Is Development of Postoperative Venous Thromboembolism Related to Thromboprophylaxis Use? A Case-Control Study in the Veterans Health Administration

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Abstract

**Background:** Observational studies continue to report thromboprophylaxis underuse for postoperative pulmonary embolism/deep vein thrombosis (pPE/DVT) despite long-standing prevention guidelines. These gaps in care have led to introduction of performance measures addressing thromboprophylaxis use, plus CMS non-payment for pPE/DVTs following joint replacements. However, data are limited on whether thromboprophylaxis use differs between patients developing pPE/DVT versus those who don’t, or why prophylaxis is withheld. We investigated these questions in the Veterans Health Administration (VA).

**Methods:** Using 2002-2007 data from 28 VA hospitals, we screened administrative data for discharges with 1)pPE/DVT as flagged by the AHRQ Patient Safety Indicator Software and 2)pharmaco-prophylaxis-recommended procedures, then reviewed medical records to ascertain true pPE/DVTs (i.e., cases). We selected controls matched with cases by hospital, age, gender, Diagnosis-Related Group, and predicted probability for developing pPE/DVT, and who underwent a pharmaco-prophylaxis-recommended procedure. We assessed records for “appropriate pharmaco-prophylaxis use,” defined primarily per American College of Chest Physicians (ACCP) guidelines, and reasons for anticoagulant non-use.

**Results:** The 116 case-control pairs were similar in terms of demographics, surgery type, ACCP risk category and appropriate pharmaco-prophylaxis rates overall (62% vs. 72%; p=0.13; effect size=0.16). Of highest risk patients, respective pharmaco-prophylaxis rates among cases and controls were 88% vs. 92% among hip/knee replacements (p=0.74), and 31% vs. 48% among cancer patients (p=0.19). Of all cases and controls, 25% had no pharmaco-prophylaxis contraindications documented; reviewers identified contraindications in 14% of cases and 9% of controls (p=0.30).
Conclusions: Preventive pPE/DVT practice similarities between cases and controls suggest that pPE/DVTs occur despite implementation of guideline-adherent practices. While VA quality improvement efforts should target cancer patients and improve documentation of prophylaxis contraindications, research should address additional methods to reduce pPE/DVT.

Key Words: postoperative venous thromboembolism; venous thromboembolism, prophylaxis; processes of care; quality of care; quality indicators; patient safety
Introduction

Postoperative pulmonary embolism/deep vein thrombosis (pPE/DVT) is a common, costly and potentially life-threatening complication.\textsuperscript{1} Without thromboprophylaxis, DVT occurs in up to 15\% to 60\% and PE in 0.5\% to 5\% of major surgery patients, with the highest risk following orthopedic procedures, particularly, total hip replacement;\textsuperscript{1} pPE/DVT is associated with an excess of $21,000 in hospital charges, 5.4 hospital days, and four-fold 30-day mortality.\textsuperscript{2,3}

Multiple randomized trials and meta-analyses have shown that prophylaxis, especially pharmaco-prophylaxis, can significantly reduce this risk, with reductions of almost 70\% among general surgical patients.\textsuperscript{1,4,5} Despite this, and the long-standing existence of national evidence-based PE/DVT prevention guidelines,\textsuperscript{1,6} observational studies continue to report prophylaxis underuse.\textsuperscript{7-9}

Recognizing these gaps in care, the Joint Commission and the Surgical Care Improvement Project (SCIP) have developed chart-based process measures addressing appropriate thromboprophylaxis use.\textsuperscript{10} The Agency for Healthcare Research and Quality (AHRQ) has also included pPE/DVT as a Patient Safety Indicator (PSI). PSIs are outcome measures that use administrative data to identify potentially preventable adverse events.\textsuperscript{11} The Centers for Medicare and Medicaid Services (CMS) have subsequently added the SCIP Venous Thromboembolism (VTE) measures and the pPE/DVT PSI to their hospital pay-for-reporting program.\textsuperscript{12,13} Additionally, CMS no longer reimburses for PE/DVTs following total hip or knee replacements.\textsuperscript{14}

Given the adverse clinical consequences, as well as associated institutional penalties for pPE/DVT occurrences, we need to understand the extent to which these events are related to
prophylaxis-related process of care failures, and therefore potentially preventable through improved care. Although several recent case series have examined guideline-adherent thromboprophylaxis rates in either at-risk patients or those experiencing pPE/DVT events, data are limited, and somewhat conflicted, on whether thromboprophylaxis use differs between patients who do and those who do not develop a pPE/DVT.7-9 Physician implicit review of chart-confirmed pPE/DVT cases (N=28), using 1994 data, revealed a potential process failure in 61% versus only 2% of controls.15 However, a subsequent case-control study, using 1995 through 2004 chart data, reported similar prophylaxis adherence in cases and controls (N=172).16 Additionally, relatively few recent studies have reported on thromboprophylaxis use among high-risk patients,9,16,17 or on the reasons for or appropriateness of withholding thromboprophylaxis.18 Further, despite the Veterans Health Administration’s (VA’s) strong commitment to development and implementation of quality improvement initiatives, little is known about VTE practices in the VA.19

