Postdischarge venous thromboembolic complications following pulmonary oncologic resection: An underdetected problem

John Agzarian, MD, MPH,[a] Waël C. Hanna, MD, MBA,[a] Laura Schneider, BSc,[a] Colin Schieman, MD,[a] Christian J. Finley, MD, MPH,[a] Yury Peysakhovich, MD,[a] Terri Schnurr, RN,[b] Dennis Nguyen-Do, BPH,[a] Lori-Ann Linkins, MD, MSc,[b] James Douketis, MD,[b] Mark Crowther, MD, MSc,[b] Marc De Perrot, MD, MSc,[c] Thomas K. Waddell, MD, PhD,[c] and Yaron Shargall, MD[a]

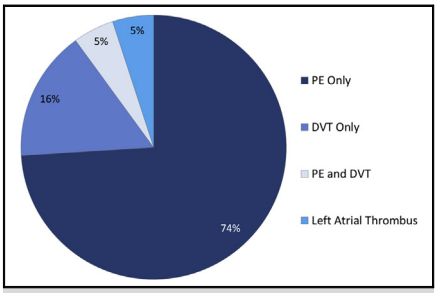
ABSTRACT

Objectives: To determine the prevalence of delayed postoperative venous thromboembolism (VTE) in patients undergoing oncologic lung resections, despite adherence to current in-hospital VTE prophylaxis guidelines.

Methods: Patients undergoing lung resection for malignancy in 2 tertiary-care centers were recruited between June 2013 and December 2014. All patients received guideline-based VTE prophylaxis until hospital discharge. Patients underwent computed tomography chest angiography with pulmonary embolism (PE) protocol and bilateral lower extremity venous Doppler ultrasonography at 30 ± 5 days after surgery to determine the incidence of postoperative VTE. Univariate analysis was used to compare the VTE and non-VTE groups.

Results: A total of 157 patients were included, 45.9% were men with a mean age of 66.7 years. VTE prevalence was 12.1% with a total of 19 VTE events, including 14 PEs (8.9%), 3 deep venous thromboses (DVTs) (1.9%), 1 combined PE/DVT, and 1 massive left atrial thrombus originating from the pulmonary vein stump after pulmonary lobectomy. PE events occurred in the operated lung 64% of the time and 4 patients (21.1%) were symptomatic at diagnosis. The 30-day mortality rate of VTE events was 5.2%, with 1 patient who died secondary to massive in situ ipsilateral PE following readmission to the hospital. Univariate analysis did not demonstrate significant differences between the VTE and non-VTE populations with regard to baseline characteristics.

Conclusions: Despite adherence to in-hospital standard prophylaxis guidelines, VTE events are frequent, often asymptomatic, and with associated significant morbidity and mortality. More research into the potential role of predischarge screening and extended prophylaxis is warranted. (J Thorac Cardiovasc Surg 2015;■:1-8)



Distribution of venous thromboembolism event types, demonstrating a high proportion of de novo pulmonary embolism (PE).

Central Message

Despite adoption of in-hospital prophylaxis standards, late VTE after lung cancer resection occurs frequently and is often asymptomatic.

Perspective

Reported rates of venous thromboembolic events after oncologic lung resection are varied. This is the first prospective study to evaluate prevalence in this population while following current in-hospital prophylaxis guidelines, and notes that prevalence is higher than previously reported and usually asymptomatic at diagnosis. Routine screening or extended postdischarge prophylaxis may be indicated.

GTS

Following pulmonary resection for lung cancer, patients who experience venous thromboembolism (VTE) events, including deep vein thrombosis (DVT) and pulmonary embolism (PE), have a mortality rate as high as 14.3%, compared with a mortality risk of 2% in uncomplicated cases void of VTE.[1] The clinical burden of postoperative VTE in thoracic surgery is likely underestimated because the majority of patients are asymptomatic or misdiagnosed.[2] There is generally little concordance of the reported incidence of VTE after thoracic surgery, with rates ranging from 1.3% to 15.2% for PE, and 4% to 14% for DVT.[1-8] Older studies, conducted between 1975 and 1993, before the routine use of heparin prophylaxis, reported a

From the [a]Departments of Surgery and [b]Medicine, McMaster University Faculty of Health Sciences, Hamilton, Ontario, Canada; and [c]Department of Surgery, University of Toronto, Faculty of Medicine, University Health Network, Toronto, Ontario, Canada.

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Address for reprints: Yaron Shargall, MD, St Joseph's Healthcare Hamilton, 50 Charlton Ave, E Juravinski Tower T-2105, Hamilton, ON, L8N 4A6 Canada (E-mail: shargal@mcmaster.ca).

