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

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Abstract

Background—We prospectively evaluated the safety and efficacy of adding pre-operative 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 pre-operative VTE chemoprophylaxis. Bleeding, transfusion, and VTE rates were compared to historical controls who had not received pre-operative chemoprophylaxis.

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

Keywords

Venous Thromboembolism; Deep Venous Thrombosis; Pulmonary Embolism; Surgical Quality Improvement; National Surgical Quality Improvement Project; Surgical Secondary Events; Heparin Induced Thrombocytopenia and Thrombosis

Introduction

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.

Cancer patients are not only more likely to develop a post-operative 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) While 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 following VTE than non-cancer 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 post-operative anticoagulation decreases the rate of symptomatic and asymptomatic VTE in surgical oncology patients, the effect of adding pre-operative anticoagulation to post-operative 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 pre-operatively with either low molecular weight heparin (LMWH) or unfractionated heparin (UFH) in cancer patients undergoing surgery.

Since 2001 our institution has been prospectively tracking post-operative complications using our Surgical Secondary Events (SSE) database (21). Adverse events are graded on a 1–5 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 – 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). While 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 directed a physician led prospective quality improvement (QI) initiative to investigate the safety and efficacy of instituting pre-operative chemical prophylaxis with LMWH or UFH in patients undergoing major operations for cancer.

Methods

Intervention

We performed a single institution prospective, non-randomized, historical cohort-comparison trial assessing the safety (primary endpoint and secondary endpoints) and efficacy (secondary endpoint) of adding pre-operative chemoprophylaxis to our peri and post-operative 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 orthopedic procedures within the Department of Surgery at Memorial Sloan Kettering Cancer Center (Colorectal, Gastric and Mixed Tumor (GMT), Gynecology (GYN), Hepatopancreaticobiliary (HPB), Orthopaedic, Thoracic, and Urology) in addition to representatives from the Department of Anesthesia and Critical Care Medicine, Hematology, Clinical Pharmacy, Pre- and peri-operative Nursing services, and Biostatistics and Epidemiology.

Service-specific inclusion criteria for administration of pre-operative VTE prophylaxis were formulated based on review of current literature and guidelines. Participating services included the Colorectal, GMT, GYN, 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 Pre-operative Surgical Testing (PST) service. Contraindications to anticoagulation included patients with any of the following conditions: 1) a diagnosed allergy to LMWH or UFH, 2) a known brain mass, 3) platelets less than 50×10^9/l, patients, 4) serum creatinine 2 mg/dl, 5) an active transfusion requirement within the last week, or 6) a diagnosis or history of Heparin Induced Thrombocytopenia and Thrombosis (HITT). In appropriate patients, orders were written for either LMWH (40 mg Enoxaparin) or UFH (5,000 units unfractionated heparin) to be given subcutaneously in the pre-operative holding area by the nursing staff within two 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 pre-operative chemoprophylaxis. LMWH 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 pre-operative agent (LMWH or UFH) or to discontinue the pre-operative anticoagulation. Patients who had been exposed to heparin within 90 days of their planned operation or had a platelet count of less than 100 $\times 10^9$/l were ordered for a pre-operative anti-heparin 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 post-operative day #1 patients receive either UFH (5,000 units, sub-cutaneous, 2 – 3 times daily) or LMWH (enoxaparin 30 – 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 15th, 2013 with a planned two-week rollout prior to beginning data capture on August 1st. 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 to a cohort of patients who underwent surgery between January 1st 2012 and June 30th 2013 (pre-intervention group) that were indentified from our institutional medical record using identical inclusion criteria to the post-intervention group (with the difference that the pre-intervention group did not, as a standard, receive pre-operative VTE chemoprophylaxis). Rates of bleeding, transfusion, DVT, PE, and missed doses of post-operative VTE prophylaxis in both groups were compared using the chi squared test. Within the post-intervention group rates of screening (defined as opening of the project-specific electronic order set), and receipt of pre-operative VTE prophylaxis were also analyzed. All analysis was conducted using Stata 12 (StataCorp LP, College Station, TX).

