Preoperative Chemoprophylaxis Is Safe in Major Oncology Operations and Effective at Preventing Venous Thromboembolism

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BACKGROUND: We prospectively evaluated the safety and efficacy of adding preoperative chemoprophylaxis to our institution's operative venous thromboembolism (VTE) prophylaxis policy as part of a physician-led quality improvement initiative.

STUDY DESIGN: Patients undergoing major cancer surgery between August 2013 and January 2014 were screened according to service-specific eligibility criteria and targeted to receive preoperative VTE chemoprophylaxis. Bleeding, transfusion, and VTE rates were compared with rates of historical controls who had not received preoperative chemoprophylaxis.

RESULTS: The 2,058 eligible patients who underwent operation between August 2013 and January 2014 (post-intervention) were compared with a cohort of 4,960 patients operated on between January 2012 and June 2013, who did not receive preoperative VTE chemoprophylaxis (pre-intervention). In total, 71% of patients in the post-intervention group were screened for eligibility; 82% received preoperative anticoagulation. When compared with the pre-intervention group, the post-intervention group had significantly lower transfusion rates (pre- vs post-intervention, 17% vs 14%; difference 3.5%, 95% CI 1.7% to 5%, $p = 0.0003$) without significant difference in major bleeding (difference 0.3%, 95% CI −0.1% to 0.7%, $p = 0.2$). Rates of deep venous thrombosis (1.3% vs 0.2%; difference 1.1%, 95% CI 0.7% to 1.4%, $p < 0.0001$) and pulmonary embolus (1.0% vs 0.4%; difference 0.6%, 95% CI 0.2% to 1%, $p = 0.017$) were significantly lower in the post-intervention group.

CONCLUSIONS: In patients undergoing major cancer surgery, institution of a single dose of preoperative chemoprophylaxis, as part of a physician-led quality improvement initiative, did not increase bleeding or blood transfusions and was associated with a significant decrease in VTE rates. (J Am Coll Surg 2016;222:129−137. © 2016 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Venous thromboembolism (VTE) is a common complication of hospitalization and is associated with significant morbidity and mortality.[1] Although the link between VTE and cancer has been known since Trosseau's seminal observations,[2] VTE remains a frequent cause of morbidity during treatment for cancer.

CME questions for this article available at http://jacscme.facs.org

Disclosure Information: Authors have nothing to disclose. Timothy J Eberlein, Editor-in-Chief, has nothing to disclose.

Support: This research was funded in part through the NIH/NCI Cancer Center Support Grant P30 CA008748 to Memorial Sloan Kettering Cancer Center.

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Members of the Memorial Sloan Kettering Cancer Center Venous Thromboembolism Task Force are listed in the Appendix.

Received July 1, 2015; Revised October 26, 2015; Accepted November 9, 2015.

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http://dx.doi.org/10.1016/j.jamcollsurg.2015.11.011
ISSN 1072-7515/15

Abbreviations and Acronyms

DVT = deep venous thrombosis
GMT = gastric and mixed tumor service
HITT = heparin-induced thrombocytopenia
HPB = hepatopancreaticobiliary service
LMWH = low molecular weight heparin
PE = pulmonary embolism
QI = quality improvement
SSE = surgical secondary events
UFH = unfractionated heparin
VTE = venous thromboembolism

Cancer patients are not only more likely to develop a postoperative VTE than patients undergoing surgery for other indications,[3] but those with a VTE are also more likely to develop a subsequent VTE than patients without an underlying malignancy.[4] Although different malignancies have different thrombotic potential, cancer is associated with a 4-fold increase in thrombosis, and chemotherapy is associated with a 6.5-fold increase in thrombosis.[5] Additionally, cancer patients have a much higher risk of death after VTE than noncancer patients.[6] Surgery and systemic chemotherapy, the mainstays of modern cancer care, are both associated with increased risk of VTE in cancer patients.[5,7,8] Though numerous studies[9-17] have demonstrated that postoperative anticoagulation decreases the rate of symptomatic and asymptomatic VTE in surgical oncology patients, the effect of adding preoperative anticoagulation to postoperative VTE prophylaxis is largely unknown.

