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Perioperative Pharmacologic Prophylaxis for Venous Thromboembolism in Colorectal Surgery

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Abstract

Background—To determine the effectiveness of pharmacologic prophylaxis on preventing clinically relevant venothromboembolic (VTE) events and deaths after surgery. Surgical Care Improvement Project recommends that VTE pharmacologic prophylaxis be given within 24 hours of the operation. The bulk of evidence supporting this recommendation uses radiographic endpoints.

Study Design—The Surgical Care and Outcomes Assessment Program (SCOAP) is a Washington State quality improvement initiative with data linked to hospital admission/discharge and vital status records. We compared the rates of death, clinically relevant VTE and a composite adverse event (CAE) in the 90-days after elective, colon/rectal resections, based on the receipt of pharmacologic prophylaxis (within 24 hours of surgery) at 36 SCOAP hospitals (2005-2009).

Results—Of 4,195 (61.1±15.6 yrs; 54.1% women) patients, 56.5% received pharmacologic prophylaxis. 90-day death (2.5% vs. 1.6%, p-value=0.03), VTE (1.8% vs. 1.1%, p-value=0.04), and CAE (4.2% vs. 2.5%, p-value=0.002) were lower in those who received pharmacologic prophylaxis. After adjustment for patient and procedure characteristics, the odds were 36% lower for CAE (OR 0.64, 95% CI 0.44-0.93) with pharmacologic prophylaxis. In any given quarter, hospitals where patients more often received pharmacologic prophylaxis (highest tertile of use) had the lowest rates of CAE (2.3% vs. 3.6%, p=0.05) compared to hospitals in the lowest tertile.

Conclusions—Using clinical endpoints this study demonstrates the effectiveness of VTE pharmacologic prophylaxis in patients having elective colorectal surgery. Hospitals that used pharmacologic prophylaxis more often had the lowest rates of adverse events.

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Keywords

Venous thromboembolism; venous thromboembolism pharmacologic prophylaxis; Surgical Care Improvement Project

INTRODUCTION

Venous thromboembolism (VTE) is the second most common postoperative complication[1] and one of the most common preventable causes of in-hospital death.[2, 34] To prevent VTE, the American College of Chest Physicians generates evidence-based guidelines every 4 years.[3, 5] Current guidelines recommend that unless otherwise contraindicated, heparin-based pharmacologic prophylaxis be administered to prevent deep vein thrombosis (DVT) and pulmonary embolism (PE) in patients undergoing major abdominal surgery. This recommendation, with the specification that VTE pharmacologic prophylaxis be given within 24 hours of the operation has been adopted by the Surgical Care Improvement Project (SCIP) initiative as a "pay for performance" initiative. The bulk of evidence supporting this recommendation uses an endpoint of VTE "events" determined by radiolabelled fibrinogen uptake or venography rather than clinically relevant VTE (symptomatic DVT and symptomatic or fatal PE). In part because of the use of radiographic endpoints and concerns regarding bleeding risk there has been skepticism about the wider use of VTE pharmacologic prophylaxis in patients having surgery.[6-8] Skeptics note that as many as 66% of patients who get a VTE have received appropriate pharmacologic prophylaxis[9] and in at least one center, despite increasing use of pharmacologic prophylaxis the rate of symptomatic VTE on the surgical service actually increased over a 10-year period.[10] These concerns may explain why the rate of use of pharmacologic prophylaxis is highly variable despite the SCIP mandate.[11-14]

Given the relative paucity of VTE studies using clinical endpoints and unclear effectiveness of pharmacologic prophylaxis in community practice settings, we performed an observational, comparative effectiveness evaluation across most Washington State hospitals. The study is based in Washington State's Surgical Care and Outcomes Assessment Program (SCOAP), a prospectively-gathered clinical registry and quality improvement (QI) activity now implemented at nearly all statewide hospitals where surgery is performed (n= 55).[15] The purpose of this study was to evaluate the relationship between the use of pharmacologic prophylaxis and clinical VTE in patients having elective colorectal surgery and to determine the relationship between increasing hospital use of pharmacologic prophylaxis and outcomes.