We therefore undertook this study to better understand the relationship between adherence with guideline-related processes of care and pPE/DVT development, and to explore VTE prevention practices in the VA.
Methods

Study Design and Data Sources

As part of a larger VA study examining the validity of selected PSIs, we conducted a retrospective case-control study using data from October 1, 2002 through September 30, 2007. We obtained acute-care hospital administrative discharge data from the VA National Patient Care Database Patient Treatment File (PTF), and electronic medical record (EMR) data using VistAWeb, a program enabling centralized access to VA-wide facility data.

Hospital Sampling

Our hospital sampling method is described in detail elsewhere. Briefly, we applied the AHRQ PSI software (v.3.1a) to the PTF-derived database to obtain individual PSI counts and composite scores (a combined measure of 11 PSIs). We selected a geographically diverse sample of 28 of 158 VA acute-care hospitals using a stratified sampling method based on observed and expected PSI counts and composite scores. The final hospital sample included hospitals from 19 of 21 VA regional healthcare networks (otherwise known as VA Integrated Service Networks), and 20 states representing a mix of rural (e.g., Togus, ME) and more urban areas (e.g., Los Angeles, CA). (All the US Census Bureau-designated regions and divisions of the lower 49 mainland states were represented.)

PE/DVT Case and Control Identification

Case and control identification required several steps. (See Figure 1.) First, as part of a previous study examining the positive predictive value of the PSI pPE/DVT, we randomly selected 112 PSI software-flagged pPE/DVT cases (4 per sample hospital); two trained nurse-abstractors reviewed these EMRs to identify true pPE/DVTs (N=48). Second, we excluded cases with ineligible procedures (i.e., those not appropriate for prophylaxis; N=25) (see below
for eligibility), and third, we confirmed there were no upper extremity DVT cases. This left 23 cases for matching. We then screened additional flagged cases in batches of 112, repeating step 2 (screening for eligible procedures), then steps 1 and 3 (nurse-abstractor confirmation of PE/lower extremity DVT) until we obtained approximately 100 cases. This target sample size was based on power calculations which assumed a pharmaco-prophylaxis use difference of 20% between cases and controls and rate of approximately 50% among cases.25

We used the SCIP-recommended procedures for thromboprophylaxis as initial reference to determine surgeries for inclusion.26 (See Appendix 1.) Additional selection was based on study clinician opinion (AB, AC) with expert surgical input (KI); only major surgeries were included. We excluded neurosurgical procedures since they often do not receive pharmacologic prophylaxis, and included lower extremity orthopedic procedures associated with fractures (excluding below knee) and lower extremity amputations lasting beyond 1 hour.

In total, we screened 560 PSI-software flagged cases (5 groups of 112, including the initial 112) (Figure 1); among those with eligible procedures, 128 were confirmed as true pPE/DVTs. We excluded 8 upper extremity DVTs, plus three cases occurring more than 30 days after surgery.

Using the PTF, we then matched true pPE/DVT cases one-to-one with controls (i.e., patients not experiencing a pPE/DVT), based on hospital, age (within 5 years), gender, and diagnosis-related group ([DRG], which accounts for procedure type). Within strata defined by these variables, we selected the control with the closest predicted probability of developing a pPE/DVT based on a logistic regression model that included age, gender, DRG, and discharge comorbidities.27 We similarly screened out controls based on procedure eligibility as described for cases. We lacked an appropriate match for one case; our final sample comprised 116
matched cases and controls. Our cases came from 27 of the 28 sample hospitals. The average number of cases per site was 4.1 (standard deviation 2.7) or median 3.5 (range 0-10).

EMR Abstraction

Starting with preliminary tools and guidelines from AHRQ, we developed separate but comparable abstraction instruments for cases and controls. Specific to cases, the instrument included questions about case ascertainment per the PSI definition. There had to be documentation in the discharge summary, radiology reports or physician progress notes that the patient experienced a VTE postoperatively. All but two cases had radiographic confirmation; these two cases were reviewed by study clinicians (AB, AC) and retained as true events. See Kaafarani, et al. for further EMR abstraction details.

