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Association Between Missed Doses of Chemoprophylaxis and VTE Incidence in a Statewide Colectomy Cohort

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Chemoprophylaxis reduces the incidence of postoperative venous thromboembolism (VTE), the leading cause of preventable inpatient death. Single-institution studies suggest that missed doses of inpatient chemoprophylaxis are common and associated with developing VTE.^{1,2} One health system-wide study found that missed doses were common at both academic and community hospitals.³ The concept of “defect-free” VTE prophylaxis has emerged, which includes prescription of optimal risk-appropriate prophylaxis and administration of every dose as prescribed.⁴

The Illinois Surgical Quality Improvement Collaborative (ISQIC) is a collaborative of 56 academic and community hospitals dedicated to improving the quality of surgical care in Illinois. ISQIC implemented a novel comprehensive postoperative inpatient VTE prophylaxis process measure to address shortcomings of existing quality measures such as the inability to accurately identify missed chemoprophylaxis doses.^{4,5} A previous analysis of ISQIC hospitals identified failure to provide defect-free postoperative inpatient VTE chemoprophylaxis in 18% of colectomies, with missed doses being a major contributor.⁶

The association between missed doses of postoperative chemoprophylaxis and VTE has not been examined in a large, multi-institutional cohort, and previous studies have lacked power to examine this association in detail. The objectives of this study were to (1) assess the incidence of missed doses of inpatient VTE chemoprophylaxis after colectomy in a statewide patient cohort, and (2) examine the association between missed chemoprophylaxis doses and postoperative VTE.

METHODS

We retrospectively reviewed 2 prospectively maintained databases, the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) procedure targeted dataset for colectomy (100% capture of cases for all hospitals) and the ISQIC online data

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platform ([ISQICdata.org](https://www.isqicdata.org)). In these databases, the same trained surgical clinical reviewers (SCRs) abstracted cases from ISQIC hospitals, with regular audits of both registries for data reliability and quality. SCRs abstracted the ISQIC measures at the same time as abstraction of NSQIP measures, and the ISQIC dataset was designed specifically to be easily merged with the NSQIP dataset. Eligible patients were those ≥ 18 years who underwent a colectomy between 1/2015 and 6/2017, excluding cases that included a proctectomy and patients from hospitals with missing or discontinuous abstraction.

Abstractors used a validated ISQIC process measure evaluating comprehensive postoperative inpatient VTE prophylaxis.^{5,6} The measure evaluates whether patients: (1) received defect-free postoperative inpatient chemoprophylaxis, (2) had an appropriate clinical exception to chemoprophylaxis, or (3) did not receive defect-free chemoprophylaxis and had no eligible exception. Preoperative prophylaxis was not evaluated in this measure. Acceptable chemoprophylaxis included FDA-approved forms of VTE chemoprophylaxis at standard doses and intervals, including heparin or low-molecular-weight heparin. Abstraction ended with nonadherence to the measure (ie, the first failure of postoperative chemoprophylaxis administration without appropriate exception) or discharge. In other words, the first time a dose was missed, nonadherence was noted and abstraction ceased.

Abstractors also collected demographic and clinical variables, including 30-day postoperative VTE through ACS NSQIP. Hospital characteristics were obtained from the American Hospital Association 2016 hospital survey and Center for Medicare Services 2016 Impact File. Cluster-corrected chi-square tests and multivariable logistic regression with robust clustered standard errors were used to assess associations between VTE incidence and missing ≥ 1 postoperative chemoprophylaxis dose, while adjusting for patient- and hospital-level confounders (Supplemental Tables 1, <http://links.lww.com/SLA/C459> and 2, <http://links.lww.com/SLA/C460>). Known risk factors for VTE and those with $P < 0.10$ on univariate analysis were included in multivariable analysis. Analyses were performed in the overall cohort and in subsets undergoing colectomy for indications known to be at differing risk for VTE.^{7,8}

RESULTS

Among 5327 patients from 39 hospitals undergoing colectomy for any indication, with appropriately prescribed chemoprophylaxis, 13.3% of patients missed ≥ 1 dose of chemoprophylaxis (Supplemental Fig. 1, <http://links.lww.com/SLA/C459>). The overall incidence of VTE was 2.1%. Among all colectomy patients missing ≥ 1 chemoprophylaxis dose, the VTE rate was 3.1% versus 1.9% for patients who received all doses, but this difference did not reach statistical significance on cluster-corrected analysis ($P = 0.12$) or multivariable regression (odds ratio (OR) 1.55 [0.97–2.46], Supplemental Table 3, <http://links.lww.com/SLA/C461>).

In the high-risk cohort of 2884 patients who underwent colectomy for cancer or inflammatory bowel disease, missing ≥ 1 chemoprophylaxis dose (13.8% missed a dose) was significantly associated with increased VTE events compared to those who received all doses, and this remained significant on multivariable analysis (4.0% vs 1.7%, $P = 0.016$; OR

2.41 [1.27–4.57]). In contrast, among 1266 patients with the lower-risk operative indication of diverticulitis, 10.0% missed 1 dose, with a 1.5% overall VTE rate and no association with missed doses (1.6% vs 0.8%, $P = 0.49$).

DISCUSSION

We found that 13% of post-colectomy inpatients did not receive all prescribed doses of inpatient VTE chemoprophylaxis in a large statewide patient cohort. At least 1 missed dose of chemoprophylaxis was associated with an over twofold increased incidence of VTE among patients at high-risk for VTE, specifically those undergoing colectomy for cancer or inflammatory bowel disease, but not in lower VTE risk patients. This is the first confirmation of an association between missed doses of postoperative chemoprophylaxis and VTE in a large, multi-institutional cohort, and identifies a specific population of patients for whom providing defect-free postoperative VTE chemoprophylaxis is particularly important.

One limitation of this study was the inability to examine the association between the specific number of chemoprophylaxis doses missed and VTE events. Nonadherence to the measure was defined as the first missed dose of chemoprophylaxis. This decision was made to balance the cumulative burden of data collection placed on data abstractors who were asked to evaluate all colectomy patients for measure adherence. Another limitation was the lack of data regarding postdischarge prophylaxis, which is especially important in the high-risk group. Although we were unable to identify how many doses were missed or if postdischarge prophylaxis was prescribed or administered, this study was still able to demonstrate that missing even 1 dose of inpatient, postoperative chemoprophylaxis is associated with increased VTE events in high-risk patients. Examining the relationship between VTE events and both the number of missed doses and the administration of postdischarge chemoprophylaxis are important areas for further study. Additionally, as a retrospective observational study, there is the possibility of unmeasured confounders (eg, advanced disease, difficult operation, use of enhanced recovery protocols) influencing the administration of doses and/or the VTE rate. Finally, these results reflect an association and cannot be assumed to indicate causation.

Missed doses of inpatient VTE chemoprophylaxis have been identified as a major contributor to nonadherence to best practice VTE prophylaxis in postoperative patients.⁶ The reasons for missed doses vary and most commonly are due to patient refusal and ordering errors.⁶ This study demonstrates that missed doses of VTE chemoprophylaxis may have serious consequences, particularly in patients at higher risk for VTE. Hospitals and providers should verify that patients receive all prescribed doses of postoperative VTE chemoprophylaxis, identify why doses are missed, and institute quality improvement efforts (eg, education and awareness interventions for patients and nurses^{9,10}) to ensure patients receive all appropriate doses of chemoprophylaxis. Improving adherence to VTE prophylaxis is a critical area for QI that is associated with lower rates of a preventable adverse outcome.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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