No large studies have directly investigated either the safety or the efficacy of a single preoperative dose of chemical VTE prophylaxis. Despite this relative lack of evidence, guidelines from the European Society of Medical Oncology,[18] the American Society of Clinical Oncology,[19] and the American College of Chest Physicians[20] recommend institution of VTE prophylaxis preoperatively with either low molecular weight heparin (LMWH) or unfractionated heparin (UFH) in cancer patients undergoing surgery.

Since 2001, our institution has been prospectively tracking postoperative complications using our Surgical Secondary Events (SSE) database.[21] Adverse events are graded on a 1 to 5 scale that is a modification of the Clavien-Dindo classification,[22] with increasing severity indicated by the level of intervention required to treat the event. Grade 1 and 2 events, those requiring bedside care and either oral (grade 1) or intravenous (grade 2) medicine are defined as minor events. Grades 3 to 5 require invasive intervention (grade 3), result in chronic organ disability (grade 4), or death (grade 5); all are defined as major events.

The American College of Surgeons National Surgical Quality Improvement Project (NSQIP) provides member hospitals with risk-adjusted rankings on the incidence of postoperative adverse events, including VTE.[23] Widely adopted, NSQIP provides bench-marking of events between hospitals and has led to a decrease in adverse events at participating institutions.[24] Although Memorial Sloan Kettering Cancer Center (MSKCC) was recently recognized by NSQIP for achieving meritorious outcomes in surgical patient care,[25] higher than expected rates of DVT and PE were identified.[25]

In response, the MSKCC VTE Task Force was convened and it directed a physician-led prospective quality improvement (QI) initiative to investigate the safety and efficacy of instituting preoperative chemical prophylaxis with LMWH or UFH in patients undergoing major operations for cancer.

METHODS

Intervention

We performed a single institution prospective, nonrandomized, historical cohort-comparison trial assessing the safety (primary and secondary endpoints) and efficacy (secondary endpoint) of adding preoperative chemoprophylaxis to our peri- and postoperative VTE policies, which were not altered. The MSKCC VTE Task Force included an attending surgeon from the surgical services performing major adult abdominal, thoracic, or orthopaedic procedures within the Department of Surgery at Memorial Sloan Kettering Cancer Center (colorectal, gastric, and mixed tumor [GMT], gynecology, hepatopancreaticobiliary [HPB], orthopaedic, thoracic, and urology) in addition to representatives from the Departments of Anesthesia and Critical Care Medicine, Hematology, Clinical Pharmacy, Pre- and Perioperative Nursing Services, and Biostatistics and Epidemiology.

Service-specific inclusion criteria for administration of preoperative VTE prophylaxis were formulated based on review of current literature and guidelines. Participating services included the colorectal, GMT, gynecology, HPB, thoracic, and urology services. Final inclusion criteria during the QI initiative are listed in Table 1. Patients were screened by the nurse practitioners on the Preoperative Surgical Testing service. Contraindications to anticoagulation included patients with any of the following conditions: a diagnosed allergy to LMWH or UFH; a known brain mass; platelet counts $< 50 \times 10^9$/L; serum creatinine ≥ 2 mg/dL; an active transfusion requirement within the last week; or a diagnosis or history of heparin-induced thrombocytopenia and thrombosis (HITT). In appropriate patients, orders were written for

Table 1. Service-Specific Inclusion Criteria for Services Included in the 6-Month Pilot of Preoperative Venous Thromboembolism Prophylaxis

Service	Inclusion criteria
Colorectal	All inpatient procedures
GMT	All inpatient procedures
GYN	Any laparotomy; laparoscopy with BMI > 40 kg/m^2 and expected OR time > 3 h
Thoracic	All inpatient procedures
Urology	Radical nephrectomy and radical cystectomy

GMT, gastric and mixed tumor service; GYN, gynecology service; OR, operating room.

either LMWH (40 mg enoxaparin) or UFH (5,000 units unfractionated heparin) to be given subcutaneously in the preoperative holding area by the nursing staff within 2 hours of operation. Orders were written using an order set created specifically for this QI project that included both the service-specific inclusion criteria as well as the contraindications to preoperative chemoprophylaxis. Low molecular weight heparin was the default anticoagulant during the trial, with UFH reserved for patients who were planned to receive an epidural catheter. Patients on pre-existing anticoagulation remained at their standard dosing. Patients undergoing emergent operations were excluded from the pilot.