For both cases and controls, the instrument contained identical questions about demographics, patient- and procedure-related risk factors, perioperative thromboprophylaxis use, plus contraindications to pharmaco-prophylaxis, including: a history of recent (within 4 weeks) or active intra-cerebral, gastrointestinal, respiratory, or urinary tract bleeding, a known bleeding disorder (inherited or acquired, e.g., severe liver disease), or platelet count <75,000. The two nurse-abstractors were also encouraged to write-in additional documented reasons for lack of pharmaco-prophylaxis use. For controls, records were also examined out to 90 days following discharge to look for late VTE events. (We initially tested inter-rater reliability on approximately 10% of cases; average agreement across records was 92%. Further abstraction details are described elsewhere.)

Analyses

We compared cases and controls on several variables including demographics, patient-related risk factors, surgery type, American College of Chest Physicians (ACCP) risk category
We conducted similar analyses comparing prophylaxis use between and within surgical specialties, with subcategorization of orthopedic procedures, and compared risk factors within surgery type.

We categorized thromboprophylaxis use into mutually exclusive groups: “appropriate pharmaco-prophylaxis,” “mechanical prophylaxis only,” and “no prophylaxis.” We used the SCIP VTE measures specifications (v.2.6b), derived from the seventh version of the ACCP guidelines (ACCP 7), to define appropriateness. Appropriate pharmaco-prophylaxis required both proper timing of administration (within 24 hours of the procedure) and use of recommended anticoagulants; the “mechanical prophylaxis only” group similarly required use of appropriately timed and recommended forms of mechanical prophylaxis. (See Appendix 2.) For procedures not represented in the SCIP measures (e.g., lower extremity amputations), we referred directly to ACCP 7 for recommended anticoagulants. Of note, the SCIP specifications differ from ACCP guidelines in being more explicit with respect to appropriate timing of prophylaxis administration, outlining appropriate prophylaxis options for a specific set of major surgeries, and not accounting for patient VTE risk factors (e.g., SCIP considers mechanical prophylaxis as appropriate in all urologic patients, even high risk ones). Since ACCP guidelines recommend that mechanical prophylaxis be used as an adjunct to anticoagulants, especially in high-risk patients, we also calculated the percentage on both appropriate pharmacologic and mechanical prophylaxis.

Study clinicians (AB, AC) reviewed EMRs of all patients who did not receive appropriate pharmaco-prophylaxis and in whom nurse-abstractors did not identify a potential contraindication, (including records with delayed prophylaxis, i.e., initiated >24 hours postoperatively). They looked for other potential reasons for lack of pharmaco-prophylaxis use,
such as significant perioperative bleeding (e.g., bleeding associated systolic blood pressure drop to <90 mm Hg, or hematocrit drop to <25% immediately postoperatively, or requiring ≥4 units of blood), significant renal impairment (estimated glomerular filtration rate <30ml/min or end-stage renal disease on dialysis) or epidural anesthesia/analgesia use. This last item was included since the SCIP specifications consider withholding of pharma-co-prophylaxis in patients undergoing epidural anesthesia or with an epidural catheter in situ as appropriate, provided mechanical prophylaxis is used contrary to ACCP guidelines.\textsuperscript{1,32}

We compared groups using parametric (chi-squares and t-tests) and non-parametric tests (Wilcoxon rank-sum) as appropriate. We also calculated effect size (ES) for selected results to characterize the clinical significance of findings.\textsuperscript{33} (Effect sizes of 0.2, 0.5 and 0.8 are considered small, medium and large respectively.\textsuperscript{33}) SAS version 9.1 (SAS Institute Inc., Cary, NC) was used for all analyses.
Results

Our final patient sample was drawn from

Patient Sample Characteristics

Table 1 shows baseline characteristics of sample patients. Cases and controls were similar with respect to gender, race/ethnicity, and age; all patients were at least 40 years old. The most common pre-admission risk factors overall were current neoplasm and obesity (i.e., BMI ≥ 30). Individual risk factors were similar between cases and controls, except for more prior VTEs in cases (16% vs. 5%; p=0.01) and more obesity in controls (36% vs. 22%; p=0.03). Cases and controls were comparable with respect to major surgery type; orthopedic surgery was the most common category (>54% of cases and controls) followed by general surgery (>27% of cases and controls; Table 1.) Eighty-two percent of cases and 77% of controls were in the ACCP highest risk category (p=0.42); all were at least high risk.

There were few significant differences in risk factors between cases and controls by surgery type, other than higher prior VTE rates among orthopedic cases, and impaired mobility among lower extremity amputation cases. (Data not presented; available from authors.) Notably, current neoplasm was especially common among patients undergoing thoracic (100% of cases, 88% of controls), urologic (88% of cases, 71% of controls) and general surgery (44% of cases, 52% of controls). We found no late VTE events among controls.