METHODS

Study design

This study was approved by the University of Washington Human Subject Review Committee and the Washington State Department of Health. A prospective cohort study was conducted using the SCOAP in-hospital clinical registry linked to hospital administrative discharge database, and the state's vital records system. SCOAP draws data from the medical record by trained, audited abstractors using standardized definitions (http://www.scoap.org/documents/index.html). The Washington State comprehensive health abstract reporting system (CHARS) includes administrative information on all hospitalizations and patient identifiers that allows for tracking of subsequent hospitalizations. SCOAP index cases were linked to CHARS to identify patients who were re-hospitalized at any center after a SCOAP index admission and to the vital status registry to determine if they had died. The CHARS dataset also contains International Classification

of Diseases, Ninth Revision (ICD-9) procedure and diagnosis codes. Records of inpatient hospitalization between 4th quarter of 2005 and 1st quarter of 2009 at 36 SCOAP hospitals (Appendix 1, online only) were used to assess outcomes for patients undergoing elective colon/rectal resections.

Variable Definitions

Patient risk factors—SCOAP records were used to obtain sociodemographic characteristics, clinical comorbidities, and operative details. We used the Deyo modification of the Charlson Comorbidity Index to calculate a weighted index of comorbid conditions for each patient.[16] Scores range from 0 to 3+, where 0 indicates the absence of comorbid conditions and the score was truncated at 3 and above.

Duration of operation—Anethesia record and operating room (OR) log was used to identify the OR incision and end times. Duration was measured from incision to final wound closure.

Type/Method of operation—Operation type was specified as right hemicolectomy, left hemicolectomy, low anterior resection, abdominal perineal resection, total abdominal colectomy, colostomy takedown, and perineal proctectomy. Method of operation was specified as laparoscopic, open, laparoscopic converted to open, and laparoscopic/hand-assited.

Use of pharmacologic prophlaxis—VTE pharmacologic prophylaxis administration was obtained by directed chart review of all patients. SCIP criteria were used to define the use of pharmacologic prophylaxis, specifically chemical agents administered 24 hours before or after the operative start time in a patient not otherwise contraindiacted for use.[17] Acceptable pharmacologic prophylaxis included unfractionated heparin, low molecular weight heparin (enoxaparin, dalteparin, tinzaparin), and synthetic factor Xa inhibitor (fondaparinux). Use of warfarin was not counted as acceptable as defined by the SCIP criteria.[18] Use of agents that did not conform to SCIP criteria (sequential pneumatic compression devices) was also recorded.

Outcomes—Given recent evidence that the risk of operation-related VTEs does not return to baseline for 12 weeks,[19] the primary outcome was 90-day death rate, new VTE diagnosis or VTE-related intervention, as well as the composite of these adverse events (CAE). Complication potentially related to the use of VTE pharmacologic prophylaxis (intra-operative or post-operative red blood cell transfusions) was also recorded. Readmissions for VTE were defined as any hospital admission within 90 days of discharge from the index hospitalization. At index and subsequent hospitalizations, VTE diagnosis or VTE-related interventions were defined as either a documented new use of anticoagulation therapy (at therapeutic dose) for presumed/confirmed DVT or PE (from SCOAP), and/or specific ICD-9 codes as previously described related to VTE diagnosis and/or treatment (Appendix 2, online only).[20] The 90-day mortality was defined as all-cause death ≤90 days of procedure as ascertained from Washington State Vital Records.

