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The identification of risk factors for venous thromboembolism in gastrointestinal oncologic surgery

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ARTICLE INFO

Article history:
Received 15 March 2016
Received in revised form
6 June 2016
Accepted 26 June 2016
Available online 4 July 2016

Keywords:
VTE
Venous thromboembolism
ACS-NSQIP
Malignancy
Gastrointestinal

ABSTRACT

Background: The aim of this study was to examine the incidence and factors associated with occurrence of venous thromboembolism (VTE) in patients undergoing major gastrointestinal (GI) surgery for malignancy.

Methods: The American College of Surgeon's National Surgical Quality Improvement Program, Participant User File database was queried from 2005 to 2012 to study major GI operations performed for cancer. Predictors of VTE and their relation to survival were studied.

Results: In 79,300 patients, the incidence of deep venous thrombosis was 1.7%, and pulmonary embolism was 0.9% during the 30-d postoperative period. The highest rate of VTE occurred after esophagectomy (5.9%) followed by pancreatectomy (3.2%), hepatectomy (3.2%), gastrectomy (2.5%), enterectomy (2.3%), colectomy, and proctectomy (2.0%). On multivariate analysis, disseminated cancer, age $\geq$ 80 y, body mass index $>$ 35 kg/m^2, functional status, post operative sepsis, pulmonary dysfunction, and longer operative time were associated with occurrence of VTE. Occurrence of VTE was associated with mortality on multivariate analysis (odds ratio 2.4, 95% confidence interval 2.0-3.0, $P < 0.001$).

Conclusions: Absolute incidence of VTE after major GI surgery is low but is associated with significant mortality and postoperative complications. Disseminated cancer, post operative sepsis, longer operative time, and increased body mass index >35 kg/m^2 further increased the risk of VTE in patients undergoing surgery for malignancy. Surveillance strategies should be implemented for those cancer patients who have multiple risk factors for VTE.

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Introduction

Venous thromboembolism (VTE) remains a fairly common disease that leads to reduced survival and increased health care costs. The annual incidence of VTE in the United States is about 1 per 1000, with slightly higher numbers in the African American population.[1,2] VTEs have been found to be a leading cause of increased length of stay and a common cause of excess mortality.[3] Independent risk factors for VTE include both surgery and malignant neoplasm.[2,4,5] In a recent review article,

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0022-4804/$ – see front matter © 2016 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jss.2016.06.089

VTE was not only found to be a leading cause of mortality for cancer patients, but it was also associated with a 50% higher total cost for cancer patients than those who did not develop a VTE.[6]

Although much of the existing literature demonstrates a link between cancer and VTE, typically, the VTE complications have been analyzed according to specific organ malignancy or surgical specialty. A more generalized study from 2006 used the California Cancer Registry Database to find that VTE incidence varied depending on the cancer type. However, VTE was found to be highest among those with metastatic disease.[7] When looking at the incidence of VTE secondary to surgery alone, the annual incidence rises eight fold compared with VTEs in the nonsurgical population.[8] Several studies have demonstrated increased plasma levels of inflammatory mediators that may play a key role in the development of VTE.[9-11] Regardless, sparse literature exists that specifically examines the overall cancer patient population that undergoes major gastrointestinal (GI) surgery.

The aim of our study was to use the American College of Surgeon's National Surgical Quality Improvement Program Participant User Data File (ACS-NSQIP, PUF) to compile the largest population of cancer patients that underwent major GI surgery and analyze the incidence of VTE in this specific population. We sought to identify characteristics that may lead to increased risks of VTE in this already high-risk population and factors associated with worse outcomes. Identifying these characteristics in this patient subset may help lead to better risk stratification and ultimately improved preventative measures.

