JPPT | Single-Center Retrospective Study

Optimization of Thromboprophylaxis Use in Hospitalized Pediatric Patients Through Implementation of a Venous Thromboembolism Risk Assessment Tool

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OBJECTIVE Venous thromboembolism (VTE) is a leading cause of hospital-acquired morbidity for pediatric patients. Pharmacological thromboprophylaxis increases the risk of adverse events such as bleeding complications. There exists a need for a universal VTE risk assessment tool to aid in thromboprophylaxis prescribing while minimizing the risk of adverse events. The objective of this study is to investigate if implementation of a VTE risk assessment tool is associated with a change in the rate of thromboprophylaxis prescribing.

METHODS This retrospective study evaluated the change in thromboprophylaxis prescribing pre and post implementation of a VTE risk assessment tool. Patients were excluded if they were pregnant, diagnosed with VTE ≤48 hours of admission, presented with VTE symptoms, or if they were diagnosed with multisystem inflammatory syndrome in children (MIS-C) or coronavirus disease (COVID-19).

RESULTS A total of 186 pediatric patients were included in this study. Thromboprophylaxis was prescribed in 16/93 (17.12%) and 75/93 (80.6%) patients in the pre- and post-implementation group, respectively (95% CI, 0.523–0.745; $p < 0.001$). No VTE events occurred in either group. Bleeding complications occurred in 3.2% and 7.5% of patients in the pre- and post-implementation groups, respectively. The risk tool was used in 80.6% of patients; providers used the tool correctly in 48% of patients and incorrectly in 52% of patients.

CONCLUSION Implementation of a VTE risk assessment tool was associated with a statistically significant change in the rate of thromboprophylaxis prescribing. Incorrect use may be minimized by providing provider reeducation and making modifications to the order set.

ABBREVIATIONS BMI, body mass index; COVID-19, coronavirus disease; MIS-C; multisystem inflammatory syndrome in children; VTE, venous thromboembolism

KEYWORDS anticoagulants; pediatrics; pharmacy; retrospective studies; risk assessment; risk factors; venous thromboembolism

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Introduction

Venous thromboembolism (VTE) includes both deep vein thrombosis and pulmonary embolism.[1] VTE events have a bimodal peak within the pediatric population with the first peak occurring in early infancy and a second peak occurring during adolescence.[2,3] Adolescent VTE accounts for ~50% of all pediatric events.[3] Many risk factors for VTE have been identified with the most common being the presence of a central venous catheter.[2] Other risk factors include exogenous estrogen, immobility, inflammatory disease, trauma, obesity, and prior VTE, among others.[1] Thromboprophylaxis consists of both pharmacological and non-pharmacological methods. Non-pharmacological methods include early ambulation and mechanical prophylaxis using sequential compression devices. Pharmacological prophylaxis includes the use of anticoagulants such as unfractionated heparin and low-molecular-weight heparins. The use of pharmacological prophylaxis increases the risk of adverse events such as bleeding complications, and universal use of pharmacological thromboprophylaxis in pediatrics is not recommended.[1]

The incidence of VTE within the pediatric population is estimated to be 0.07 to 0.14 per 10,000 children.[2] Although this incidence is very low, it dramatically increases to ~58 per 10,000 children with hospitalized pediatric patients.[2] Additionally, VTE has been found to be a leading cause of hospital-acquired morbidity within the pediatric population.[1,3] VTE events also increase hospital costs, length of stay, and may lead to patient death.[1,3] Risk assessment tools have been previously published, although there is lack of evidence on the