Results

In total, 2,058 patient in the post-intervention group (August 1st, 2013 – January 31st, 2014) were compared to 4,960 patients in the pre-intervention group (January 1st, 2012 – June 30th, 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 two 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 pre-operative 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 pre-operative 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 and twenty nine patients in the pilot were evaluated and eligible for pre-operative coagulation but had no order placed by pre-surgical testing. The most common reason for not placing an order was "Attending Review 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 a HITT test that had not resulted by the time the nurse practitioner reviewed the patient's lab results and eligibility for pre-operative 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 pre-operative 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 pre-operative anticoagulation, for a total of 1,206 patients who received pre-operative chemoprophylaxis in the post-intervention group.

The 2,058 patients in the post-intervention cohort, when compared to the 4,960 patients in the pre-intervention cohort (only 40 of whom received pre-operative 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 – 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% – 2.6%, p = 0.001) and blood transfusion (17% vs 14%; difference 3.1%; 3.1%; 95% CI 1.3% – 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% – 1.4%, p<0.0001), and PE (1% vs 0.4%; difference: 0.6%; 95% CI 0.2% – 1%, p = 0.017). There were no changes to institutional or service-specific guidelines regarding utilization 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% – 4.8%, p < 0.0001). The pre-intervention group had a higher rate of missed post-operative VTE

prophylaxis doses (3.9% vs 3.3%; difference 0.7%; 95% CI: 0.4% – 0.9%, p < 0.0001) as well as a higher percentage of patients with at least one missed postoperative dose (39% vs 31%; difference 8%; 95% CI: 6% – 11%, p <0.0001) (Table 4).

In total, 373 patients in the post-intervention group met our study's criteria (platelets   100 $\times 10^9$/l or exposure to heparin within 90 days) for HITT screening prior to the administration of pre-operative 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 (8/373, 2%) or positive (2/373, 0.5%). Borderline or positive patients did not receive additional confirmatory testing. Subsequent to non-negative HITT tests, two patients had heparin listed as an allergy in their chart and electronic medical record, seven patients, including the two patients with a positive test, received post-operative heparin, and no patients developed clinical HITT.

Discussion

We conducted this single institutional, non-randomized, prospective QI project to evaluate the safety and efficacy of adding a single pre-operative dose of either LMWH or UFH to current peri- and post-operative 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 pre-operatively, few studies have examined the additive effect of pre-operative chemoprophylaxis to peri and post-operative chemoprophylaxis. The initial studies of VTE prophylaxis in general surgery and surgical oncology patients all included pre-operative VTE prophylaxis (9–13), but they occurred in an era when elective surgery patients were routinely admitted to the hospital prior to surgery, thus 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 two hours prior to 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 pre-operative 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 pre-operative 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 publically reported quality measure. DVT prophylaxis is known to be imperfect (26) and there is well characterized surveillance bias regarding publically reported VTE rates (26–31). Reporting controversies aside, VTE remains an important public health concern resulting in substantial morbidity (1). Missed prophylaxis doses remain the major modifiable risk factor for the development of DVT and PE in the general surgery population (32, 33).

NSQIP provides risk adjusted outcomes that allow institutions to track individual performance compared to 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 pre-operative anticoagulation. After comparing VTE prophylaxis guidelines (18–20) to our institutional guidelines, we began a QI initiative to primarily study the safety, and secondarily, the efficacy, of adding a single dose of pre-operative VTE prophylaxis to our current institutional VTE prophylaxis policy in select patients. We found that the single dose of pre-operative 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 pre-operative 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 anti-coagulant, which often resulted in disruptions to the flow of routine clinical care given its contraindication in patients receiving neuraxial analgesia. LMWH was chosen as the preferred chemoprophylaxis agent for the QI initiative because of its 10-fold lower association with HITT. While there were no instances where the LMWH was administered inadvertently in a patient planned for an epidural, the additional surveillance and failsafe mechanisms necessary to insure 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 pre-operative chemoprophylaxis. Our post-operative chemoprophylaxis agents were not changed during either the pre or post-intervention time frames; both UFH and LMWH may be used beginning on post-operative day one.