Attending surgeons had the opportunity to change the ordered preoperative agent (LMWH or UFH) or to discontinue preoperative anticoagulation. Patients who had been exposed to heparin within 90 days of their planned operation or had a platelet count $< 100 \times 10^9$/L were ordered for a preoperative antiheparin antibody testing to rule out undiagnosed HITT. Preoperative prophylactic anticoagulation was not ordered until this result was known, and if positive, both the attending surgeon and the hematology service were alerted. Postoperative VTE prophylaxis was administered according to existing institutional VTE prophylaxis policies, which were not altered. Beginning on postoperative day 1, patients receive either UFH (5,000 units, subcutaneous, 2 to 3 times daily) or LMWH (enoxaparin 30 to 40 mg subcutaneously, once daily) for the duration of their hospital stay. Dosing adjustments are made in consultation with the hematology and nephrology services, as necessary, and patients have sequential compression devices placed in the operating room.

Study of the intervention

This QI initiative began on July 15, 2013, with a planned 2-week rollout before beginning data capture on August 1. The primary endpoint was the rate of major bleeding events (grade ≥ 3 in our SSE database).[21] Secondary endpoints included the rate of DVT and PE, the rate of documented bleeding complications (regardless of grade), and the rate of blood transfusion. Adverse events, including those diagnosed post-discharge, were collected from our institutional SSE database as well as administrative data compiled after discharge. As per our standard practice, patients in the post-intervention cohort did not receive surveillance for asymptomatic VTEs.

Analysis

Patients in the post-intervention group were compared with a cohort of patients who underwent surgery between January 1, 2012 and June 30, 2013 (pre-intervention group), who were identified from our institutional medical record using identical inclusion criteria to those used for the post-intervention group (with the difference that the pre-intervention group did not, as a standard, receive preoperative VTE chemoprophylaxis). Rates of bleeding, transfusion, DVT, PE, and missed doses of postoperative VTE prophylaxis in both groups were compared using the chi-square test. Within the post-intervention group, rates of screening (defined as opening of the project-specific electronic order set), and receipt of preoperative VTE prophylaxis were also analyzed. All analysis was conducted using Stata 12 (StataCorp LP).

RESULTS

In total, 2,058 patients in the post-intervention group (August 1, 2013 to January 31, 2014) were compared with 4,960 patients in the pre-intervention group (January 1, 2012 to June 30, 2013). Service-specific inclusion criteria during the pilot are shown in Table 1. Table 2 shows clinical characteristics for both groups, including the percentage of operations performed by the included services, which did not significantly differ between the 2 timeframes.

Of the 2,058 patients undergoing surgery in the post-intervention group, 1,463 (71%) were evaluated by the pre-surgical testing service for eligibility to receive preoperative anticoagulation (Table 3). Service-specific evaluation rates ranged from 43% of eligible patients on the gynecology service to 84% of patients on the colorectal service. The majority of evaluated patients (1,148 of 1,463, 78%) received preoperative anticoagulation, ranging from 52% of patients on the urology service to 84% of patients on the thoracic service. Services with the least complex inclusion criteria (colorectal, GMT, and thoracic) had the highest rates of evaluation. One hundred twenty-nine patients in the pilot were evaluated and were eligible for preoperative coagulation, but had no order placed by pre-surgical testing. The most common reason for not placing an order was "Attending Review

Table 2. Case Volume for the Pilot and Comparison Cohorts

Variable	Pre-intervention group (January 1, 2012 to June 30, 2013) (n = 4,960)	Post-intervention group (August 1, 2013 to January 31, 2014) (n = 2,058)	p Value
Age, y, median (IQR)	62 (52–71)	62 (52–71)	NS
Male sex, n (%)	2,400 (48)	925 (45)	0.009
BMI, kg/m^2, median (IQR)	27 (24–31)	27 (24–31)	NS
LOS, d, median (IQR)	5.0 (3.0–7.0)	4.0 (2.0–7.0)	NS
Race, n (%)			
Asian	285 (5.7)	133 (6.5)	0.002
Black	250 (5.0)	128 (6.2)	
Native American	2 (<0.1)	0 (0)	
White	4,239 (85)	1,687 (82)	
Unknown	184 (3.7)	110 (5.3)	
All cases, n	4,960	2,058	
By service, n (%)			
Colorectal	1,200 (24)	474 (23)	NS
GMT	943 (19)	369 (18)	
GYN	509 (11)	314 (15)	
Thoracic	1,794 (36)	689 (33)	
Urology	514 (10)	212 (10)	