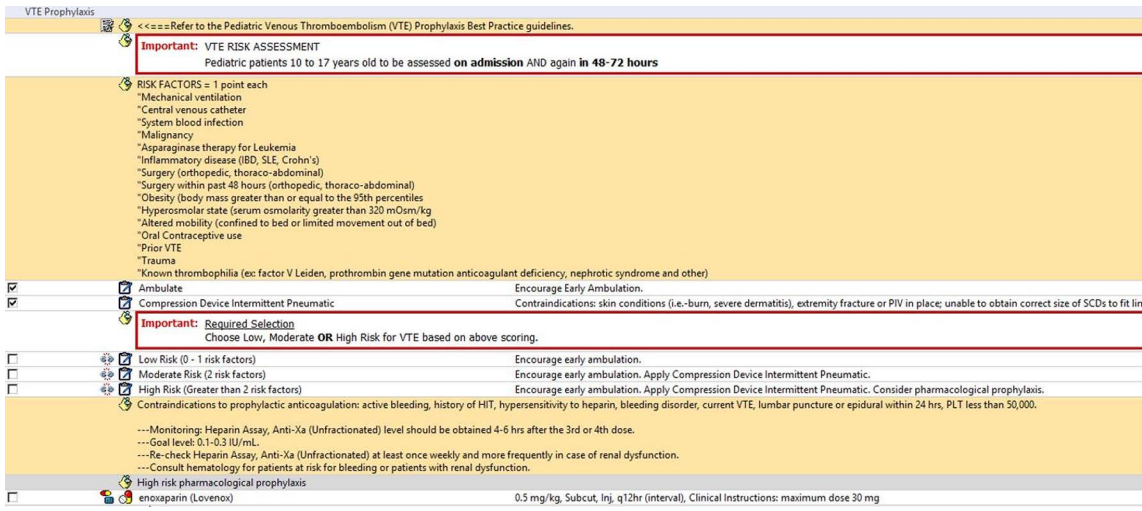
right approach to prevent VTE events in the pediatric population.[1] In a 2020 study, Jaffray et al[4] used a risk assessment model to retrospectively review pediatric cases of hospital-acquired VTE (n = 728) compared with controls (n = 839).[4] They identified many significant risk factors, using the model, and concluded that future validation of the tool could identify those at low risk and high risk and assist in guiding thromboprophylaxis.[4] Many tools are extrapolated from adult studies. In a 2018 study, Park et al[5] studied medical (n = 110) and surgical (n = 124) adult patients pre and post implementation of a risk assessment tool. They found increased rates of thromboprophylaxis prescribing after implementation of the risk assessment tool as well as an overall decrease in VTE events.[5] Because data are lacking within the pediatric population, there exists a need for the development and validation of a universal VTE risk assessment tool to identify patients at high risk for VTE development while decreasing the risk of adverse effects from pharmacological thromboprophylaxis administration. The goal of this study was to assess if implementation of a VTE risk assessment tool was associated with a change in the rate of thromboprophylaxis prescribing pre and post implementation.

Materials and Methods

In March 2019, St. Joseph's Children's Hospital in Tampa, Florida, implemented a VTE risk assessment tool (Figure). The tool was first piloted in the pediatric intensive care unit and was further expanded to our general pediatric floors in January 2021. Prior to creating the tool as part of our admission order set, a VTE risk assessment guideline was developed by our hematology/oncology physicians and pharmacist. The guideline was then taken to various pediatric subspecialty groups and hospital quality groups to finalize the content prior to being published within the hospital system. After publishing the guideline, a monthly meeting was commenced to create and implement the order set within our electronic medical record. The meeting now occurs quarterly to monitor use and obtain feedback from providers. Most providers have reported that the tool is straightforward and easy to use. Education on the risk tool and guideline was distributed to team members via lecture presentations during committee group and physician specialty group meetings, and via distribution of printed materials. Printed materials included the VTE Risk Assessment Guideline and a Cerner Job Aid to assist in use of the risk assessment tool. These printed materials are available on the hospital intranet and were sent out to providers via email communication.