Screening for HITT also proved to be a significant disruptor to workflow with "positive" screens in pre-surgical testing a frequent impediment to the ordering of pre- pre-operative 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.

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 as 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 as the majority of unscreened patients did not receive pre-operative 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 utilization as well as the frequency of missed post-operative 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 post-operative 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 pre-operative 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 chance in imaging utilization 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 post-operative 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 pre-operative VTE prophylaxis is safe in our patient population. Off 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 non-specific 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 to 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% – 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 two have made changes. With the institutional change to UFH, the HPB service has added service-specific exclusion criteria (platelets $< 100 \times 10^9$/L, INR > 1.5, Plavix or Aspirin within 7 days prior to operation, bilirubin > 4mg/dl in the 3 weeks prior to operation, current bilirubin > 2mg/dl, or a history of cirrhosis) in addition to institutional exclusion criteria, and HPB patients not excluded by either set of criteria now receive pre-operative anticoagulation. Though their patients were not included in the QI initiative, upon seeing that pre-operative 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 presurgical

testing. Their criteria have been revised and currently laparotomies are the only GYN cases to receive pre-operative anticoagulation. The current institutional inclusion criteria, finalized after internal distribution of these results and reflecting these two changes, are shown in Table 5.

Summary

The addition of a single dose of pre-operative VTE prophylaxis did not result in a significant increase in major bleeding complications in patients undergoing major cancer surgery. When compared to a pre-intervention cohort that did not receive the pre-operative dose of either UFH or LMWH VTE chemoprophylaxis, the post-intervention cohort that received pre-operative 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 post-operative imaging and missed doses of postoperative VTE prophylaxis, we believe the addition of pre-operative DVT prophylaxis 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) pre-operatively to all eligible patients.

Acknowledgments

Abbreviations

VTE	Venous Thromboembolism
DVT	Deep Venous Thrombosis
PE	Pulmonary Embolism
NSQIP	National Surgical Quality Improvement Project
SSE	Surgical Secondary Events
GMT	Gastric and Mixed Tumor Service
GYN	Gynecology Service
pRBC	Packed Red Blood Cells
PCEA	Patient controlled epidural analgesia
HITT	Heparin induced thrombocytopenia
HPB	Hepatopancreaticobiliary service
ELISA	enzyme linked immunosorbent assay
QI	quality improvement

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Appendix 1. Members of the Memorial Sloan Kettering Cancer Center Venous Thromboembolism Task Force

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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; HPB, Hepatopancreaticobiliary Service

Table 2

Case Volume for the Pilot and Comparison Cohorts

	Pre-intervention group (January 1, 2012 – June 30, 2013) (n = 4,960)	Post-intervention group (August 1, 2013 – 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	4239 (85)	1687 (82)	
Unknown	184 (3.7)	110 (5.3)	
All cases, n	4,960	2,058	
By service, n (%)			
Colorectal	1200 (24)	474 (23)	NS
GMT	943 (19)	369 (18)	
GYN	509 (11)	314 (15)	
Thoracic	1794 (36)	689 (33)	
Urology	514 (10)	212 (10)	

GMT, Gastric and Mixed Tumor Service; GYN, Gynecology Service; LOS, length of stay.

Table 3

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

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

[*] 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.

Table 4

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

	Pre-intervention (n=4,960)	Post-intervention (n=2,058)	Absolute difference	95% CI	p Value
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 are considered to have received preoperative anticoagulation, according to the final service-specific inclusion criteria.

*
Bleeding includes SSE entries of Anemia, GI bleeding, Hemorrhage, Hematoma, Hematuria, Bladder, Vaginal Bleeding, and Hemothorax.

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, Plavix or Aspirin within 7 days prior to operation, bilirubin > 4 mg/dL in the 3 weeks prior to 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.