Overall Thromboprophylaxis Rates (Table 2)

Overall, more controls than cases received appropriate pharmaco-prophylaxis (72% vs. 62%), although the difference was not statistically significant (p=0.13; ES=0.16). Mechanical prophylaxis alone was used in 32% of cases and 22% of controls (p=0.11); 6% of both cases and
controls did not receive any prophylaxis. Fifty-three percent of cases and 58% of controls received both appropriate pharmacologic and mechanical prophylaxis (p=0.60).

**Surgical Specialty-Specific Thromboprophylaxis Rates (Table 2)**

Orthopedic patients were significantly more likely to receive appropriate pharmaco-prophylaxis compared to other surgical groups (p<0.01), with similar rates among cases and controls (>87%). Urologic patients had the lowest rates (0% and 29% for cases and controls, respectively). There was a non-significant trend toward higher prophylaxis rates among controls versus cases for the non-orthopedic surgical groups.

We saw opposite results with respect to mechanical prophylaxis only use. Non-orthopedic surgical patients (other than lower extremity amputations and thoracic patients) had significantly higher mechanical prophylaxis rates compared to orthopedic patients (p<0.001); urologic patients had the highest rates (88% of cases and 71% of controls).

Rates of no prophylaxis were comparable between cases and controls by specialty group, ranging from 0% to 50% for cases undergoing orthopedic procedures versus lower extremity amputations. With respect to use of both pharmacologic and mechanical prophylaxis, trends were similar to those seen with appropriate pharmaco-prophylaxis.

**ACCP Highest Risk Groups**

Eighty-one percent of both cases and controls undergoing orthopedic procedures represented hip or knee replacements. Among these joint replacement patients, 88% of cases and 92% of controls received pharmaco-prophylaxis (p=0.65); all received some form of prophylaxis; approximately three-quarters of both groups received a combination of appropriate pharmacologic and mechanical prophylaxis. (See Table 2.)
While 83% of those with a prior VTE in both groups received pharmaco-prophylaxis, only 31% of cases and 48% of controls with a neoplasm received appropriate pharmaco-prophylaxis (p=0.19; ES=0.33). Of those in the highest ACCP risk category based on either procedure or patient risk factors, 68% of cases and 75% of controls received pharmaco-prophylaxis (p=0.33); 56% of cases and 62% of controls received both pharmacologic and mechanical prophylaxis (p=0.46).

Reasons for Lack of Appropriate Pharmaco-Prophylaxis (Table 3)

Nurses identified contraindications in only approximately 25% of both cases and controls who did not receive appropriate pharmaco-prophylaxis. Table 3 shows results after clinician EMR review. Clinicians identified bleeding contraindications in 12% of all cases (N=14) and 9% of controls (N=10). Of these, about 60% of both cases (N=8) and controls (N=6) had these reasons explicitly documented, and 57% (N=8) and 70% (N=7) respectively, represented patients with cancer. Another 2 cases had documentation of not receiving pharmaco-prophylaxis because of fall risk. Among patients with contraindications, all but one case, a patient with peripheral vascular disease, received appropriate mechanical prophylaxis. Two additional cases developed VTEs within 24 hours postoperatively. We felt we could not conclude that they lacked a contraindication to pharmaco-prophylaxis. Given the relatively short time frame between the procedure and the VTE event, postoperative documentation of the acute complication would likely have taken precedence over documentation of contraindications. (Had we excluded these patients from the original sample, our results would not have appreciably changed.) Thus, accounting for contraindications and early VTE occurrence, a total of 78% of cases and 80% of controls were appropriately managed (p=0.75). This represented 56% of cases and 72% of controls with malignancy (p=0.19; ES=0.32). Accounting for contraindications, assessments
of appropriate management increased for all surgical groups except thoracic cases and lower extremity amputation controls. (See Figure 2.)

Of the remaining patients, either no reason was given or identified in the record as to why they did not receive appropriate pharmaco-prophylaxis (16% of both cases and controls), or potential reasons for withholding prophylaxis were not consistent with accepted contraindications (i.e., the presence of an epidural catheter or use of aspirin as prophylaxis instead of anticoagulants; 6% of cases and 4% of controls) No identifiable cause for lack of pharmaco-prophylaxis use was found proportionately most often in lower extremity amputation patients. **Of note, among patients with “delayed” prophylaxis (i.e., started in hospital but >24 hours postoperatively; 2 cases and 8 controls) we did not find documentation of resolution of a contraindication (accepted or otherwise), except for 2 controls in whom it was started after an epidural catheter was removed.**
Discussion

This is one of the few studies of VA surgical patients to examine thromboprophylaxis use and the first VA study to our knowledge to evaluate the association of process failures with outcomes. Among this high-risk group of veterans undergoing major operative procedures, we did not find a significant difference in pharmaco-prophylaxis use between cases and controls. Overall, appropriate pharmaco-prophylaxis rates were modest, although rates of appropriate management were high when accounting for contraindications; 62% of cases and 72% of controls received guideline-recommended PE/DVT pharmaco-prophylaxis, with a further 16% of cases and 8% of controls appropriately managed given contraindications. Had we approximated SCIP criteria by considering mechanical prophylaxis use as appropriate in all urologic patients or patients receiving epidural anesthesia and excluding non-SCIP eligible procedures (i.e., lower extremity amputations and fractures), 83% of our cases and 90% of controls would have received appropriate prophylaxis (not accounting for SCIP exclusion criteria).