This was a retrospective chart review of patients admitted to St. Joseph's Children's Hospital from January 2019 to December 2021. Patients screened between January 2019 and December 2020 were included in the pre-implementation group, while patients screened between January 2021 and December 2021 were included in the post-implementation group. Patients were included in the study if they were admitted to a general pediatric floor within the predefined study period and if they were 10 to 17 years of age. Patients were not included if they were admitted to an intensive care unit. This age range used for inclusion, 10 to 17 years, has been identified as the peak age for incidence of VTE in pediatrics.[2,3] The VTE risk assessment tool was only available to order for patients within this specific age range in our electronic medical record system. Patients were excluded from the study if they presented with VTE symptoms at admission or were diagnosed with

Figure. Facility VTE Risk Assessment Tool.



VTE, venous thromboembolism.

VTE within 48 hours of admission. Further, patients were excluded if they had coronavirus disease (COVID-19), multisystem inflammatory syndrome in children (MIS-C), or if they were pregnant.

Patients were assessed for VTE risk factors upon hospital admission by their providers and were placed into either low, moderate, or high-risk levels for VTE. Based on the assigned risk level, recommendations for thromboprophylaxis orders were available to providers. Early ambulation was recommended for low risk (0–1 risk factors). Early ambulation plus mechanical prophylaxis was recommended for moderate risk (2 risk factors). Lastly, the high-risk category (≥3 risk factors) recommended early ambulation, mechanical prophylaxis, and pharmacological prophylaxis (if appropriate). Providers were encouraged to reassess patients when risk factors changed and at least weekly. The VTE risk assessment tool was ordered as part of the pediatric admission order set although it was up to the providers' discretion to use this order set.

The primary outcome of this study was to determine if implementation of a VTE risk assessment tool was associated with a change in the rate of VTE thromboprophylaxis prescribing, including early ambulation, mechanical prophylaxis, and pharmacological prophylaxis. Secondary objectives included the incidence of VTE events and bleeding complications, assessing appropriate provider use of the risk assessment tool, and determining if those receiving pharmacological prophylaxis were being monitored appropriately. Appropriate provider use of the tool was determined by reviewing if a risk category was selected and if the correct thromboprophylaxis orders were selected, based on the physician-selected risk category. Correct monitoring consisted of a baseline complete blood count and basic metabolic panel, and anti-Xa concentrations drawn after the third or fourth dose of enoxaparin. Mobility was assessed by using the Braden Q Assessment.[6] The Braden Q Assessment is a tool designed to assess pediatric patients for risk of pressure ulcers. A patient's mobility is one component of the tool and hospitalized patients are routinely assessed upon admission. Patients are placed into one of the following mobility categories: completely immobile, very limited, slightly limited, or no limitations in mobility. Those scored as very limited or completely immobile were classified as having altered mobility. Oral contraceptive use was determined by reviewing home medication lists, and not necessarily whether patients continued receiving therapy once admitted to the hospital. Patient charts, previous diagnoses, and clinical notes were reviewed for identification of prior VTE, malignancy, inflammatory diseases, and known thrombophilia. Patients were documented as having surgery if they underwent any type of surgical procedure. Obesity was identified in patients with a body mass ≥95th percentile. Body mass was determined by using pediatric growth charts and the body mass index formula (BMI = kg/m^2). Serum osmolarity was reviewed as part of the VTE risk assessment tool because a hyperosmolar state can increase the risk of developing a VTE. Hyperosmolar state was defined as a serum osmolarity >320 mOsmol/L and was calculated with the patient's baseline laboratory test results, using a serum osmolarity calculator.

Statistical analysis was completed with the MiniTab 18 software and Microsoft Excel. A two-proportions test was used to calculate a sample size of 186 patients (93 per group) to detect a 20% difference with 80% power. A p value of 0.05 was used to determine statistical significance for all hypothesis testing. Categorical data were analyzed by using the chi-square test or Fisher exact test as appropriate. Continuous data were analyzed by using a *t* test and descriptive statistics were used for all other reported data points.

