Identifying Esophagectomy Patients at Risk for Predischarge Versus Postdischarge Venous Thromboembolism

Jeremiah T. Martin, MBBCh, FRCSI, Angela L. Mahan, MD, Victor A. Ferraris, MD, Sibu P. Saha, MD, Timothy W. Mullett, MD, Joseph B. Zwischenberger, MD, and Ching-Wei D. Tzeng, MD

Department of Surgery, Division of Cardiothoracic Surgery, University of Kentucky, Lexington, Kentucky

Background. Current guidelines recommend postoperative venous thromboembolism (VTE) chemoprophylaxis for moderate-risk patients (3% rate or greater) and extended-duration chemoprophylaxis for high-risk patients (6% or greater). Large-scale studies of and recommendations for esophagectomy patients are lacking. This study was designed to evaluate the timing, rates, and predictors of postesophagectomy VTE.

Methods. Patients undergoing esophagectomies for cancer were identified from the 2005 to 2012 American College of Surgeons National Surgical Quality Improvement database. Timing and rates of VTE (deep venous thrombosis or pulmonary embolism, or both) were calculated. Events were stratified as predischarge or postdischarge. Perioperative factors associated with 30-day rates of predischarge and postdischarge VTE were analyzed.

Results. Of 3,208 patients analyzed, the surgical approach was Ivor-Lewis (n = 1,131, 35.3%), transhiatal (n = 945, 29.5%), three-field (n = 587, 18.3%), thoracoabdominal (n = 364, 11.3%), and nongastric conduit reconstruction (n = 181, 5.6%). Rates were 2.0% pulmonary embolism, 3.7% deep venous thrombosis, and 5.1% VTE. Overall median length of stay was 11 days (versus 19 days, $p < 0.001$, if predischarge VTE). Predischarge VTE occurred on median day 9, whereas postdischarge VTE occurred on day 19 ($p < 0.001$). Only 17% of VTE occurred after discharge. Multivariate analysis identified being male (odds ratio [OR] 2.09, $p = 0.018$), white race (OR 1.93, $p = 0.004$), prolonged ventilation (OR 3.24, $p < 0.001$), and other major complications (OR 1.90, $p = 0.005$) as independent predictors of predischarge VTE. Older age (OR 1.06 per year, $p = 0.006$) and major complications (OR 3.14, $p = 0.004$) were independently associated with postdischarge VTE.

Conclusions. Postesophagectomy VTE occurs in a clinically significant proportion of esophageal cancer patients with identifiable risk factors for predischarge and postdischarge events. Elderly patients and patients with major complications are most likely to benefit from extended-duration chemoprophylaxis.

(Ann Thorac Surg 2015;100:932–8)

Venous thromboembolism (VTE) remains a significant cause of potentially preventable morbidity and mortality among surgical patients, especially those with active cancer [1–3]. The incidence of VTE varies with type of cancer and surgical procedure [4–6], and despite decreasing hospital lengths of stay with modern postoperative care [7], it continues to be major clinical issue after discharge [4, 8, 9]. Methods of prophylaxis against VTE may be classified as either mechanical (eg, sequential compression device, compression stockings) or chemical (eg, unfractionated and low molecular weight heparin), known as chemoprophylaxis. Numerous national and international consensus groups [10] advocate perioperative VTE chemoprophylaxis from the time of surgery to the date of discharge and even extended-duration chemoprophylaxis for select patients to prevent this complication, which is a clinically significant cause of decreased quality of life [11], delayed adjuvant therapy [12], and even death after the index hospitalization [9].

High-risk operations are associated with increased risk of postdischarge VTE, and distinct sets of predictors for predischarge and postdischarge VTE can be used to identify patients who might benefit from extended-duration chemoprophylaxis [6, 13, 14]. Guidelines exist for extended chemoprophylaxis, including those from the National Comprehensive Cancer Network (NCCN). However, these have not seen uniform clinical application [1, 4, 7, 15, 16]. Additionally, these guidelines apply to broad categories of high-risk surgical patients, and none has been specifically developed to guide the care of patients undergoing esophagectomy. For esophagectomy, traditional surgical training has always taught the need

Accepted for publication April 6, 2015.

Presented at the Fifty-first Annual Meeting of The Society of Thoracic Surgeons, San Diego, CA, Jan 24–28, 2015.

Address correspondence to Dr Martin, 740 S Limestone St, A301, Lexington, KY 40509; e-mail: j.martin@uky.edu.

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2015.04.042

for awareness of postoperative major complications such as anastomotic leak, aspiration, and respiratory failure, whereas VTE receives less attention as a complication when consenting patients for surgery.

