical significance. The rate of major bleeding at 30 days in the alert group was similar to the control group.

We recently studied a novel serial three-screen alerting strategy to increase VTE prophylaxis utilization in high-risk hospitalized patients whose physicians had initially declined to order any prophylactic measures after an initial electronic alert [9]. If the physician initially declined to order prophylaxis after our original, one-screen electronic alert, he or she was instructed on the

second screen to enter a rationale for omitting VTE prophylaxis. The third screen of the three-screen alert included a final opportunity to prescribe graduated compression stockings or intermittent pneumatic compression devices. Of a total cohort of 880, the responsible physicians for 425 hospitalized patients received the one-screen electronic alert, whereas 455 who declined prophylaxis after the initial screen received the second and third screens of the three-screen alert. Our enhanced serial three-screen alert strategy generated VTE prophylaxis orders for an additional 58.4% of the 455 patients whose physicians initially declined to order any prophylactic measures following the one-screen alert. There was no significant difference in the rate of symptomatic VTE at 90 days between the two cohorts.

Although our novel serial three-screen electronic alerting strategy improved VTE prophylaxis utilization compared with our original one-screen alert, a substantial proportion of physicians still declined to order any prophylactic measures. Alert-based computerized decision support systems offer a variety of options for further improving VTE prophylaxis among high-risk hospitalized patients. However, further investigation is required to determine the optimal approach to alert-based computerized decision support for VTE prevention.

Although the prescription of prophylaxis is a critical step in VTE prevention, clinicians must also ensure adherence to orders for prophylaxis. We recently completed a study at Brigham and Women's Hospital where we discovered that pharmacological prophylaxis adherence, defined as the ratio of doses given to doses ordered, was greater with enoxaparin once daily (94.9%) when compared to unfractionated heparin (UFH) three times daily (87.8%) or UFH twice daily (86.8%) ($p < 0.001$) [10]. Medical and surgical patients at moderate or high risk for VTE receiving physician-ordered enoxaparin for VTE prophylaxis were more likely to receive all of their scheduled doses compared with patients receiving physician-ordered UFH prophylaxis ($p < 0.001$).

We were surprised to learn that patient refusal was the most common reason for omitted physician-ordered enoxaparin or UFH prophylaxis doses. Patient refusal accounted for 44.5% of the UFH orders and 39.4% of enoxaparin orders that were omitted. We hypothesize that patients were not adequately educated about the rationale for prescribing these medications and that they refused doses because of anticipated discomfort, inconvenience, or anxiety. Patients may have also refused prophylactic injections because of their lack of understanding regarding their individual risk of VTE. We have designed a Patient Education Initiative to evaluate whether 1-on-1 inpatient education with a standardized script reviewing the individual's risk for VTE and rationale for prophylaxis will improve adherence. This cohort study will enroll 500 hospitalized patients at moderate or high risk for VTE who are ordered for prophylaxis with low-molecular weight heparin (LMWH) or UFH. The primary endpoint is medication adherence with LMWH and UFH following the patient education intervention compared with our recently completed cohort study in which no education program was offered.

Although much of the emphasis placed on prevention has focused on in-hospital prophylaxis, a recent study demonstrated that 74% of patients developed VTE as an outpatient [6]. Of these patients, a substantial proportion had undergone surgery (23%) or hospitalization (37%) in the 3 months preceding the diagnosis of VTE [6]. Current practice is to administer VTE prophylaxis while the patient is in the hospital. Upon discharge, it is assumed that the risk of VTE abates, and consequently, prophylaxis is discontinued. In reality, the risk persists as many patients continue to have limited mobility as well as other ongoing risk factors for VTE. Several studies have validated extended out-of-hospital prophylaxis with warfarin or low-molecular weight heparin in the prevention of VTE among orthopedic patients [11,12] and those undergoing abdominal or pelvic surgery for malignancy [13]. Comparatively, data regarding the prevention of VTE in medical patients after discharge have been limited. The Extended Clinical Prophylaxis in Acutely Ill Medical Patients (EXCLAIM) trial, conducted primarily in North America and Europe, was designed to evaluate the efficacy and safety of extended pharmacological prophylaxis in medical patients after hospital discharge [14]. Acutely ill hospitalized medical patients who had been receiving prophylactic subcutaneous enoxaparin were randomized to continue prophylaxis or to receive a placebo for approximately 1 month after discharge [14]. Extended duration prophylaxis with enoxaparin resulted in a 73% relative risk reduction in symptomatic VTE with a small incremental increase in risk of bleeding [14].

Although the EXCLAIM Trial demonstrated that extended prophylaxis in medical patients after hospital discharge reduced the risk of VTE, this practice has not been widely utilized. The Discharge Alert Quality Improvement Initiative has completed enrollment and will determine whether alerting physicians about the importance of continued VTE prophylaxis in at-risk medical patients just prior to hospital discharge will lower the incidence of outpatient VTE. Hospitalized medical patients with discharge planned within 48 hours were evaluated with the previously validated VTE risk score. If the cumulative VTE risk score was ≥ 4 , orders were reviewed to detect ongoing mechanical or pharmacological prophylactic measures.

The intervention took place within 48 hours of planned hospital discharge. If randomized to the alert, the responsible physician was notified that: 1) his or her patient is at high risk for VTE and 2) VTE prophylaxis should be considered in the discharge orders. If randomized to no alert (control patients), the responsible physician was not contacted. The primary endpoint is clinically diagnosed DVT or PE at 90 days. Safety endpoints include total mortality and bleeding events at 90 and 30 days, respectively.

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