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Risk factors associated with venous thromboembolism in 49,028 mastectomy patients

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ABSTRACT

Venous thromboembolism (VTE) is a potentially preventable disease that carries significant morbidity and mortality. Although malignancy is associated with increased risk for VTE, it varies according to cancer type. Despite the fact that breast cancer is the most common form of cancer in women, the incidence and risk factors associated with VTE in patients undergoing mastectomy have not been well characterized. To address this we utilized the ACS-NSQIP database to identify and characterize independent risk factors for VTE in 49,028 mastectomy patients. We identified 116 cases of VTE in the 49,028 cases analyzed (0.23%). Obesity (BMI > 30, OR $= 1.91$, $p < 0.001$), inpatient status (OR $= 3.75$, $p < 0.001$), venous catheterization (OR $= 2.67$, $p = 0.012$), prolonged operative time >3 h (OR $= 4.36$, $p < 0.001$), and immediate reconstruction (OR $= 3.23$, $p < 0.001$) were found to be independent risk factors for VTE. While the incidence of VTE is rare in mastectomy patients, the heightened awareness and increased VTE prophylaxis should be considered in high risk groups.

Introduction

Venous thromboembolism, which includes both deep venous thrombosis (DVT) and pulmonary embolism (PE), is a potentially preventable disease that carries significant morbidity and mortality. The overall age-adjusted incidence of VTE in the general population in the United States is approximately 1 in 1000.[1] Malignancy increases the risk of VTE by up to seven-fold.[2,3]

The incidence of VTE in breast cancer patients ranges from 0.3% to 2.3%.[4–7] Although the incidence of VTE in this patient population is small, the consequences of VTE can be devastating. The mortality rate from VTE in post-mastectomy patients has been reported to be up to 20%.[8] Despite this, a recent survey of 606 reconstructive breast surgeons in the United States revealed overall compliance with established American College of Chest Physicians (ACCP)[9] guidelines for post-surgical VTE prophylaxis to be only 25%.[10]

The relatively low compliance with VTE prophylaxis guidelines may be related to the fact that the incidence of malignancy-associated VTE varies by type of malignancy. The incidence of breast cancer-associated VTE is low relative to other types of cancer such as pancreatic which has a reported VTE rate of up to 8.1%.[7] However, VTE remains the second most common cause of death in patients with breast cancer, second only to the cancer itself.[11] In addition, up to 80% of patients with VTE will suffer from long-term symptoms of post-thrombotic syndrome to include pain, edema and ulceration.[12,13] In spite of this, the amount of literature that has been published on the subject of VTE in breast cancer patients post-mastectomy is limited.[14]

In addition to surgery, patients with breast cancer often undergo treatments that further increase their risk of VTE. Hormonal therapy, chemotherapy and placement of central venous catheters have all been shown to be independent risk factors for VTE in cancer patients.[15] As such, the objective of this study is to review recent multi-institutional data to determine the current incidence of post-mastectomy VTE and identify specific risk factors that predispose to development of VTE in this patient population. Being cognizant of

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these risk factors will allow for better pre-operative risk-stratification as well as increased intra-operative vigilance, ultimately to prevent development of VTE.

Methods

Data source: the National Surgical Quality Improvement Program

The American College of Surgeons National Surgical Quality Improvement Program[e] (ACS-NSQIP) is a validated, risk-adjusted data source for deriving quality indicators in surgical care.[16] Participating hospitals prospectively collect data on 240 variables, including preoperative risk factors, intraoperative variables, and 30-day postoperative mortality and morbidity outcomes.[16,17]

A surgical clinical reviewer at each hospital collects, validates, and submits the data to the central database. After the data are submitted, validity, completion, and uniformity are ensured through built-in software checks and user information prompts. Furthermore, inter-rater reliability site visits are conducted to continue auditing of the data on a periodic basis.

Each hospital must submit a minimum of 1680 surgical cases per year, and these cases must be drawn from 10 subspecialties, including plastic surgery, unless the institution does not offer the specialty.[18] In order to avoid sampling bias, the calendar year is divided into eight-day cycles so that completed cases have equal chances to be selected any day of the week. There are 46 cycles per year. The first consecutive 40 cases must be submitted per cycle, and cases must be submitted for 42 cycles per year, amounting to 1680 cases annually.[18] Low volume hospitals may submit 22 cases for every eight-day cycle if they demonstrate they cannot meet the 1680 case minimum.[18]

Study population

The study population included all mastectomy cases collected by ACS-NSQIP from 2005 to 2009. Table 1 displays the CPT Codes used to identify Mastectomy Cases from the NSQIP Database.