Analysis

Patient level analysis—Patient characteristics were summarized using frequency distributions for categorical variables, and means and standard deviations for continuous variables stratified by receipt of perioperative VTE pharmacologic prophylaxis. 90-day mortality, VTE events and CAE were summarized using frequency distributions stratified by use of pharmacologic prophylaxis. Pearson chi-square statistics were used to compare characteristics and unadjusted event rates. Logistic regression models were created to

evaluate the association between the receipt of pharmacologic prophylaxis and outcomes adjusting for patient, clinical, and operative characteristics identified as statistically significant ($p<0.05$) on univariate evaluation or found to be important in previous studies. For sensitivity analysis, we calculated the propensity score for receipt of VTE pharmacologic prophylaxis among all patients without regard to the outcome using the same variables. Patients were divided into quartiles of propensity scores and within each stratum the 90-day CAE rates were calculated based on receipt of perioperative VTE pharmacologic prophylaxis.

Hospital level analysis—We evaluated the use of VTE pharmacologic prophylaxis at each hospital in each calendar quarter using descriptive statistics and multivariate adjustments (adjusting for patient history of VTE and comorbid conditions within each hospital for that quarter). Hospitals were divided in tertiles according to the frequency of use of VTE pharmacologic prophylaxis and the rates of VTE were calculated for each calendar quarter based on the level of use (highest, mid, lowest tertile) of prophylaxis

Not all 36 hospitals began data entry at the same time and quality improvement interventions were occuring during this evaluation period and for the hosptal-level analysis each hospital's calandar quarter was considered as a separate unit of analysis.

STATA was used for all analyses (Version 11, STATACorp, College Station, TX).

RESULTS

A total of 4,195 patients (mean age 61.1±15.6 yrs; 54.1% women) underwent elective colorectal resections. Patients who received perioperative VTE pharmacologic prophylaxis (n=2,369; 56.5%) and those who did not (n=1,826; 43.5%) were similar with respect to age, sex, smoking status, BMI, comorbidities such as hypertension and coronary artery disease, Charlson comorbidity indices, hospital factors such as length of stay and intraoperative duration, and indication for procedure (Table 1). Those who received perioperative VTE pharmacologic prophylaxis were more likely to have had previous history of DVT or PE (4.1% vs. 2.9%, *p*-value=0.04).

The overall rates of 90-day death and VTE events were 2.0% and 1.4%, respectively. The unadjusted rates of 90-day death (2.5% vs. 1.6%, p-value=0.03), VTE events (1.8% vs. 1.1%, p-value=0.04) and CAE (4.2% vs. 2.5%, p-value=0.002) were lower among those who received VTE pharmacologic prophylaxis. The rate of intra- or post-operative transfusions were more common in those who did not receive the pharmacologic prophylaxis (7.0% prophylaxis vs.10.9% no prophylaxis, *p*-value<0.001). Only 31.7% of 90-day VTE events, 56.6% of deaths and 46.7% of CAE occurred during the initial in-patient hospital stay, while corresponding rates of 80%, 59.0% and 70.8% were identified at 30 days, respectively.

There was a 41% reduction in the unadjusted odds of 90-day CAE (OR 0.59, 95% CI 0.42-0.83) (Table 2). After adjustment for calendar year, history of VTE and other patient and procedure characteristics (such as duration of operation, and method and type of operation) the odds of 90-day CAE were 36% lower with VTE pharmacologic prophylaxis (OR 0.64, 95% CI 0.44-0.93) [adjusted odds of 30-day CAE (OR 0.54, 95% CI 0.35-0.83)]. 1,641 (39.5%) of patients had pneumatic compressions alone. When adjusting for the same covariates, there was no significant reduction in the odds of VTE based on the use of pneumatic compressions (OR 0.82, 95% CI 0.43-1.57). Sensitivity analysis using propensity quartile matching found that 90-day CAE rates were consistently lower if perioperative VTE pharmacologic prophylaxis was given. Adjusting for propensity score found a significant

reduction in the odds of 90-day CAE when VTE pharmacologic prophylaxis was used (OR 0.61, 95% CI 0.43-0.89).

