BRIEF REPORT

Development and Implementation Results of a Venous Thromboembolism Prophylaxis Guideline in a Tertiary Care Pediatric Hospital

Arash Mahajerin, MD,a Emily C. Webber, MD,a Jennifer Morris, PharmD,b Kathryn Taylor, PharmD,c Michele Saysana, MDd

ABSTRACT

OBJECTIVES: Incidence of pediatric venous thromboembolism (VTE) is increasing due to increased survival of children with chronic diseases and use of interventions (eg, central venous lines), with VTE risk. Our objective was to create VTE prophylaxis guidelines with targeted identification of children at high risk to support appropriate mechanical and pharmacologic prophylaxis and integrate into the electronic medical record (EMR) as a hospital-wide quality improvement project.

METHODS: Patients aged 12 to 17 years were included. We evaluated institutional data regarding VTE incidence and risk factors. We evaluated literature for populations at high risk for VTE. Guidelines were formulated, and an EMR tool to assess risk and support the guidelines was created and implemented.

RESULTS: The EMR tool was used to screen 48% of qualified admissions for the first month and 81% in the final study month. On average, 69.1% of qualified admissions were screened monthly during the first 18 months of the program. No adverse events were reported due to pharmacologic prophylaxis.

CONCLUSIONS: Many risk factors are common between children and adults and certain pediatric populations warrant prophylactic consideration. Pediatric VTE prophylaxis guidelines can be successfully implemented into the EMR to identify high-risk populations. Future studies should assess the long-term impact of implementation.
The incidence of venous thromboembolism (VTE), including deep vein thrombosis and pulmonary embolism, is increasing in tertiary care pediatric hospitals. Our institutional data revealed an incidence of 71/10,000 admissions from 2005 to 2009 for patients aged 0 to 18 and 112/10,000 admissions for those 12 and older. The higher adolescent VTE incidence concurs with known bimodal peaks in neonates and adolescents.

The rising incidence is attributed to increased survival of patients with chronic conditions and increased utilization of life-saving measures with known VTE association (eg, central venous lines). Well-established risk factors include VTE history, thrombophilic state, autoimmune disease with antiphospholipid antibody (APA) positivity, CVL, bacteremia or other serious bacterial infection, overweight/obesity, estrogen therapy, immobilization ≥72 hours, chronic total parenteral nutrition (TPN), and mechanical ventilation.

We developed a multidisciplinary committee to formulate VTE prophylaxis guidelines for 12- to 17-year-old patients based on our institution's high VTE incidence in this age group. The goals of the group were to develop a VTE screening and prophylaxis program, to monitor utilization of VTE prophylaxis, and to address adverse events attributed to these modalities. In this report we describe guideline and electronic medical record (EMR) tool development and utilization.

**METHODS**

The institution did not require institutional review board approval for guideline development. We began by reviewing current literature for prophylaxis guidelines in adults and children. This included the American College of Chest Physicians *Chest* guidelines, other children's hospitals' guidelines, and institutional retrospective data of VTE risk factors. We also reviewed existing institutional pathways for adult VTE prophylaxis, traumatic brain injury, and spinal cord injury and met with representatives from all major medical and surgical divisions.

**Patient Cohort to Be Screened and VTE Risk Factors**

The 2 risk factors with the largest contribution to VTE are CVL and immobility. We determined these 2 factors must be present to consider pharmacologic prophylaxis. Mobility has a range of definitions posing a challenge to identify an accurate standard. American College of Chest Physicians guidelines (9th edition) support thromboprophylaxis of chronically immobilized patients (defined by Robinson as >30 days) in postacute or subacute situations, given similar VTE incidence compared with acutely ill hospitalized patients. For clarity, we identified acutely "nonambulatory" or chronically nonambulatory patients with decreased range of motion from baseline and unable to do passive range of motion exercises as candidates for thromboprophylaxis. Patients who are chronically nonambulatory but at baseline during hospitalization did not meet criteria for VTE thromboprophylaxis consideration for immobility.