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Abbreviations and Acronyms

CT = computed tomography
CTPA = computed tomography pulmonary angiogram
DVT = deep venous thrombosis
LMHW = Low-molecular-weight heparin
PE = pulmonary embolism
UFH = unfractionated heparin
VTE = venous thromboembolism

mortality rate from PE as high as 15.2% in the lung cancer population.[3,4] More recent literature reports the incidence of PE in this population to be 5%, and that of DVT to be 4% to 14%,[5-8] although most of these studies reported only clinically evident events. A contemporary screening-based study, using spiral helical computed tomography (CT) scanning 7 to 15 days postoperatively, detected both symptomatic and asymptomatic events, and reported a markedly higher incidence of PE at 14%[2] while following current VTE prophylaxis guidelines.[9]

Pertaining to the thoracic surgery population, the American College of Chest Physicians ninth edition guidelines for VTE prevention recommend the use of in-hospital routine VTE prophylaxis with either low-dose unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) (Grade 1B),[9] with no recommendations for continuation after hospital discharge. This is despite an American College of Surgeons National Surgical Quality Improvement Program database review indicating that after lung cancer resection, 23% of VTE events occur after discharge and another study by Yang and colleagues reported that VTE.[1] In contrast, for patients undergoing major orthopedic procedures, there is prospective evidence to support long-term prophylaxis up to 35 days[10] after discharge.[11-15] These findings have been echoed in abdominal and pelvic cancer surgery, where prospective randomized trials have demonstrated that VTE prophylaxis up to 30 days after surgery results in significantly fewer VTE events.[1,16]

The aim of this multicenter pilot study was to prospectively determine the postoperative prevalence and clinical burden of clinically evident and occult VTE following oncologic lung resection, using delayed screening investigations 30 days postoperatively. We also examine the use of VTE prophylaxis in this population to determine whether current thromboprophylaxis guidelines are being appropriately followed. By assessing symptomatic and subclinical events, we hypothesize that the detected prevalence of VTE will be higher than previously suspected, despite adhering to standard prophylaxis guidelines. As part of a 3-phase project, we aim to use these findings to investigate the role of extended VTE thromboprophylaxis in the thoracic surgery patient population.

METHODS

Patient Selection

Between June 2013 and December 2014, patients undergoing lung resection for primary or secondary lung malignancies in 2 tertiary-care centers (St Joseph's Healthcare Hamilton, Hamilton, ON, Canada, and Toronto General Hospital, Toronto, ON, Canada) were recruited to participate in this prospective cohort study. Adults aged 18 years or older undergoing open or minimally invasive lobar or sublobar resection (eg, wedge resection, segmentectomy, lobectomy, bilobectomy, or pneumonectomy) were considered for enrollment. Patients were excluded if they had a known allergy to contrast dye, UFH, or LMWH; were at an increased risk of hemorrhage; had a history of heparin-induced thrombocytopenia; had known renal impairment (defined as creatinine clearance <55 mL/min/m^2 as calculated by the Cockroft-Gault method); had a platelet count <75,000; or were pregnant. Patients were deemed ineligible if they demonstrated any history of prior VTE during the 3 months before surgery, had previous inferior vena cava filter insertion, and/or were concurrently on therapeutic anticoagulation. The study was approved by the Hamilton Integrated Research Ethics Board and University Health Network Research Ethics Board before patient enrollment.

VTE Prophylaxis Management

Each study subject received American College of Chest Physicians guideline-compatible thromboprophylaxis consisting of mechanical prophylaxis via graduated compression stockings, along with chemical prophylaxis consisting of either subcutaneous injection of 5000 units dalteparin once daily, or 5000 units UFH every 8 hours. The initial dose of chemical prophylaxis was administered intraoperatively within 2 hours of the beginning of each operation, defined as the time at which the initial skin incision was made, in accordance with hospital and anesthesia-specific guidelines for perioperative DVT prophylaxis. For patients with thoracic epidurals, catheter removal was coordinated with the last administered dose of chemical thromboprophylaxis according to hospital-specific nursing guidelines. In the case of dalteparin, the epidural catheter was removed at least 2 hours before administration of the next dose, after checking patient international normalized ratio and partial thromboplastin time. Specific to UFH, epidural catheters were typically removed in the morning after holding the first dose of heparin. The regimen of UFH was then resumed 2 hours after catheter removal. Prophylaxis continued only until hospital discharge. All patients were ambulated on the first postoperative day and daily thereafter by a physiotherapist.

Outcomes Measurement

Each study participant was scheduled for 2 early postoperative outpatient follow-up visits. Patients were initially seen 2 weeks postoperatively for a clinical assessment of symptoms suggestive of VTE. This clinical assessment was repeated 4 weeks postoperatively, followed by objective radiographic screening for PE and DVT, often on the same visit date. All participants underwent a chest CT pulmonary angiogram (CTPA) with contrast using a 64-slice multidetector CT (Lightspeed CT; GE Healthcare Milwaukee, Wis) and bilateral above-knee lower extremity venous Doppler ultrasonography at 30 ± 5 days after surgery. Before undergoing CTPA examination, all patients provided blood samples to rule out significant postoperative bleeding and/or the development of postprocedural renal impairment. Patients who developed symptoms suggestive of VTE events before the 30-day mark, either during hospitalization or during outpatient clinical follow-up, underwent an urgent CTPA examination based on the clinical judgment of the treating surgeon.