Methods

After obtaining exemption from our institutional review board, we performed a review of the ACS-NSQIP PUF database. The ACS-NSQIP PUF database is a risk-adjusted outcomes-based program designed to measure and improve the quality of surgical care. The program collects data on over 130 preoperative, intraoperative, and postoperative clinical variables. In addition, 30-d postoperative mortality and morbidity data are collected in the database. Currently, there are over 300 hospitals that participate in this program.[12]

We queried ACS-NSQIP PUF database from 2005 to 2012 for major abdominal surgeries under the Current Procedural Terminology codes listed (Table 1) and studied those with diagnoses of cancer according to the International Classification of Diseases, Ninth Revision listed in Table 2. Emergency cases were excluded from the study, and major abdominal surgeries were categorized by system into the following: esophagectomy, gastrectomy, pancreatectomy, enterectomy, hepatectomy, colectomy and proctectomy. VTE was defined as the occurrence of either pulmonary embolism or deep venous thrombosis (DVT)/thrombophlebitis. In the ACS-NSQIP PUF guideline, DVT/thrombophlebitis is defined as the identification of a new blood clot or thrombus within the venous system, which may be coupled with inflammation. The clot can be found in the superficial or deep venous systems. Furthermore, the diagnosis must have been confirmed by either a duplex, venogram or a computed tomography scan, and the patient must be treated with anticoagulation therapy and/or placement of a vena cava filter or clipping of the vena cava.[13]

Table 1 – Major abdominal procedures by CPT code.

Esophagus	43107, 43108, 43112, 43113, 43116, 43117, 43118, 43122, 43123, 43124
Stomach	43620, 43621, 43622, 43631, 43632, 43633, 43634
Small bowel	44120, 44121, 44125, 44126, 44127, 44128, 44625, 44202, 44203
Large bowel	44140, 44141, 44143, 44144, 44145, 44146, 44147, 44150, 44151, 44155, 44156, 44157, 44158, 44160, 44626, 44204, 44205, 44206, 44207, 44208, 44210, 44211, 44212, 44213, 45395, 45397, 45110, 45111, 45112, 45113, 45114, 45116, 45119, 45120, 45121, 45123
Hepatobiliary	47120, 47122, 47125, 47130, 47140, 47141, 47142
Pancreas	48140, 48145, 48146, 48148, 48150, 48152, 48153, 48154, 48155

CPT = Current Procedural Terminology.

Demographics and comorbidities were compared between those who developed postoperative VTE requiring therapy and those who did not. We noted clinically relevant intraoperative events and postoperative factors between the two groups. Variables were selected based on clinical relevance and were largely limited by the availability within the ACS-NSQIP database. All clinical variables in the ACS-NSQIP database are defined in the user guide.[13]

Categorical variables were analyzed between the group with VTE-requiring therapy and the group without VTE using chi-square tests. Continuous variables were analyzed with the Student's *t*-test and the Mann–Whitney *U*-test, where appropriate. A univariate binomial logistic regression analysis was performed for all factors studied. In addition, a multivariate stepwise logistic regression analysis was used to generate odds ratios (ORs) for factors associated with VTE-requiring therapy. A P value ≤ 0.05 was considered statistically significant. All statistical analyses were performed on Statistical Package for Social Sciences (SPSS) for Windows version 22 (SPSS Inc, Chicago, IL).

Results

Based on our selection criteria, we identified 79,300 patients. The most common type of surgery was colectomy and/or proctectomy (n = 56,030) followed by pancreatectomy

Table 2 – Cancer diagnosis by ICD-9 code.

Esophagus	150.0, 150.1, 150.2, 150.3, 150.4, 150.5, 150.8, 150.9
Stomach	151.0, 151.1, 151.2, 151.3, 151.4, 151.5, 151.6, 151.8, 151.9
Small bowel	152.0, 152.1, 152.2, 152.3, 152.8, 152,9
Large bowel	153.0, 153.1, 153.2, 153.3, 153.4, 153.5, 153.6, 153.7, 153.8, 153.9, 154.0
Hepatobiliary	155.0, 155.1, 155.2, 156.0, 156.1, 156.2, 156.8, 156.9
Pancreas	157.0, 157.1, 157.2, 157.3, 157.4, 157.8, 157.9

ICD-9 = International Classification of Diseases, Ninth Revision.

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