Several pediatric populations have been previously described to have increased VTE risk. Patients with diabetic ketoacidosis or sickle cell anemia and a CVL are at increased VTE risk.10-12 Two small case series demonstrated increased VTE risk in patients with cystic fibrosis (CF) and *Burkholderia cepacia*.13,14 The risk of VTE in patients with inflammatory bowel disease (IBD) is 3 times that of the general population; approximately two-thirds of IBD-associated VTE occurs during active flares of disease.15 Patients with congenital heart disease involving dilated cardiomyopathy, atrial fibrillation, single-ventricle pathology, and/or palliative surgical shunts have higher VTE incidence.16,17 Certain patients are at high risk for VTE regardless of CVL presence and immobility. These include acute spinal cord injury 24 hours postinjury without plan for surgical intervention or 24 hours postsurgery, traumatic brain injury with stable computed tomography of the head, and 48 hours postprocedure and 72 hours postinjury and patients 48 hours after major surgery.

**Prophylaxis Modalities and Contraindications**

Literature review recommends intermittent pneumatic compression devices during wakeful nonambulatory periods. Graduated compression stockings are less efficacious than intermittent pneumatic compression devices.20 Selecting the appropriate graduated compression stocking size for a pediatric population is challenging, and erroneous sizing can result in skin damage and increase VTE risk.21 For pharmacologic prophylaxis, we use enoxaparin. For patients <60 kg, we use 0.5 mg/kg per dose subcutaneous twice daily.22 For patients >60 kg, we use 30 mg subcutaneous twice daily or 40 mg subcutaneous once daily.

We determined contraindications (Table 1) by reviewing established contraindications (eg, active bleeding), adult guidelines in our health system, and consensus opinion with the divisions mentioned previously. We also reviewed American Society of Regional Anesthesia and Pain Medicine 2010 guidelines regarding regional anesthesia and enoxaparin.

**Adverse Events**

All medication-related adverse events, including enoxaparin, are reviewed in a standard process. Adverse bleeding was defined via International Society of Thrombosis and Haemostasis major bleeding criteria,24 and minor bleeding was defined as any overt bleeding not fulfilling major bleeding criteria but requiring intervention or physician notification.

**Final Risk-Stratification**

We used a logistic regression model previously published that evaluated risk factors in a retrospective case-control study of VTE at our institution.2 Subanalyses of adolescents showed retained significance of risk factors.2 Tier 1 risk factors were identified through bivariate analyses and retained significance in a multivariable logistic regression model: immobilization ≥72 hours, estrogen therapy, and length of stay ≥7 days. Tier 2 risk factors were significant by bivariate analyses but did not retain significance in the multivariable model: bacteremia, BMI >85th percentile, chronic TPN, initial ICU admission,
TABLE 1 Contraindications to Thromboprophylaxis

<table>
<thead>
<tr>
<th>Mechanical thromboprophylaxis</th>
<th>1. Bilateral amputee</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2. Bilateral lower extremity trauma or medical issue</td>
</tr>
<tr>
<td></td>
<td>3. Peripheral arterial insufficiency</td>
</tr>
<tr>
<td>Pharmacologic thromboprophylaxis</td>
<td>1. Anesthesia/analgesia (neuraxial), single dose within past 24 h</td>
</tr>
<tr>
<td></td>
<td>2. Anesthesia/analgesia (neuraxial), within past 6 h</td>
</tr>
<tr>
<td></td>
<td>3. Anticoagulated</td>
</tr>
<tr>
<td></td>
<td>4. Aspirin or other irreversible platelet inhibitor within past 7 d</td>
</tr>
<tr>
<td></td>
<td>5. AVM, aneurysm, CNS mass, Moyamoya</td>
</tr>
<tr>
<td></td>
<td>6. Bleeding (active, major) requiring transfusion, bleeding into vital organ, hemodynamic instability</td>
</tr>
<tr>
<td></td>
<td>7. Bleeding disorder/tendency or history of unexplained or spontaneous hemorrhage</td>
</tr>
<tr>
<td></td>
<td>8. Blood pressure (increased): SBP or DBP greater than 95th percentile for age, height, gender</td>
</tr>
<tr>
<td></td>
<td>9. Catheter placement (indwelling) epidural/spinala</td>
</tr>
<tr>
<td></td>
<td>10. Catheter removal epidural/spinal within past 2 h</td>
</tr>
<tr>
<td></td>
<td>11. Coagulopathy: INR $&gt;$1.5, aPTT $&gt;$44 s, platelet count $&lt;$50,000/mm$^3$, or fibrinogen $&lt;$100 g/dL</td>
</tr>
<tr>
<td></td>
<td>12. Comfort measures only</td>
</tr>
<tr>
<td></td>
<td>13. HIT history</td>
</tr>
<tr>
<td></td>
<td>14. Hepatic disease without known INR</td>
</tr>
<tr>
<td></td>
<td>15. Neurosurgery, head trauma within 3 d</td>
</tr>
<tr>
<td></td>
<td>16. Spinal hematoma or spinal stabilization surgery within past 24 h</td>
</tr>
</tbody>
</table>