Pharmaco-prophylaxis rates varied widely by surgery type, with the highest rates among orthopedic patients; general surgery, thoracic and urologic patients had comparatively lower rates. Among the highest ACCP risk groups, very high pharmaco-prophylaxis rates were seen among joint replacement patients and those with a VTE history (>80%), with much lower rates among cancer patients (39% overall). These lower rates persisted even after accounting for contraindications. (Although the clinical significance, i.e., effect size, of case-control differences was slightly larger among cancer patients, both groups were relatively undertreated.)

Clinical trial results strongly support the process-outcome link between perioperative PE/DVT pharmaco-prophylaxis use and decreased occurrence of DVT, PE and death, with much weaker evidence supporting mechanical prophylaxis and only with respect to DVT risk.
reduction. Thus, the ACCP guidelines generally recommend mechanical prophylaxis alone only when the bleeding risk is unacceptably high. Although we did find a trend towards lower pharmaco-prophylaxis use (and conversely higher mechanical prophylaxis use) in cases compared to controls (both overall and within each **non-orthopedic** surgical group), these differences were not statistically significant. **Interestingly, when we performed a post hoc analysis among the non-orthopedic patients, we found borderline significant differences in pharmaco-prophylaxis rates (32% in cases vs. 53% in controls, p=0.049, ES=0.39).** However, once we accounted for contraindications, differences in appropriate prophylaxis use disappeared (64% vs. 66%, p=1.0, ES=0.03). Thus, while more cases did not receive pharmaco-prophylaxis, which may have contributed to at least some events, several of these were appropriately treated and therefore not clearly preventable. Moreover, these findings remain consistent with existing observational studies, both case-control and case series, that show that many pPE/DVT events occur despite seeming best practices.18,25,34

A similar disconnect between observational study and clinical trial results with respect to process-outcome links has been noted for various conditions.35-37 Clinical trials occur in a structured setting with a relatively homogeneous population; few interventions are as effective in actual practice. Further, as hypothesized by Shackford et al., guideline recommended measures may simply be “insufficient to prevent VTE in some high-risk patients.”16 However, we are not advocating for a decrease in prophylaxis use. Rather, our findings suggest opportunities for improvements in preventive care, particularly among cancer patients and those undergoing non-orthopedic procedures. Although each surgical specialty has its own guidelines, the ACCP VTE prophylaxis guidelines are considered the standard of care in the US. Clinicians during our study period (2002-2007) would have been influenced by both the
sixth (released in 2001) and seventh (released in 2004) versions of these guidelines, which contained very similar recommendations. Orthopedic procedures have the highest procedure-associated VTE risk, the strongest evidence base for prevention and, therefore, the strongest recommendations for pharmaco-prophylaxis. However, ACCP 6 and 7 also strongly recommend pharmaco-prophylaxis for patients undergoing major general and thoracic procedures, especially if they are over age 40 or have other VTE risk factors; patients over 40 with a prior VTE or cancer are considered at highest risk, similar to orthopedic patients. For major urologic or vascular procedures, the guidelines recommend anticoagulant use if patients have VTE risk factors. Thus, several of our high- and highest-risk cases and controls did not receive guideline-recommended care (even accounting for contraindications). Of note, our findings would be similar even accounting for the recommendations of the recently published ACCP 9, other than one notable exception; aspirin is now considered an acceptable anticoagulant alternative in patients undergoing major orthopedic surgery. Among patients undergoing knee arthroplasty, we had one case and one control who received only aspirin.