Results

A total of 186 pediatric patients were included in the primary analysis of this study. Ninety-three patients were included in both the pre- and post-implementation groups. Owing to the time constraints of this project, not all patients admitted between the prespecified study period were included in the analysis. A random number generator was used to identify a random list of patients and data were collected until 93 patients were included in each study group. A total of 207 patients were screened for inclusion in the study. Ninety-nine patients were included in the pre-implementation group with 2 patients excluded for COVID-19 diagnosis, 1 patient excluded for MIS-C diagnosis, 1 patient excluded for pregnancy, and 3 patients excluded for VTE at admission. One hundred eight patients were included in the post-implementation group with 10 excluded for COVID-19 diagnosis, 1 excluded for MIS-C diagnosis, and 3 excluded for prior VTE at admission. This led to 93 patients included in the pre-implementation group and 93 patients included in the post-implementation group (Supplemental Figure).

Baseline characteristics were equally balanced between the 2 groups except for female sex with a higher percentage within the post-implementation group (47.3% versus 62.4%; p = 0.037). The post-implementation group had more cases of obesity (22.6% versus 24.7%; p = 0.730), central line presence (3.2% versus 8.6%; p = 0.212), and malignancy (2.2% versus 4.3%; p = 0.682) than the pre-implementation group, although these were not considered statistically significant (Table).

The primary outcome of thromboprophylaxis prescribing was identified in 16 (17.2%) patients in the pre-implementation group and 75 (80.6%) patients in the post-implementation group, identifying a 63.4% prescribing difference (95% CI, 0.523–0.754; p < 0.001). The pre-implementation group had 15 cases of early ambulation orders and 1 case of mechanical prophylaxis orders, while the post-implementation group had 75 cases of early ambulation orders and 34 cases of

Table. Baseline Characteristics

	Pre-Implementation Group (N = 93)	Post-Implementation Group (N = 93)	p Value
Female, n (%)	44 (47.3)	58 (62.4)	0.037
Age, mean, yr	13.89	14.29	0.211
Obesity, n (%)	21 (22.6)	23 (24.7)	0.730
Surgery, n (%)	26 (28)	23 (24.7)	0.617
Prior VTE, n (%)	1 (1.1)	1 (1.1)	1.000
Central Line, n (%)	3 (3.2)	8 (8.6)	0.212
Malignancy, n (%)	2 (2.2)	4 (4.3)	0.682

VTE, venous thromboembolism

mechanical prophylaxis orders. Neither group had any pharmacological thromboprophylaxis orders. No patients in either group developed a new VTE event. Three (3.2%) patients in the pre-implementation group and 7 (7.5%) patients in the post-implementation group had bleeding events, although none of these bleeding events were due to pharmacological prophylaxis, as neither group had pharmacological thromboprophylaxis orders. Bleeding events included menorrhagia, hematuria, post-cardiac surgery bleeding, and a hemorrhagic ovarian cyst.

Overall, in the post-implementation group 75 (80.6%) patients had the VTE risk scoring tool ordered, while 18 (19.4%) did not. Of the 80.6% of patients who had the VTE risk tool ordered, 48% of patients had the tool used correctly, while 52% had the tool used incorrectly. Reasons for incorrect use included no selection of a risk category with thromboprophylaxis orders (35.9%), incorrect thromboprophylaxis orders based on the risk category selected (46.2%), and no thromboprophylaxis orders although a risk category was selected (17.9%).

Further, risk category selected was compared with scoring by the authors during our retrospective chart review. There were 11 cases in which our retrospective categorization differed from the provider-selected risk category in the patient medical record. In 7 cases, retrospective review identified more risk factors (higher risk category) than the provider selection, while in 4 cases fewer risk factors were identified (lower risk category) than with the provider selection. There were 2 cases where retrospective review identified patients eligible for pharmacological prophylaxis, although no pharmacological prophylaxis orders were placed. In the first case, 3 risk factors were retrospectively identified including presence of a central line, surgery, and obesity. The provider assessed the patient as low risk and thus only early ambulation was ordered for this patient. In the second case, 4 risk factors were identified including presence of a central line, malignancy, surgery, and obesity. The patient was admitted under observation for surgical wound debridement and was discharged the following day. The patient was classified as low risk and no thromboprophylaxis orders were placed for this patient.