Over the course of the study period (Figure 1), the use of VTE pharmacologic prophylaxis increased (35.8% in Q0 to 70.4% in Q13), while overall rates of 90-day CAE decreased (4.3% in Q0 to 1.7% in Q13). Patients treated at hospitals in the top VTE pharmacologic prophylaxis "use tertiles" in a given quarter had a significantly lower 90-day CAE compared to patients at the lowest "use tertile" hospitals (2.3% vs. 3.6%, p=0.05) (Figure 2**)** and after adjustment for patient characteristics, the highest tertile use-hospitals (in a given quarter) had a 37% lower odds of CAE than lowest tertile use-hospitals (OR 0.63, 95% CI 0.40-0.99).

DISCUSSION

Our evaluation of statewide patients undergoing colorectal surgery with and without VTE pharmacologic prophylaxis found that VTE pharmacologic prophylaxis given within 24 hours of colorectal resection (SCIP criteria) was associated with significantly lower 90-day mortality and CAEs, despite the fact that patients receiving VTE pharmacologic prophylaxis were "higher risk" for VTE. VTE pharmacologic prophylaxis was not associated with rates of bleeding events and those hospitals where doctors used pharmacologic prophylaxis more often than others (highest tertile use) had the lowest rates of VTE or death. Almost all the prior studies used to support SCIP guidelines have used surrogate, radiographic endpoints. While studies looking only at fatal PEs[7, 21] and meta-analysis pooling the results of many smaller studies have suggested a reduction in clinically relevant endpoints in the general surgery patient population, [8, 22] this is the first large-scale modern study evaluating the comparative effectiveness of SCIP VTE metrics using clinically relevant endpoints. Our finding, based on the clinical records of patients from nearly the entire State of Washington, across all types of hospital and communities reinforces the recommendation for adherence to existing VTE prevention guidelines.

Approximately 10 to 40% of inpatient general surgical patients have been found to have "radiographically determined" DVT.[3] Autopsy studies have attributed 10% of all surgical hospital deaths to PE.[23] Given its prevalence, a national campaign to encourage the use of pharmacologic prophylaxis has been led by the Centers for Medicare & Medicaid Services through the SCIP initiative. Furthermore, the National Quality Forum established a nationwide preventative performance measure standard for VTE,[24] and Agency for Healthcare Research and Quality's highest ranked safety practice was the "appropriate use of prophylaxis to prevent VTE."[25]

Despite these efforts, use of VTE pharmacologic prophylaxis has been variable.[26-28] In a cross-sectional study of the 11,613 surgical patients at risk, the 2008 ENDORSE study demonstrated that only 59% of surgical patients received the recommended pharmacologic prophylaxis.[29] While self-reported rates of adherence to SCIP VTE prophylaxis criteria may be as high as 88% nationwide[30], a recent study based on audits of actual performance demonstrated a 56% adherence.[18] Physician resistance may be a component of the variable use since most of the supporting data for the recommendation have been based on radiographic endpoints and correlation to clinically relevant VTE reduction (outside of specific studies looking at fatal PEs and cancer patients[7, 21, 31]) has only been demonstrated in meta-analysis of underpowered studies.[6, 8, 22] Unlike radiographic DVTs, there is less agreement about the effect of pharmacologic prophylaxis on clinically relevant outcomes.[32, 33] The first study with a sufficient sample size to evaluate the clinical impact of VTE pharmacologic prophylaxis was the International Multicentre Trial (IMT). Clouded in controversy, the authors first reported in 1975[34] that patients receiving heparin had a 3-fold