Nevertheless, our rates of appropriate pharmaco-prophylaxis are generally higher than those reported in recent case series of surgical patients. A multinational trial using chart review (the ENDORSE study) and two large US studies using administrative data from similar time periods reported overall appropriate pharmaco-prophylaxis rates between 18% and 55%. Rates also varied by specialty with the highest rates among orthopedic patients (38% to 74%) and the lowest rates tending to be among urologic patients (26% to 32%). The ENDORSE study also found that patients with prior VTE had a higher likelihood of receiving recommended prophylaxis than cancer patients. Among studies of surgical patients experiencing VTE, two single site studies, one using 2009 data (N=89), and the other, the
previously noted case-control study, found that 63% and 40% respectively received appropriate pharmaco-prophylaxis; an additional 25% and 23% respectively were appropriately managed given contraindications.\textsuperscript{18}

There are several possible explanations for the discrepant rates, especially with the larger case series, including slightly different appropriateness definitions (all were based on ACCP 6 or 7 guidelines),\textsuperscript{31,32} data sources used, patient characteristics, and included procedure types. Our population’s higher VTE risk likely led to higher prophylaxis rates. For example, in the ENDORSE study, rates of prior VTE, active cancer, and orthopedic procedures were only 3%, 17% and 13% respectively.\textsuperscript{9}

Other important findings of our study were that relatively few of the patients who did not receive pharmaco-prophylaxis had documented contraindications and that approximately half of these cases and controls had no identifiable reason for lack of use even after careful clinician review. Few previous studies have investigated this aspect of prophylaxis, other than reporting bleeding risk.\textsuperscript{9,39} In a setting with an established VTE prophylaxis protocol including an order sheet with check boxes to indicate contraindications, Weigelt et al. found only 1% of cases were missing documentation of contraindications.\textsuperscript{18} However, Shackford et al. found up to 37% of VTE cases had no contraindications documented or identified.\textsuperscript{16}

Our study design is unique compared to related recent studies in surgical patients in that we used a well-established administrative-data based indicator, the AHRQ PE/DVT PSI, to flag PE/DVT cases.\textsuperscript{16,18,34} However, given the PSI’s recognized relatively high rate of misidentification of events (and under-detection of events), we then confirmed cases through chart review.\textsuperscript{23,41,42}
Our study had a few limitations. First, our sample size may have been too small to show statistical significance. However, the calculated effect size for the level of difference observed for the whole sample was relatively small at 0.16. Effect size is independent of the sample size. Thus, even if we had found a statistically significant result by including twice as many cases and controls, this difference is too small to be clinically meaningful. Additionally, as noted, other studies support this lack of difference in management of cases and controls.

Second, although we matched cases and controls on VTE risk using administrative data, chart-abstracted data demonstrated some individual risk factor differences between groups, notably with respect to prior VTE and obesity. However, by chart data all patients were in the high or highest ACCP VTE risk categories, with similar distributions by group. Third, despite using very accurate medication data (obtained from bar-coded medication administration logs), we may be overestimating appropriate pharmaco-prophylaxis rates since we assessed prophylaxis use up to 3 days postoperatively, but not beyond this. Further, while standard prophylaxis dosing for unfractionated and low molecular weight heparin had to be adhered to, target INRs were frequently not documented. Since we could not determine warfarin dosing appropriateness, we deemed any regular warfarin use as appropriate. Nevertheless, our rates are still higher than the ENDORSE study which did not consider dosage and only examined prophylaxis use at a single time-point. Additionally, our methods of assessing appropriateness are similar to other recent chart review studies. Finally, it is possible that some controls may have had subclinical VTE. However, our findings are consistent with related studies that included only symptomatic VTEs. While we focused on in-hospital outcomes, related studies used 30-day outcomes. More recent data have also raised concern about events occurring up to 90 days following surgery, especially hip replacements. We therefore examined EMRs of all
controls up to 90 days post-discharge and found no VTE events; all had evidence of ongoing VA use after discharge to at least 90 days, unless they died in-hospital or prior to day 90. (None of the deaths were attributed to a VTE.)

Our findings and those of others suggest that even with 100% compliance with current SCIP VTE measures, or even with modifications to increase use of pharmaco-prophylaxis, pPE/DVTs will still occur. It may be important to incorporate other factors such as VTE risk, or anticoagulant dosage and duration into VTE process measures in order to realize the full potential of such measures in improving patient safety. Moreover, penalizing providers for pPE/DVT events, such as following joint replacements, may be inappropriate since the vast majority occur despite appropriate pharmaco-prophylaxis. Additionally, our finding that clinicians often failed to document reasons for lack of pharmaco-prophylaxis is concerning from a medico-legal standpoint. We expect this will improve over time as provider awareness of performance monitoring and public reporting increases, since this information is necessary to satisfy the SCIP-VTE measures for certain surgery types.

Further work is needed to understand why these pPE/DVT events are happening. This may occur at the local level by means of observational studies, including local quality improvement activities that carefully assess process factors, using prospective data collection to determine whether important strategies such as early mobilization are actually being implemented. Clinical trials are also necessary to examine additional strategies to reduce VTE events.