aPTh partial thromboplastin time; AVM, arteriovenous malformation; CNS, central nervous system; DBP, diastolic blood pressure; HIT, heparin-induced thrombocytopenia; INR, international normalized ratio; SBP, systolic blood pressure.

<For twice-daily enoxaparin dosing.
<For once-daily enoxaparin dosing.

**Implementation**

We created 3 risk groups: high, moderate, and low with a stratification algorithm and thromboprophylaxis recommendations (Fig 1). Guidelines were first implemented in the EMR by using an order set. Specific risk factors were displayed in plain text. Although this solution supported thromboprophylaxis orders, it did not support risk category documentation. Thus, a more integrated tool was developed that captured risk category and applied logic rules to support the algorithm (Fig 1).

Providers are presented the screening form at time of patient admission, with an option to defer for 24 hours if the admitting provider does not have enough information to make an accurate risk assessment. The provider selects risk factors and contraindications. Logic rules from the algorithm are applied by the EMR and present the risk category and specific prophylaxis recommendations. The provider can select the recommended prophylaxis orders. This tool was implemented on August 9, 2013. Rates of screening were tracked by querying the EMR for the number of qualified admissions per month, number of risk assessment forms completed, associated risk categories, and orders for prophylaxis interventions. This review is an ongoing, monthly process with the goal of increasing screening rates to $\approx$90%.

**RESULTS**

**Implementation Outcomes**

The study period was defined as the first 17 months of EMR tool use. During this time, 149 qualified patients, on average, were admitted each month and an average of 69.1% were screened. Figure 2 shows screening rates of qualified admissions. The first month rate was 48% and increased to 81% in the last month. Figure 3 shows the screened populations’ risk category distribution.

Overall, physician orders for mechanical and pharmacologic prophylaxis increased in the screened population; however, not all physician orders correlated with the suggestions from the EMR tool. After reconfiguring the report, data on VTE prophylaxis orders were captured for the last 12 months of the study period. On average, 10.4 patients per month were screened as moderate risk but 27.3 patients per month received sequential compression devices (SCDs). This suggests SCDs were ordered for patients not screened using the VTE risk assessment tool but met other criteria per provider discretion. Regarding pharmacologic prophylaxis, the average number of high-risk patients per month (2.4) approximately correlated with the average number of patients per month who were screened and received enoxaparin (2.1). No major or minor adverse bleeding events related to enoxaparin have been reported to date, although the rate of enoxaparin use was low.

In the first year after implementing the EMR screening tool, none of the screened patients developed a VTE. In the 12 months before implementation, there were 8 patients who developed a VTE, 3 of whom were between 12 and 17 years and would have been identified as high risk by the EMR tool. During the first 12 months after implementation, 6 patients developed a VTE but all were $<$12 years old and therefore not screened.