Discussion

In our single center retrospective study, implementation of a VTE risk assessment tool led to a statistically significant increase in thromboprophylaxis prescribing. There were no cases of VTE events, and all bleeding complications reported were not due to pharmacological thromboprophylaxis, although these results may be limited by our small patient population. The risk tool was used in 80.6% of patients and thus, we could not assess use of the VTE risk assessment tool in 19.4% of patents in the post-implementation group. Incorrect use of the VTE risk assessment tool occurred in 52% of patients in the post-implementation group. Reasons for incorrect use included omission of a risk category, thromboprophylaxis orders that did not match the selected risk category, and omission of thromboprophylaxis orders with selection of a risk category. When assessing this information, it was identified that the design of the tool could have increased the likelihood of these errors. Owing to the limitations of the electronic medical record system, 2 thromboprophylaxis orders were preselected within the order set (early ambulation and mechanical prophylaxis). Therefore, providers who selected the low-risk category would have to intentionally remove the mechanical prophylaxis orders. This could have led to the mismatch between the risk category selected and the thromboprophylaxis orders. In addition, when entering the order set, risk-category selection can be bypassed. Thus, if the risk category was not selected, these preselected orders would still be placed for the patient. This may have been the cause of patients having thromboprophylaxis orders without a selected risk category.

Although no patients received pharmacological prophylaxis, the preferred agent at our institution is

low-molecular-weight heparin. If a patient were to qualify for pharmacological thromboprophylaxis, enoxaparin 0.5 mg/kg/dose subcutaneously twice daily is initiated. Currently, our order set places the maximum dose at 30 mg twice daily, although this maximum dose varies on the basis of providers' discretion and patient-specific factors (e.g., obesity). Monitoring at our institution includes a baseline complete blood count and basic metabolic panel, and anti-Xa concentrations. Anti-Xa concentrations are obtained 4 to 6 hours after the third or fourth dose with a recommended range of 0.1 to 0.3 units/mL.

There are several limitations to our study. First, the design of the risk assessment tool order set within the electronic medical record as discussed above. Another limitation of this study was the small sample size and time constraints of completing the project. Because this was only a year-long project, the number of patients able to be assessed was limited. Thus, not all patients admitted during the prespecified study period were assessed and a random selection of 186 patients was included within the analysis. The small study population could also be the reason there were no differences in VTE events or bleeding complications in either group. The retrospective single center study design also limited the generalizability of the results. In addition, the retrospective chart review design makes it difficult to assess all patient risk factors because there may be information omitted within the patient chart, making room for error when comparing the retrospective risk assessment with the providers' risk category selection.

The results of this study have identified areas of improvement for the risk assessment tool order set. Because the tool was not used for ~19.4% of patients, reeducation may lead to an increase in the use of the tool on admission and may increase the rates of thromboprophylaxis prescribing. Our electronic medical record system limited the build of the order set and preselection of 2 orders was required (early ambulation and mechanical prophylaxis). One recommendation we can make with the tool is to rebuild the order set to remove the preselection of orders. In addition, by reformatting the order set to require selection of a risk category and linking the associated thromboprophylaxis orders, omissions would be prevented.

Conclusion

In conclusion, this retrospective chart review of implementation of a VTE risk assessment tool was associated with a statistically significant change in the rate of thromboprophylaxis prescribing. Although incorrect use of the tool was identified, by providing provider reeducation and making modifications to the order set, incorrect use can be minimized. Further studies with a larger patient population are needed to assess the change in VTE and bleeding risk with implementation of a VTE risk assessment tool in the pediatric population.

Article Information

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Ethical Approval and Informed Consent. Given the nature of this study, institutional review board/ethics committee review and informed consent were not required.

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