Conclusion

Similarities in pPE/DVT preventive practices between cases and controls suggest that pPE/DVTs events occur even with implementation of evidence-based practices. However,
despite high overall rates of guideline-adherent care, certain high-risk patient groups were relatively undertreated, and documentation of prophylaxis contraindications was frequently absent. While these deficiencies should be addressed through VA quality improvement efforts, further research is necessary to uncover additional methods to prevent pPE/DVT.
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Figure Legends:

Figure 1. Selection of PE/DVT Cases

*From groups 2-5, three additional cases were excluded for PE/DVT occurring >30 days post-operatively and one because of no control match, yielding a final sample of 116.

Figure 2. Percent Appropriately Managed Accounting for Contraindications

CI to PPx = contraindication to prophylaxis; Approp Pharm PPx = appropriate pharmacologic prophylaxis; Ortho = orthopedic; Gen Sx = general surgery; LE Amp = lower extremity amputation
Table 1. Patient Sample Characteristics

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<th>Characteristic</th>
<th>Cases (N=116)</th>
<th>Controls (N=116)</th>
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<tr>
<td>Non, white</td>
<td>19 (16.3)</td>
<td>13 (11.2)</td>
</tr>
<tr>
<td>Other/Missing</td>
<td>14 (12.1)</td>
<td>18 (15.5)</td>
</tr>
<tr>
<td>Patient Risk Factors Present on Admission, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current neoplasm‡</td>
<td>32 (27.6)</td>
<td>29 (25.0)</td>
</tr>
<tr>
<td>Obesity (BMI ≥ 30)*§</td>
<td>25 (21.6)</td>
<td>42 (36.2)</td>
</tr>
<tr>
<td>Prior venous thromboembolism*</td>
<td>18 (15.5)</td>
<td>6 (5.1)</td>
</tr>
<tr>
<td>History of recent trauma</td>
<td>7 (6.0)</td>
<td>12 (10.3)</td>
</tr>
<tr>
<td>Hypercoaguable state‖</td>
<td>1 (0.9)</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>ACCP 6/7 Highest Risk Category* ‡</td>
<td>95 (81.9)</td>
<td>90 (77.6)</td>
</tr>
</tbody>
</table>

* p<0.05, significant difference between cases and controls

Column percents are shown.

SD = standard deviation; BMI = body mass index.

† Median time from admission to VTE diagnosis was 6.5 days (inter-quartile range 9.0); median time from diagnosis to discharge was 10.0 days (inter-quartile range 14.0).

‡ This included known neoplasms present on admission and masses present on admission that were diagnosed as malignancies.

§ BMI based on admission height and weight.
Includes congenital and acquired states other than malignancy; 1 case and 1 control had a known Factor V Leiden mutation (and a prior VTE)

#Based on procedure (hip or knee replacement or hip fracture surgery) and/or age >40 and having a prior VTE/molecular hypercoagulability or current neoplasm. Major trauma and acute spinal cord injury patients are also at the highest risk. Only one control fit these latter criteria.
Table 2. Rates of Thromboprophylaxis Among All Surgical Patients and by Surgery Type

<table>
<thead>
<tr>
<th>Surgery Type</th>
<th>N</th>
<th>Appropriate Pharmaco-prophylaxis* n (%)</th>
<th>Mechanical Prophylaxis Only† n (%)</th>
<th>No Prophylaxis n (%)</th>
<th>Appropriate Pharmaco- &amp; Mechanical* n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Controls</td>
<td>Cases</td>
<td>Controls</td>
<td>Cases</td>
</tr>
<tr>
<td>All Procedures</td>
<td>116</td>
<td>116</td>
<td>72 (62.1)</td>
<td>83 (71.6)</td>
<td>37 (31.9)</td>
</tr>
<tr>
<td>Orthopedic</td>
<td>63</td>
<td>63</td>
<td>55 (87.3)</td>
<td>55 (87.3)</td>
<td>8 (12.7)</td>
</tr>
<tr>
<td>Knee Replacement</td>
<td>31</td>
<td>25</td>
<td>28 (90.3)</td>
<td>23 (92.0)</td>
<td>3 (9.7)</td>
</tr>
<tr>
<td>Hip Replacement</td>
<td>20</td>
<td>26</td>
<td>17 (85.0)</td>
<td>24 (92.3)</td>
<td>3 (15.0)</td>
</tr>
<tr>
<td>General Surgery</td>
<td>34</td>
<td>31</td>
<td>13 (38.2)</td>
<td>17 (54.8)</td>
<td>19 (55.9)</td>
</tr>
<tr>
<td>Urologic</td>
<td>8</td>
<td>7</td>
<td>0</td>
<td>2 (28.6)</td>
<td>7 (87.5)</td>
</tr>
<tr>
<td>Thoracic</td>
<td>5</td>
<td>8</td>
<td>2 (40.0)</td>
<td>5 (62.5)</td>
<td>2 (40.0)</td>
</tr>
<tr>
<td>LE Amputation§</td>
<td>6</td>
<td>7</td>
<td>2 (33.3)</td>
<td>4 (57.1)</td>
<td>1 (16.7)</td>
</tr>
</tbody>
</table>

No significant differences between cases and controls, for “all procedures” or procedure-specific comparisons. Row percents are shown.