GMT, gastric and mixed tumor service; GYN, gynecology service; IQR, interquartile range; LOS, length of stay.

Requested" (55 patients, 42% of evaluated patients who were eligible, but had no anticoagulation order placed), signifying the pre-surgical testing nurse practitioner wanted to defer the anticoagulation decision to the attending surgeon. This often occurred in the context of an HITT test that had no results by the time the nurse practitioner reviewed the patient's lab results and eligibility for preoperative chemoprophylaxis. An additional 30 patients (23% of screened patients who were not ordered anticoagulation) had no contraindication noted by the pre-surgical testing service but were not ordered for preoperative anticoagulation; the remaining 44 patients (34% of screened patients who were not anticoagulated) had strict contraindications to anticoagulation (active bleeding, n = 13; brain lesion, n = 9; serum creatinine ≥ 2 mg/dL, n = 9; HITT or other heparin allergy, n = 7; thrombocytopenia, n = 6). Of the 595 patients who were not evaluated by pre-surgical testing, 58 (10%) received preoperative anticoagulation, for a total of 1,206 patients who received preoperative chemoprophylaxis in the post-intervention group.

Table 3. Preoperative Screening and Anticoagulation for Eligible Patients in the Post-Intervention Group

Variable	n	Screened, n (% eligible)	Received chemoprophylaxis, n (% eligible; % screened)
All cases	2,058	1,463 (71)	1,148 (56; 78)*
Service			
Colorectal	474	397 (84)	311 (65; 78)
GMT	369	259 (70)	200 (54; 77)
GYN	314	135 (43)	112 (35; 83)
Thoracic	689	544 (79)	459 (67; 84)
Urology	212	128 (60)	66 (31; 52)

*An additional 58 patients who were not screened were subsequently ordered for, and received, preoperative chemoprophylaxis.
GMT, gastric and mixed tumor service; GYN, gynecology service.

The 2,058 patients in the post-intervention cohort, when compared with the 4,960 patients in the pre-intervention cohort (only 40 of whom received preoperative chemoprophylaxis), did not have a statistically significant difference in the rate of major bleeding events (pre- vs post-intervention, 0.8% vs 0.5%; difference 0.3%; 95% CI −0.15 to 0.7%, p = 0.2). Additionally, patients in the post-intervention cohort had lower rates of both documented bleeding (4.2% vs 2.5%; difference 1.7%; 95% CI 0.8% to 2.6%, p = 0.001) and blood transfusion (17% vs 14%; difference 3.1%; 3.1%; 95% CI 1.3% to 4.9%, p = 0.001), as well as lower rates of documented DVT (1.3% vs 0.2%; difference 1.1%; 95% CI 0.7% to 1.4%, p < 0.0001), and PE (1% vs 0.4%; difference 0.6%; 95% CI 0.2% to 1%, p = 0.017). There were no changes to institutional or service-specific guidelines regarding use of imaging for investigation of VTE during the study period, and imaging rates were also lower in the post-intervention group (11% vs 7.6%; difference 3.4%; 95% CI 1.9% to 4.8%, p < 0.0001).

The pre-intervention group had a higher rate of missed postoperative VTE prophylaxis doses (3.9% vs 3.3%; difference 0.7%; 95% CI 0.4% to 0.9%, $p < 0.0001$) as well as a higher percentage of patients with at least 1 missed postoperative dose (39% vs 31%; difference 8%; 95% CI 6% to 11%, $p < 0.0001$) (Table 4).