**DISCUSSION**

The objective was to create and implement VTE screening and prophylaxis guidelines for hospitalized patients 12 to 17 years. Our results demonstrate successful guideline development and implementation in a tertiary care children’s hospital. Interval improvements continue as part of ongoing optimization of the screening tool to increase provider utilization. The 2012 Chest guidelines do not address pediatric risk categorization, except for long-term TPN, hemodialysis, perioperative...
management in specific surgical diseases (eg, cardiac defects), and some acquired defects (eg, coronary artery aneurysm in Kawasaki disease). Children's Hospital of Philadelphia published guidelines for adolescents with 14 years as a cutoff and required altered mobility and presence of 1 other risk factor for pharmacologic prophylaxis consideration. Our guidelines differed in using logistic regression to evaluate the relative strength of risk factors. Another key difference was CVL as an additional prerequisite for pharmacologic thromboprophylaxis. This additional step created a more tiered risk-stratification to prevent overutilization of enoxaparin.

Challenges to guideline adoption are well demonstrated. A recent study evaluating thromboprophylaxis in the PICU found utilization was different than recommendations by institutional guidelines. The authors suggest multiple reasons, but foremost was lack of evidence of efficacy and underestimation of VTE risk in pediatrics. In acknowledgment of these issues, the screening tool is optional and staff were educated periodically to increase awareness about incidence and risk of VTE.

We recognize limitations to our study. First, the guidelines target adolescents and may not be generalizable to other high-risk patient cohorts (eg, neonates). Second, there is existing debate regarding known VTE risk factors, such as mobility and CVL, making it difficult to reach consensus for guideline definition. The definition of immobility for patients who are chronically nonambulatory was vexed by minimal scientific data. We excluded those able to receive physical therapy, but there is conflicting evidence regarding whether passive physical therapy reduces VTE incidence. Multiple studies cite CVL as

---

**FIGURE 1** VTE risk assessment and prophylaxis algorithm. ASCI, acute spinal cord injury; EVD, external ventricular drain; hx, history; ICP, intracranial pressure; LOS, length of stay; MI, myocardial infarction; PNS, pediatric neurosurgery; TBI, traumatic brain injury. Dilated cardiomyopathy, atrial fibrillation, single ventricle pathology, and palliative surgical shunts.
the most significant VTE risk factor, but previous research on pharmacologic prophylaxis for pediatric patients with CVL has not consistently shown benefit. However, many of these studies used pharmacologic prophylaxis in restricted patient populations (e.g., cancer29 or infants after cardiac surgery30), with 1 broad-based trial (Prophylaxis of Thromboembolism in Kids Trial [PROTEKT]) closed prematurely due to poor accrual and lack of benefit.31 It remains to be seen whether broad-based VTE prophylaxis programs will demonstrate benefit for VTE (CVL-related or not), but early evidence suggests potential.32 Third, due to VTE complexity, not all high-risk conditions, such as nephrotic syndrome, were integrated into the initial guideline and updating is required. Last, we included tier 2 risk factors despite lack of significance in our own single-institution multivariate analysis.3 Other pediatric and adult studies have shown significance of these factors.35 Including these risk factors allowed for more accurate risk stratification. Therefore, we required presence of at least 2 to prevent overemphasis and overutilization of pharmacologic prophylaxis. Finally, the optional completion of the screening tool inhibits reliability of the screening process. Additionally, the ability of the EMR to prompt VTE rescreening later in hospitalization is being addressed to optimize compliance.
These EMR optimizations will enhance accuracy of the data captured and improve reliability of the guidelines and EMR tool. Future review will assess the impact of these changes, evaluate VTE incidence and safety events, and incorporate future feedback from providers to continue to reach our goal of 90% screening. Further studies are needed to evaluate the relative value of VTE screening and prophylaxis in preventing VTE in hospitalized adolescents. As more hospitals develop and implement VTE screening tools, the resulting aggregate data will help facilitate larger scale, multisite studies to truly evaluate the efficacy of VTE screening and prophylaxis interventions.

**REFERENCES**