Data elements

The following data elements were abstracted from the database for analysis: age, race, body mass index (BMI), presence of diabetes, smoking, pregnancy, diagnosis of congestive heart failure, history of hypertension and chronic obstructive pulmonary disease (COPD), inpatient/outpatient status, preoperative chemotherapy and/or radiotherapy, concurrent implementation of venous catheter (as determined by CPT codes 36555, 36557, 36560, 36575, 36576, 36590, 36620, 36640), long operative time, and whether immediate breast reconstruction was performed (Table 2). The presence or absence of deep vein thrombosis (DVT) and/or pulmonary embolism (PE) diagnosed within 30 days postoperatively was abstracted as an outcome measure. Of note, the NSQIP definition of DVT required diagnosis by a duplex, venogram, or CT scan with concomitant "treatment by anticoagulation therapy and/or placement of a vena cava filter or clippling of the vena cava". Confirmation of PE required clinical documentation by a high probability V/Q scan, positive spiral CT exam, pulmonary arteriogram, or CT angiogram.

[e] Disclaimer: American College of Surgeons National Surgical Quality Improvement Program and the hospitals participating in the ACS NSQIP are the source of the data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors.

Table 1
CPT codes used in mastectomy identification.

CPT code	Description
19300	Mastectomy for gynecomastia
19301	Partial mastectomy (lumpectomy, tylectomy, quadrantectomy, segmentectomy) (note: 2008 typo reads "partial mastectomy")
19302	Partial mastectomy W/LN removal (with axillary lymphadenectomy)
19303	Mastectomy, simple, complete
19304	Mastectomy, subcutaneous
19305	Mastectomy, radical (including pectoral muscles, axillary lymph nodes)
19306	Mastectomy, radical, urban type (including pectoral muscles, axillary and internal mammary lymph nodes)
19307	Mastectomy, modified radical (including axillary lymph nodes, with or without pectoralis minor muscle, but excluding pectoralis major muscle)

BMI was calculated from the ACS-NSQIP variables height and weight (BMI = mass[kg]/height[m]^2). Diabetes patients requiring oral hypoglycemic agents and/or insulin were considered to have diabetes while those whose diabetes were controlled by diet alone are not. Patients who smoked cigarettes within the year prior to admission for surgery were considered smokers. Hypertension was defined in a patient with systolic pressure $>$140 mm Hg or diastolic pressure $>$90 mm Hg thirty days before surgery. Similarly, COPD was affirmed if previously diagnosed within 30 days. Inpatient status was included in the study as another variable. Use of chemotherapy or radiotherapy was noted if each was administered within 30 or 90 days prior to surgery, respectively. Finally, performance of an immediate breast reconstruction following the mastectomy was included to account for its potential to be a confounding variable with the operation time variable.

The continuous variables of age and intraoperative time were further dichotomized into clinically relevant groups. For BMI, a division was made at $<$30 or $\geq$30 for statistical feasibility. Significance was set at $p < 0.05$.

Statistical analysis

The primary outcome measure was VTE at thirty days and was examined across each risk factor. The Pearson's Chi-square test or 2-sided Fisher's exact tests, wherever appropriate, was used for categorical risk factors. The Student's *t*-test was used to assess the difference between means for continuous risk factors. Subsequently, each risk factor was analyzed using univariate logistic regression. Factors with a *p*-value less than 0.05 were then entered into multivariate logistic regression analysis to derive adjusted odds ratios (AOR) and their 95% confidence intervals (CI). The statistical analysis software STATA (version 11, College Station, TX) was used for all analyses.

Results

Incidence of venous thromboembolism

Of the 971,455 cases collected by ACS-NSQIP from 2005 to 2009, 49,028 included a CPT code for mastectomy. The presence of a venous thromboembolic event within 30 days of surgery was identified in 114 cases, an incidence rate of 0.23% (95% CI: 0.19%–0.27%). Of the 114 cases, 67 (59%; 95% CI: 43%–81%) had a deep vein thrombosis alone, 37 patients (32%; 95% CI: 22%–47%) had a pulmonary embolism alone, and 10 patients (9%; 95% CI: 4%–7%) had both. One patient was noted to have two DVTs. This is compared to the overall age-adjusted incidence of VTE in the general population in the United States, which is approximately 1 in 1000.[1] Fig. 1 displays the composition of venous thromboembolism in this study.