reduction in DVT and 8-fold decrease in fatal PE events. The results of the study were re-issued in 1977[35] because one of the sites[36] withdrew its data suggesting that they observed the opposite effect. Almost all subsequent studies have been either underpowered or used radiographic endpoints. A meta-analysis of 46 randomized trials including more than 15,000 surgical patients demonstrated a greater than 60% reduction of DVT (diagnosed with radiolabelled fibrinogen), 40% reduction in PE and more than 60% reduction in fatal PE events.[22] Mismetti et al., in their meta-analysis study, found an even greater reduction of 71-75% in the relative risk of symptomatic and clinical VTEs concordant with reduction in asymptomatic DVTs detected radiographically.[8] However, outside of studies looking specifically at immediate postoperative fatal PEs, no study of appropriate size has reproduced the results from the IMT. One problem is that the incidence of PE is so rare that to evaluate an intervention that might reduce the risk by half (2% to 1%) might require randomization of 6,600 total patients. Secondly, identification of all clinically relevant DVTs and PEs is a challenge. Fatal PEs are usually found through autopsy, and other clinically symptomatic DVTs and PEs that do not lead to death are hard to identify. The risks also continue for some time[19] making accurate numbers of VTE-related events difficult to obtain. Another challenge to determining the comparative effects of SCIP criteria for VTE prevention is because of concerns about bleeding[8, 22, 35, 37] and/or ethical concerns about randomizing patients to non-guideline recommended care. Clinicians also remain skeptical about the disconnect between evidence-based process measures and outcome in real-world settings. For example, a recent study demonstrated a lack of association between a hospital's use of SCIP process-of-care measures to prevent surgical infection and postoperative infection rates.[38] On the contrary, our study demonstrates that greater use of one of the SCIP measures for VTE prophylaxis was associated with a reduction in clinically relevant endpoints. We not only found outcome improvements at the patient level, but also when considered at the hospital level, suggesting the value of QI interventions around this metric.

Our study is limited by several aspects of the data collection and VTE identification process. A recent study evaluating the risk of VTEs using the University HealthSystem Consortium (UHC) database found that the rates of VTE were lowest among patients not receiving the pharmacologic prophylaxis (0.0% to 0.9%).[39] While there was an increase in VTE pharmacologic prophylaxis use from 2003/2004 to 2007/2008 (74% to 89%), there was increased number of VTEs (2.4% to 3.2%) in colorectal resections. The UHC study reported raw numbers of VTEs in the two different time periods and is only risk adjusted for patient's severity of illness score. Other risk factors (such as previous history of VTEs, type and method of the operations, and temporal trends) associated with the use of VTE pharmacologic prophylaxis and VTEs were not adjusted for. More importantly, this study did not distinguish whether the anticoagulation medication was used for prophylaxis or therapy. Given that this study looked only at the postoperative period, they may have identified patients who had a diagnosis of VTEs and was started on VTE pharmacologic therapy. Our study was limited by a lack of information on duration of VTE pharmacologic prophylaxis, in and out of hospital. SCOAP has more recently included these metrics, but this was not available for this analysis. Clinicians within and between hospital may have variable approaches to evaluating patients at risk for VTE. Clinicians who had a lower threshold for diagnostic testing for VTE among symptomatic patients may also be more likely to adhere to SCIP VTE prevention measures. If so, this may have limited the finding that pharmacologic prophylaxis decreases the risk of VTE. Use of VTE pharmacologic prophylaxis by staff at a hospital can also be a marker for better use of other process measures that help reduce morbidity and mortality. We could not disentangle these from the effect of VTE pharmacologic prophylaxis. We used all-cause mortality-both alone and in combination with VTE-because most deaths that are directly caused by an acute PE occur before a timely diagnosis and treatment can be implemented.[40] The use of "all cause"

mortality may have included some patients who died of causes unrelated to VTE. For this reason, we performed analyses with and without death as an endpoint and found similar findings. Some of the limitations of this study arise from the use of administrative data (CHARS) to evaluate post-discharge outcomes by its design (retrospective), and the way health conditions and interventions are defined (using ICD-9 diagnostic and procedural codes). Because of this we did not have any information on how the diagnoses of VTEs were made. Also we could not separate out whether the transfusion was given intra-op or post-op. Given that the rate of transfusion was higher in the no prophylaxis group, it may well be instead that the intra-op bleeding led to lack of prophylaxis. Lastly, studies have demonstrated that patients discharged from the hospital have continual risk of VTEs.[41-45] With recent studies demonstrating equivalent results of outpatient management of VTEs, fewer VTE-related hospitalizations may have occurred over time.[46] The detection scheme used in this study would have missed VTEs that were diagnosed and treated in the outpatient setting, those occurring beyond 90 days, or diagnoses that were misclassified, but it seems unlikely that such misclassification would be associated with the receipt of VTE pharmacologic prophylaxis.

