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Venous thromboembolic events: How low can you go?

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ABSTRACT

Background: We evaluated postoperative venous thromboembolism (VTE) chemical prophylaxis adherence to assess the preventability of VTEs.
Methods: A case-control study was performed using the 2011–2015 ACS-NSQIP single institution database. Cases were identified as patients who experienced postoperative VTE within 30 days following surgery. Controls were matched 2:1 on procedure, age, and BMI. Association between inpatient chemical prophylaxis adherence and postoperative VTE was evaluated with conditional logistic regression.
Results: Seventy-three cases were matched to 145 controls. Complete inpatient VTE chemical prophylaxis adherence did not differ between cases and controls (45.2% vs. 46.2%, p = 1.00). Odds of postoperative VTE increased if a patient's prophylaxis was interrupted (OR 6.34, 95% CI 1.82–22.13). However, 53.7% of instances of interrupted prophylaxis were medically justified by concern for bleeding, spine operation, or for additional upcoming procedure.
Conclusions: Nearly half of patients who experienced postoperative VTEs received appropriate guideline-driven care. Most interruptions in chemical prophylaxis were justified medically. This further questions the preventability of postoperative VTEs and the utility of this outcome as a valid measure of hospital quality.

1. Introduction

Postoperative venous thromboembolisms (VTEs) represent a major "preventable" complication with substantial cost to patients and healthcare systems.[1] In 2008, the Centers for Medicare and Medicaid Services (CMS) initiated a non-payment policy for hospital-acquired VTEs. Appropriate administration of mechanical and chemical prophylaxis can decrease VTEs in certain patient populations, and current recommendations include establishing preoperative risk and prescribing appropriate prophylaxis ranging from early ambulation to 30 days of chemical prophylaxis.[2] However, recent research has shown that some patients experience postoperative VTEs despite risk-appropriate prophylaxis.[3] In addition, the rate of postoperative VTEs remains largely unchanged even when the dose and duration of chemical prophylaxis are increased.[4]

As part of the Surgical Care Improvement Project (SCIP), VTE prophylaxis within the 24 h surrounding surgery was assessed as marker of hospital quality. However, there was no association between this measure and reduced VTE outcomes, and this SCIP measure was discontinued in 2015.[5] Whether adherence to VTE prophylaxis throughout the inpatient postoperative period is associated with VTE occurrence is less well described. Currently, the rate of hospital acquired "potentially-preventable" VTEs, defined as the proportion of patients with VTEs who did not receive VTE prophylaxis between date of admission and VTE diagnosis, is publically reported.

The Caprini score is a validated tool that assesses patient-specific risk factors for VTE and stratifies patients to appropriate prophylactic regimens. The need to include additional risk factors in the Caprini score, such as emergent surgery or multiple surgeries, has been proposed and warrants further investigation.[6] When prescribing postoperative chemical prophylaxis, delay in initiation of prophylaxis and prophylaxis that is started but interrupted should be avoided whenever possible. However, chemical prophylaxis is held in surgical patients for many reasons including concern for bleeding and additional procedures.[7–10] For most of these reasons there are no guidelines regarding when to withhold chemical prophylaxis or when it is safe to resume. Instead, the

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decision requires clinical risk-benefit assessment.

Despite risk-stratified, guideline-driven chemical prophylaxis, VTEs still occur, especially in high-risk patient populations. Therefore, the actual preventability of postoperative VTEs needs to be reassessed. Our aim is to evaluate adherence to inpatient chemical VTE prophylaxis and the association with VTE occurrence.

2. Materials and methods

2.1. Study population

Using the 2011–2015 American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) single-institution database, we identified all patients who experienced postoperative VTE within 30 days of surgery. The study was limited to a single institution because access to hospital records was necessary to perform the chart review portion of this study. Cases were excluded if chart review revealed VTE was present on admission. Controls were defined as patients without evidence of VTE within 30 days following surgery and matched 2:1 on Current Procedural Terminology (CPT) codes, age within 8 years, and BMI within 8 kg/m.[2] Matching was performed due to the constraints of chart review.

2.2. Study variables

Patient and procedural factors were obtained from the ACS-NSQIP database and electronic medical record (EMR). Three individuals collected this information by an electronic medical record extraction using information from the date closest to the upcoming surgery and by manual chart review. Data was entered into a secure database to ensure consistency. A Caprini score was calculated for each patient from information obtained during the patient's preoperative anesthesia clinic visit and nursing intake form on the day of surgery. The Caprini score is a well-validated tool to assess postoperative VTE risk and shown to significantly correspond to incidences of postoperative VTEs especially among critically ill and high-risk patients.[11–13] VTE chemical prophylaxis administration records, reasons for missed doses, and characteristics of VTEs including location and association with central venous catheter were obtained from chart abstraction. For the purposes of this analysis, postoperative length of stay was defined as the number of inpatient hospital days from day of surgery to day of VTE diagnosis for cases where VTE was diagnosed prior to hospital discharge and from day of surgery to day of discharge for cases where VTE was diagnosed after discharge as well as for controls.