In total, 373 patients in the post-intervention group met our study's criteria (platelets $\leq 100 \times 10^9$/L or exposure to heparin within 90 days) for HITT screening before administration of preoperative chemoprophylaxis using an enzyme linked immunosorbent assay (ELISA) for heparin-dependent antiplatelet antibodies. Of the 373 patients screened, only 10 (2.6%) had an ELISA that was either borderline (8 of 373, 2%) or positive (2 of 373, 0.5%). Borderline or positive patients did not receive additional confirmatory testing. Subsequent to non-negative HITT tests, 2 patients had heparin listed as an allergy in their chart and electronic medical record; 7 patients, including the 2 patients with a positive test, received postoperative heparin; and no patients developed clinical HITT.

DISCUSSION

We conducted this single institutional, nonrandomized prospective QI project to evaluate the safety and efficacy of adding a single preoperative dose of either LMWH or UFH to current peri- and postoperative VTE prophylaxis policies. Though the European Society of Medical Oncology,[18] the American Society of Clinical Oncology,[19] and the American College of Chest Physicians[20] all recommend beginning VTE prophylaxis preoperatively, few studies have examined the additive effect of preoperative chemoprophylaxis to peri- and postoperative chemoprophylaxis. The initial studies of VTE prophylaxis in general surgery and surgical oncology patients all included preoperative VTE prophylaxis,[9-13] but they occurred in an era when elective surgery patients were routinely admitted to the hospital before surgery, placing them at increased risk of VTE. In fact, the trial design for the early VTE prophylaxis studies comparing different medications all included a dose 12 hours before the operation and another dose within 2 hours before skin incision.[9-13] Previous trial designs and dosing strategies are not reflective of current practice patterns, making it difficult to extrapolate the potential added effect of the single dose of preoperative heparin to modern VTE prophylaxis. As a result of the discrepancy between initial trial design and our current practice, as well as the magnitude of the surgery we typically perform, there was significant concern among our attending staff as to whether providing our patients with preoperative VTE chemoprophylaxis was safe. As a result, we structured this QI intervention primarily as a safety assessment.

Additionally, there is considerable controversy regarding the mandated use of VTE rates as a publicly reported quality measure. Prophylaxis for DVT is known to be imperfect,[26] and there is well characterized surveillance bias regarding publicly reported VTE rates.[26-31] Reporting controversies aside, VTE remains an important public health concern resulting in substantial morbidity.[1] Missed prophylaxis doses

Table 4. Postoperative Adverse Events, Deep Vein Thromboses, and Pulmonary Embolism by Timeframe

Variable	Pre-intervention (n = 4,960)		Post-intervention (n = 2,058)		Absolute difference, %	95% CI, %	p Value
	n	%	n	%			
Any bleeding*	210	4.2	52	2.5	1.7	0.8, 2.6	0.001
Bleed grade 3+	42	0.8	11	0.5	0.3	−0.1, 0.7	0.2
Any transfusion	860	17	285	14	3.5	1.7, 5	0.0003
pRBC transfusion	829	17	280	14	3.1	1.3, 4.9	0.001
Any VTE	108	2.2	13	0.6	1.5	1.0, 2.1	<0.0001
DVT	63	1.3	4	0.2	1.1	0.7, 1.4	<0.0001
PE	50	1	9	0.4	0.6	0.2, 1.0	0.017
Any imaging ordered	546	11	157	7.6	3.4	1.9, 4.8	<0.0001
Ultrasound	280	5.6	70	3.4	2.2	1.2, 3.3	<0.0001
CT	372	7.5	102	5	2.5	1.4, 3.7	0.0001
Postoperative VTE prophylaxis							
Total missed doses	3,361	3.9	1,004	3.3	0.7	0.4, 0.9	<0.0001
Patients with missed doses	1,955	39	637	31	8	6, 11	<0.0001

In this analysis, all patients in the pilot were considered to have received preoperative anticoagulation, according to the final service-specific inclusion criteria.
*Bleeding includes surgical secondary event entries of anemia, gastrointestinal bleeding, hemorrhage, hematoma, hematuria, bladder, vaginal bleeding, and hemothorax.
DVT, deep venous thrombosis; PE, pulmonary embolism; pRBC, packed RBCs; VTE, venous thromboembolism.