In conclusion, VTE pharmacologic prophylaxis was associated with significantly lower rates of 90-day mortality, clinical interventions for VTE, and composite adverse events. VTE pharmacologic prophylaxis was not associated with higher intra-op or post-op transfusion rates. This is the first time in recent decades that the impact of VTE pharmacologic prophylaxis on clinically relevant VTE endpoints in an appropriately sized cohort has been demonstrated. Our findings support the universal use pharmacologic prophylaxis in colorectal operations consistent with SCIP guidelines.

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Appendix 1

Hospitals involved in the data collection

Allenmore	Overlake
Central Washington	PeaceHealth St John
Evergreen	Providence Everett
Good Samaritan	Sacred Heart
Grays Harbor	Samaritan Healthcare
Group Health Eastside	Skagit Valley
Harborview	Stevens Healthcare
Highline	Sunnyside
Holy Family	Swedish – First Hill
Island Hospital	Tacoma General
Jefferson General	United General
Kadlec	University of Washington
Kittitas Valley	Valley Medical Center
Legacy Good Sam (Portland)	Virginia Mason
Morton General	Wenatchee Valley

Mt Carmel	Whidbey General
Northwest	Yakima Regional & Heart Medical Center
Olympic	Yakima Valley

Appendix 2

Specific ICD-9 codes related to venous thromboembolism diagnosis and/or treatment

ICD-9 coding	Description
Pulmonary Embolism	
415.1	Pulmonary embolism and infarction
38.7	Interruption of the vena cava
Deep Venous Thrombosis	
451.1	Phlebitis and thrombophlebitis of deep vessels of lower extremities
451.2	Phlebitis and thrombophlebitis of lower extremities, unspecified
451.8	Phlebitis and thrombophlebitis of other sites
451.9	Phlebitis and thrombophlebitis of unspecified site
453.2	Other venous embolism and thrombosis of vena cava
453.40-453.42	Venous embolism and thrombosis of deep vessels of lower extremity
453.8	Other venous embolism and thrombosis of other specified veins
453.9	Other venous embolism and thrombosis of unspecified site
997.2	Peripheral vascular complications (phlebitis or thrombophlebitits during or resulting from procedure)
999.2	Other vascular complications (phlebitis/thrombophlebitits/thromboembolism following infusion, perfusion, or transfusion)

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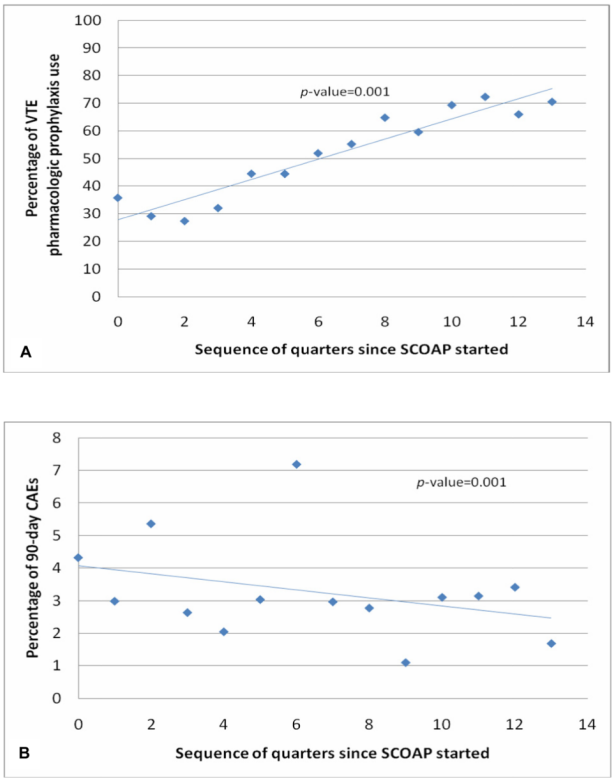

Figure 1.
Trend of (A) venous thromboembolism (VTE) pharmacologic prophylaxis use and (B) 90-d composite adverse events (CAE) over time.