Compliance with chemical prophylaxis was considered complete if the patient received appropriate prophylactic doses on each postoperative inpatient day until discharge. Missed prophylactic doses were considered delayed if chemical prophylaxis was not started within 24 h of surgery and considered interrupted if chemical prophylaxis was initiated but then held at a later date. Reasons for missed doses were categorized as concern for bleeding, spine surgery, upcoming procedure (operative, radiologic, endoscopic, or other), epidural catheter removal, patient refusal, physician error, and unknown. Physician error encompassed ordering errors where chemical prophylaxis was started a day later than intended due to how it was ordered. The reason was classified as unknown when the reason was not documented in the medication administration record or physician note. For epidural catheters, current recommendations include starting VTE prophylaxis 2 h following removal.[14] Failure to comply with this recommendation along with patient refusal, physician error, and unknown reasons were defined as without medical justification. Although unknown reasons may have been considered medically justified and simply not documented, categorizing them as without medical justification biases towards the null.

2.3. Statistical analysis

Results were analyzed at the matched case-control and procedural levels. Characteristics of cases and controls were compared using Test of Symmetry and paired *t*-test for categorical and continuous variables, respectively. A conditional logistic regression model including Caprini score, prophylaxis compliance, postoperative length of stay, additional surgeries, and emergent surgery was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the association with postoperative VTE. Statistical significance was determined using a 2-sided alpha-level of 0.05. R (version 3.2.3) was used to match cases and controls, and SAS 9.4 (SAS Institute Inc., Cary, NC) software was used for all other analyses.

3. Results

3.1. Patient characteristics

We identified 83 patients with postoperative VTEs of which 73 (86.9%) were successfully matched to 145 controls for a total of 218 patients. There were 10,377 cases evaluated by NSQIP at our single institution between 2011 and 2015, resulting in a VTE incidence rate at our institution of 0.97%. This is higher than the overall VTE incidence rate of 0.80% previously reported.[15]

Patient characteristics within case and control groups are outlined in Table 1. Overall, cases with VTE were more likely to have a higher Caprini score (6.9 vs. 6.5; $p = 0.036$) and more likely to have undergone additional surgeries within 30 days following the index operation (0.5 vs. 0.2; $p < 0.001$). Cases were also more likely to have a longer length of postoperative hospital stay (14.4 days vs. 6.6 days; $p < 0.001$). Other variables including age, sex, race, BMI, surgical specialty, emergency surgery, and prophylaxis type were not significantly different between cases and controls. Of the 73 cases of VTE, 48 (67.7%) were diagnosed before discharge and 25 (34.3%) were diagnosed after discharge. Of those diagnosed after discharge, the average time to diagnosis was 17.5 days after surgery.

3.2. Chemical prophylaxis

The majority of patients (86.5%) received Enoxaparin for VTE chemical prophylaxis with a smaller number (10.3%) receiving subcutaneous Heparin or combination (2.7%). The doses and frequency for Enoxaparin ranged from 30 mg to 40 mg daily to twice daily. The dose of subcutaneous Heparin was 5,000 mg and frequency ranged from twice to three times daily. Forty five percent of cases had complete VTE chemical prophylaxis, which was not significantly different between cases and controls (45.2% vs. 46.2%; $p = 1.000$). Of the 55.1% case and control patients who missed at least one dose of chemical prophylaxis, 47.7% had a delay in initiation compared to 13.7% whose prophylaxis was started on time but was interrupted later. Sixteen patients (7.3%) had both a delay and interruption of their prophylaxis. Controls were more likely to have a delay in initiation of prophylaxis (53.8% vs. 35.6%; $p < 0.001$), and cases were more likely to have prophylaxis interrupted (27.4% vs. 6.9%; $p < 0.001$). Among patients with postoperative VTE, the number of days with missing prophylaxis was low: 1 day (24.6%), 2–3 days (19.2%), and 4 + days (11.0%).

The reasons that patients missed a dose of chemical prophylaxis are described in Fig. 1. The most common reason overall was unknown (19.3% overall with 23.3% and 17.2% for cases and controls, respectively). Patients with VTE were more likely to have missed at