To influence national and international practice patterns, the authors felt the need to establish the clinical importance of VTE within the population of patients with cancer undergoing esophagectomy and to make recommendations to decrease VTE event rates. The hypothesis of this study was that the postoperative VTE rate after esophagectomy was clinically significant and that certain risk factors could be identified to help surgeons predict patients who were at risk for predischarge versus postdischarge events. To test this hypothesis, this study was designed to define the rates and timing of postesophagectomy VTE events and to analyze the clinical variables associated with predischarge versus postdischarge VTE.

Patients and Methods

Patients and Data Collection

All patients undergoing esophagectomy (Current Procedural Terminology [CPT] 43107 to 43124) for cancer (International Classification of Diseases 150.x or 151.x) were identified in the 2005 to 2012 American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) participant use file. Surgical approach was further classified as transhiatal (CPT 43107), three-field (CPT 43122), Ivor-Lewis (CPT 43117, 43121), thoracoabdominal (CPT 43122), and use of any nongastric conduit (CPT 43108, 43113, 43116, 43118, 43123, 43124). All available NSQIP preoperative, intraoperative, and postoperative variables were examined to identify significant differences and associated risk factors between the groups.

Definitions

Preoperative risk factors, intraoperative variables, and postoperative metrics have been previously defined [17]. Venous thromboembolism was a composite variable defined as the occurrence of clinically detected deep venous thrombosis or pulmonary embolus. Patients documented to have both deep venous thrombosis and pulmonary embolus were labeled only once for VTE. The incidence of VTE was then measured from the recorded 30-day NSQIP outcomes. Timing of VTE was further categorized relative to discharge date and classified as predischarge versus postdischarge events.

Postoperative (non-VTE) major morbidity was defined as the occurrence of any one or combination of the following NSQIP-derived variables: pneumonia, reintubation, failure to wean from ventilator, renal insufficiency, renal failure, cardiac arrest, myocardial infarction, coma, stroke, sepsis, septic shock, return to the operating room, fascial dehiscence, or organ space infection. Based on NSQIP limitations, postesophagectomy mortality was defined as death within 30 postoperative days or death during the original index admission.

Statistical Analysis

Descriptive statistics included mean and standard deviation for normally distributed continuous variables, median and interquartile range for nonparametric continuous variables, and counts and percentages for categoric variables. Univariate comparisons were performed using Student's t test, analysis of variance, χ^2 test, and Fisher's exact test, as appropriate. Logistic regression was used to measure the association between the occurrence and timing of VTE and other clinical variables. Significant variables were entered into a final logistic model to determine independent associations with predischarge and postdischarge VTE. Statistical analyses were performed using SAS 9.3 (SAS Institute, Cary NC). All tests were two-sided, and statistical significance was defined as p less than 0.05.

Results

Patients and Esophagectomies

Between 2005 and 2012, 3,208 patients underwent esophagectomy; they had a median age of 64 years (Table 1). The distribution of surgical approach was as follows: Ivor-Lewis (n = 1131, 35.3%), transhiatal (945, 29.5%), three-field (587, 18.3%), thoracoabdominal (364, 11.3%), and nongastric conduit reconstruction (181, 5.6%). Overall, 79.3% of patients were American Society of Anesthesiologists class 3 or more, and 25.8% were smokers. The major morbidity rate, excluding VTE, for patients undergoing esophagectomy was 35.7% and that was associated with an overall 3.1% (99 of 3,208) 30-day mortality rate (Table 1).

Occurrence and Timing of VTE

Overall event rates were 2.0% for pulmonary embolus, 3.7% for deep venous thrombosis, and 5.1% for VTE. Of these, 17% of VTE occurred after discharge (Fig 1). Median length of stay was 11 days for all patients versus 19 days ($p < 0.001$) for patients with predischarge VTE and versus 12 days ($p = 0.359$) for patients with postdischarge VTE. Overall median day of VTE was postoperative day 11. Predischarge VTE occurred on median day 9, whereas postdischarge VTE occurred on median day 19 ($p < 0.001$; Fig 2).

Factors Associated With Predischarge Versus Postdischarge VTE

Higher American Society of Anesthesiologists class, diabetes mellitus, preoperative dyspnea, cardiovascular history, hypertension requiring medications, and preoperative hematocrit less than 39% were identified as preoperative risk factors associated with the development of predischarge VTE on univariate analysis (Table 1). The only preoperative risk factor associated with the development of postdischarge VTE was older age. Choice of surgical approach was not associated with predischarge or postdischarge VTE ($p = 0.368$). The occurrence of postesophagectomy major complications, however, including organ space infection (as a surrogate for leak), pneumonia, failure to wean, reintubation,