remain the major modifiable risk factor for the development of DVT and PE in the general surgery population.[32,33]

The NSQIP provides risk adjusted outcomes that allow institutions to track individual performance compared with other member institutions. After adjusting for case mix and patient comorbidities, our institutional VTE rate was identified as higher than expected on repeated NSQIP semi-annual reports. Internal review identified high rates of compliance with our existing DVT-prophylaxis policies, which did not include preoperative anticoagulation. After comparing VTE prophylaxis guidelines[18-20] with our institutional guidelines, we began a QI initiative to primarily study the safety, and secondarily, the efficacy, of adding a single dose of preoperative VTE prophylaxis to our current institutional VTE prophylaxis policy in select patients. We found that the single dose of preoperative VTE prophylaxis was safe and was associated with significantly lower DVT and PE rates (Table 4). These results held true when we compared the subset of NSQIP patients in the pre- and post-intervention cohorts. These findings have resulted in the revised institutional guidelines for addition of preoperative prophylaxis in surgical patients as outlined in Table 5. We have not yet received an institutional NSQIP semi-annual report reflecting our new institutional guidelines.

Implementation challenges

A significant challenge identified during the pilot involved the use of LMWH as the primary anticoagulant, which often resulted in disruptions to the flow of routine clinical care given its contraindication in patients receiving neuraxial analgesia. Low molecular weight heparin was chosen as the preferred chemoprophylaxis agent for the QI initiative because of its 10-fold lower association with HITT. Although there were no instances in which the LMWH was administered inadvertently in a patient planned for an epidural, the additional surveillance and failsafe mechanisms necessary to ensure this interfered significantly with clinical workflow. Given the extra surveillance in patients planned for an epidural, and the fact that a significant number of surgeons were cancelling LMWH orders in favor of UFH (56% of all patients who received chemoprophylaxis received UFH), our institutional policy enacted as a result of this QI initiative uses UFH for all preoperative chemoprophylaxis. Our postoperative chemoprophylaxis agents were not changed during either the pre- or post-intervention timeframes; both UFH and LMWH may be used beginning on postoperative day 1.

Screening for HITT also proved to be a significant disruptor of workflow, with "positive" screens in pre-surgical testing a frequent impediment to the ordering of preoperative chemoprophylaxis. Despite aggressive screening we did not identify a single patient with clinical HITT, and as a result, we have abandoned routine screening for HITT.

Table 5. Current Service-Specific Guidelines for Preoperative Venous Thromboembolism Prophylaxis Adopted Based on Pilot Results

Service	Current institutional preoperative anticoagulation guidelines
Colorectal	All inpatient procedures
GMT	All inpatient procedures
GYN	Any laparotomy
HPB	All inpatient procedures without any of the following service-specific exclusion criteria: platelets $< 100 \times 10^9$/L, INR > 1.5, clopidogrel or aspirin within 7 days before operation, bilirubin > 4 mg/dL in the 3 weeks before operation, current bilirubin > 2 mg/dL, history of cirrhosis
Thoracic	All inpatient procedures
Urology	Radical nephrectomy and radical cystectomy

GMT, gastric and mixed tumor service; GYN, gynecology service; HPB, hepatopancreaticobiliary service; INR, international normalized ratio.

Limitations

Our study, an observational study with historical controls, has several limitations. Because we were comparing the pre- and post-intervention cohorts, we could not alter our institutional tracking of adverse events without adding significant observational bias, so it is possible that we are underestimating our VTE rate. We primarily captured VTEs documented in our institutional SSE database,[21] which captures inpatient and post-discharge adverse events. Additionally, we combined our SSE database entries with post-discharge administrative data compiled on our patients in order to decrease the possibility of not capturing a documented VTE. We used identical selection criteria for both the pre-intervention and post-intervention cohorts to identify patients, and after retrieving our patient list, we confirmed that all patients screened by pre-surgical testing were included in the post-intervention cohort. It is possible we used incorrect criteria to identify patients and included ineligible patients in both cohorts. However, such an error would likely bias our results against our findings because we would have included ineligible patients who were not anticoagulated and yet considered them anticoagulated in our analysis. Though we did not screen all eligible patients for inclusion, this also biases against our null hypothesis because the majority of unscreened patients did not receive preoperative VTE prophylaxis, but were analyzed as if they did.