LE = Lower Extremity; ORIF = open reduction internal fixation.
* Appropriateness definition based on administration timing and recommended medications per the SCIP Specifications Manual and ACCP guidelines.²⁶,³² (See Appendix 2.)

† Initiated within 24 hours of the first major OR and adhered to recommended SCIP specifications and ACCP guidelines with respect to mechanical prophylaxis type.

‡ ORIFs, including proximal femoral fractures, are not included in the SCIP measure.²¹

§ These are not included in the SCIP-VTE measure. Removing these patients produces similar “all procedure” rates (e.g., pharmacoprophylaxis rates would be 63% in cases and 72% in controls).
Table 3. Reason For Inappropriate or No Pharmaco-Prophylaxis

<table>
<thead>
<tr>
<th>Surgery Type</th>
<th>N</th>
<th>Bleeding* N (%)</th>
<th>No Cause Given/Identified n (%)</th>
<th>Epidural in Place† n (%)</th>
<th>Inappropriate Prophylaxis Type‡ n (%)</th>
<th>Other§ n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Controls</td>
<td>Cases</td>
<td>Controls</td>
<td>Cases</td>
<td>Controls</td>
</tr>
<tr>
<td>All Procedures</td>
<td>116</td>
<td>116</td>
<td>14(12.1)</td>
<td>10(8.6)</td>
<td>19(16.3)</td>
<td>18(15.5)</td>
</tr>
<tr>
<td>Orthopedic</td>
<td>63</td>
<td>63</td>
<td>0</td>
<td>2(3.2)</td>
<td>6(9.5)</td>
<td>5(7.9)</td>
</tr>
<tr>
<td>General Surgery</td>
<td>34</td>
<td>31</td>
<td>9(26.5)</td>
<td>4(12.9)</td>
<td>8(23.5)</td>
<td>8(25.8)</td>
</tr>
<tr>
<td>Urologic</td>
<td>8</td>
<td>7</td>
<td>4(50.0)</td>
<td>3(42.9)</td>
<td>1(12.5)</td>
<td>2(28.6)</td>
</tr>
<tr>
<td>Thoracic</td>
<td>5</td>
<td>8</td>
<td>0</td>
<td>1(12.5)</td>
<td>1(20.0)</td>
<td>0</td>
</tr>
<tr>
<td>LE Amputation</td>
<td>6</td>
<td>7</td>
<td>1(16.7)</td>
<td>0</td>
<td>3(50.0)</td>
<td>3(42.9)</td>
</tr>
</tbody>
</table>

No significant difference between cases and controls overall. Row percents are shown.

LE = lower extremity.

* Including a history of bleeding on admission, intraoperatively, postoperatively, or a bleeding history with anticoagulation (1 case and 1 control) or at bleeding risk because of thrombocytopenia (platelets <75, 1 case) or end-stage renal disease (1 case).
† These were epidural catheters that stayed in place for ≥1 day postoperatively for analgesia; 1 case had this explicitly noted by a clinician as a reason for withholding anticoagulation. An additional 3 cases (2 orthopedic and 1 LE amputation) and 5 controls (3 orthopedic, 1 general surgery and 1 LE amputation) had an epidural as anesthesia for surgery only.
‡ 1 case/1 control received ASA as prophylaxis (both underwent elective knee replacements).
§ Includes 2 cases with a PE within 1 day postoperatively who did not receive or have any pharmaco-prophylaxis ordered before the event, and 2 cases, including one patient undergoing a hip ORIF, who were deemed to be at too high fall risk.
Figure 1. Selection of PE/DVT Cases

PSI Software Flagged Cases of PE/DVT Among Sample Hospitals = 1858

Initial Case Selection (Group 1) Groups 2-5 of Case Selection

112 flagged cases selected for medical record abstraction 448 flagged cases selected for medical record abstraction

69 cases excluded: Not true postoperative PE/DVT 270 cases excluded: Ineligible procedures

48 true positives for PE/DVT 178 cases with procedures requiring

25 cases excluded: Ineligible procedures 73 cases excluded: Not true postoperative PE/DVT

23 true positives with eligible procedures 105 true positives for PE/DVT with eligible

0 cases excluded: Upper extremity DVTs 8 cases excluded: Upper extremity DVTs

23 true positives for LE PE/DVT with eligible 97 true positives for LE PE/DVT with eligible

120 true positives for LE PE/DVT with eligible procedures *
Figure 2. Percent Appropriately Managed Accounting for Contraindications