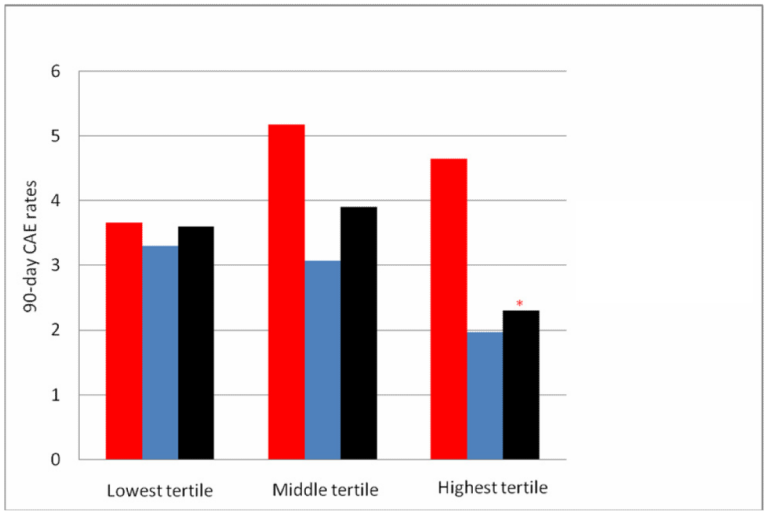

Figure 2.

90-d composite adverse events (CAE) overall (black bars) and dependent upon receipt (blue bars) or non-receipt (red bars) of venous thromboembolism (VTE) pharmacologic prophylaxis shown by hospitals who use pharmacologic prophylaxis most frequently (highest tertile) to least frequently (lowest tertile). *p Value = 0.05 in comparing overall 90-d composite adverse event rates at the hospitals with highest VTE pharmacologic prophylaxis use practices vs lowest use tertile hospitals (2.3% vs 3.6%).

Table 1

Patient and Clinical Characteristics Stratified by Receipt of Perioperative Venous Thromboembolism Pharmacologic Prophylaxis

	No perioperative VTE pharmacologic prophylaxis (n=1,826)	**Perioperative VTE pharmacologic prophylaxis (n=2,369)**	**p Value**
Age, y, mean ± SD	61.4 ± 15.7	60.9 ± 15.4	0.33
Female sex, n (%)	991 (54.3)	1,277 (53.9)	0.81
Smoker, n (%)	285 (15.8)	391 (16.7)	0.47
BMI, n (%) <20 20-25 25-30 >30	147 (8.8) 506 (30.1) 590 (35.1) 437 (26.0)	173 (7.8) 660 (29.8) 729 (32.9) 651 (29.4)	0.1
Hypertension, n (%)	787 (43.2)	1,033 (43.6)	0.78
Coronary artery disease, n (%)	211 (11.6)	258 (10.9)	0.47
Previous history of DVT/PE, n (%)	52 (2.9%)	96 (4.1%)	0.04
Length of stay, d, mean ± SD	7.6 ± 6.8	7.8 ± 9.8	0.66
OR time, min, mean ± SD	156.0 ± 95.8	155.5 ± 92.1	0.85
Charlson comorbididty index, n (%) 0 1 2 3+ Mean± SD	733 (40.1) 163 (8.9) 381 (20.9) 549 (30.1) 0.33±0.65	977 (41.2) 225 (9.5) 548 (23.1) 619 (26.1) 0.40±0.70	0.07
Indication for procedure, n (%) Malignancy IBD	716 (39.2) 140 (7.7)	916 (38.7) 208 (8.9)	0.72 0.20
Application of pneumatic compressions, n (%)	1,641 (91.0)	2,223 (94.4)	<0.001

VTE, venous thromboembolism.