There are significant differences between the pre- and post-intervention groups in the frequency of image use and in the frequency of missed postoperative VTE prophylaxis. Imaging frequency[26-31] and missed doses[26,32,33] are both known to affect VTE rates, contributing to the well-characterized surveillance bias regarding publically reported VTE rates.[26-31] Differences in imaging frequency and missed postoperative doses between the pre- and post-intervention groups (Table 4) may account for the higher VTE rate in the pre-intervention group. The primary endpoint of this QI initiative was to test whether or not preoperative VTE prophylaxis was safe in the surgical oncology patient; the VTE rate (as well as DVT and PE rates, individually) was a secondary endpoint. Because this is an observational study with historical controls, it is impossible to determine whether the change in imaging use is the result of the decreased VTE incidence (due to a decrease in clinical suspicion) or the cause of the decreased VTE incidence (due to decreased detection of asymptomatic thromboses). In the post-intervention cohort, the decreased number of total missed postoperative doses of VTE prophylaxis (as well as the decreased percentage of patients who missed any postoperative dose) could explain the decreased VTE rate. This finding, however, further reinforces that preoperative VTE prophylaxis is safe in our patient population. Of all the reasons given for skipping a dose of VTE prophylaxis (in preparation for epidural removal, as a result of a planned invasive procedure, patient refusal, patient condition, or other nonspecific reasons), patient condition was the most common condition listed by the patient's treating nurse (1,820 doses/4,365 total missed doses, 41.7% of all missed doses). When compared with the pre-intervention time period, "patient condition" was the documented reason for a skipped dose significantly less frequently in the post-intervention cohort (2.3% of missed doses vs 2% of missed doses; difference 0.3%; 95% CI 0.1% to 0.5%, $p = 0.002$).

Subsequent protocol changes

Since the internal release of these results, the services have re-reviewed their service-specific inclusion criteria, and 2 have made changes. With the institutional change to UFH, the HPB service has added service-specific exclusion criteria (platelets $< 100 \times 10^9$/L, international normalized ratio > 1.5, clopidogrel or aspirin within 7 days before operation, bilirubin > 4 mg/dL in the 3 weeks before operation, current bilirubin > 2 mg/dL, or a history of cirrhosis) in addition to institutional exclusion criteria, and HPB patients not excluded by either set of criteria now receive preoperative anticoagulation. Though their patients were not included in the QI initiative, on seeing that preoperative chemoprophylaxis did not increase major bleeding while also decreasing our VTE rate, they developed their additional service-specific exclusion criteria in Table 5. Additionally, it was difficult to operationalize the gynecology inclusion criteria, a fact reflected in the low percentage of patients screened by pre-surgical testing. Their criteria have been revised, and currently laparotomies are the only gynecology cases to receive preoperative anticoagulation. The current institutional inclusion criteria, finalized after internal distribution of these results and reflecting these 2 changes, are shown in Table 5.

CONCLUSIONS

The addition of a single dose of preoperative VTE prophylaxis did not result in a significant increase in major bleeding complications in patients undergoing major cancer surgery. When compared with a pre-intervention cohort that did not receive the preoperative dose of either UFH or LMWH VTE chemoprophylaxis, the post-intervention cohort that received preoperative VTE prophylaxis did not have a significantly different rate of major bleeding, and had significantly lower rates of any documented bleeding complication, blood transfusions, DVT, and PE. Though there were differences in postoperative imaging and missed doses of postoperative VTE prophylaxis, we believe the addition of preoperative DVT prophylaxis in appropriately selected patients undergoing major cancer surgery, is safe and effective in reducing rates of VTE. We now administer a single dose of UFH (5,000 units subcutaneously) preoperatively to all eligible patients.

APPENDIX

Members of the Memorial Sloan Kettering Cancer Center Venous Thromboembolism Task Force

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Acknowledgment: The authors wish to acknowledge Marina Kerpelev, Senior Data Solutions Analyst in the Data and Information Service at Memorial Sloan Kettering Cancer Center, for her invaluable assistance throughout this pilot.

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