Table 2

Univariate and multivariate regression analysis of 90-day venous thromboembolism events (VTE) and composite adverse events (CAE)

	Crude Odds Ratio (95% CI) 90-d CAE	Adjusted Odds Ratio (95% CI)* 90-d CAE	Crude Odds Ratio (95% CI) 90-d VTE	Adjusted Odds Ratio (95% CI)* 90-d VTE
Perioperative VTE pharmacologic prophylaxis	0.59 (0.42-0.83)	0.64 (0.44-0.93)	0.58 (0.35-0.98)	0.62 (0.36-1.06)
Age	1.04 (1.03-1.06)	1.04 (1.02-1.06)	1.01 (0.99-1.03)	1.01 (0.99-1.03)
Sex	0.97 (0.69-1.37)	1.03 (0.72-1.48)	0.96 (0.58-1.61)	0.88 (0.4-1.96)
Smoking	1.10 (0.70-1.73)	1.41 (0.86-2.32)	0.90 (0.44-1.84)	0.89 (0.4-1.96)
Previous history of VTE	1.73 (0.83-3.61)	1.49 (0.71-3.13)	2.53 (0.99-6.42)	2.32 (0.88-6.09)
Charlson Comorbidity Index 1 2 3+	 1.10 (0.55-2.23) 1.59 (0.99-2.52) 1.98 (1.31-3.01)	 0.92 (0.45-1.89) 1.19 (0.72-1.97) 1.38 (0.87-2.21)	 0.84 (0.29-2.45) 1.41 (0.73-2.71) 1.33 (0.71-2.49)	 0.85 (0.29-2.5) 1.65 (0.84-3.25) 1.36 (0.68-2.71)
Pneumatic compression	0.79 (0.43-1.44)	0.82 (0.43-1.57)	0.57 (0.26-1.27)	0.54 (0.24-1.2)
Method of operation (open)†	1.96 (1.23-3.11)	1.52 (0.94-2.48)	1.87 (0.94-3.7)	1.57 (0.77-3.21)
Type of operationa‡ Left hemicolectomy Low anterior resection Abdominal perineal resection Total abdominal colectomy Colostomy takedown Perineal proctectomy	 0.82 (0.5-1.34) 0.63 (0.41-0.97) 0.78 (0.35-1.74) 1.2 (0.63-2.29) 0.82 (0.11-6.09) 1.05 (0.14-7.94)	 0.81 (0.48-1.38) 0.83 (0.52-1.3) 0.82 (0.37-1.83) 2.45 (1.25-4.82) 1.34 (0.15-12.05) 1.31 (0.17-10.18)	 1.37 (0.65-2.91) 1.21 (0.62-2.35) 0.37 (0.05-2.8) 2.69 (1.14-6.36) 2.78 (0.36-21.62) -	 1.3 (0.63-2.69) 1.42 (0.72-2.83) 0.35 (0.05-2.65) 3.84 (1.63-9.07) 4.43 (0.48-41.27) -
Year of operation 2006 2007 2008 2009	 0.44 (0.21-0.88) 0.54 (0.28-1.05) 0.34 (0.18-0.67) 0.19 (0.07-0.48)	 0.39 (0.19-0.81) 0.49 (0.25-0.96) 0.36 (0.18-0.71) 0.20 (0.075-0.53)	 0.73 (0.24-2.25) 0.61 (0.21-1.84) 0.55 (0.19-1.61) 0.17 (0.03-0.92)	 0.63 (0.19-2.10) 0.68 (0.22-2.14) 0.63 (0.21-1.89) 0.17 (0.03-1.03)

CAE, composite adverse event; VTE, venous thromboembolism.

*Adjusted for all other variables listed.

†Compared to laparoscopic procedures.

‡Compared to right hemicolectomies.