Published in final edited form as:
Am J Med. 2012 October ; 125(10): 1010–1018. doi:10.1016/j.amjmed.2012.03.007.

Venous thromboembolism in patients with chronic obstructive pulmonary disease

Gregory Piazza, M.D., M.S.[a], **Samuel Z. Goldhaber, M.D.**[b], **Aimee Kroll, M.S.**[c], **Robert J. Goldberg, Ph.D.**[d], **Catherine Emery, R.N.**[e], and **Frederick A. Spencer, M.D.**[f]

[a]Cardiovascular Division, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

[b]Cardiovascular Division, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

[c]Department of Quantitative Health Sciences, University of Massachusetts Medical School, Worcester, MA, USA

[d]Department of Quantitative Health Sciences, University of Massachusetts Medical School, Worcester, MA, USA

[e]Department of Quantitative Health Sciences, University of Massachusetts Medical School, Worcester, MA, USA

[f]Department of Medicine, McMaster University, Hamilton, Ontario, Canada

Abstract

Purpose—Our aim was to compare clinical characteristics, prophylaxis, treatment, and outcomes of venous thromboembolism in patients with and without previously diagnosed chronic obstructive pulmonary disease.

Methods—We analyzed the population-based Worcester Venous Thromboembolism Study of 2,488 consecutive patients with validated venous thromboembolism to compare clinical characteristics, prophylaxis, treatment, and outcomes in patients with and without chronic obstructive pulmonary disease.

Results—Of 2,488 venous thromboembolism patients, 484 (19.5%) had a history of clinical chronic obstructive pulmonary disease and 2,004 (80.5%) did not. Chronic obstructive pulmonary disease patients were older (mean age 68 years vs. 63 years) and had a higher frequency of heart failure (35.5% vs. 12.9%) and immobility (53.5% vs. 43.3%) than patients without chronic obstructive pulmonary disease (all $p<0.0001$). Chronic obstructive pulmonary disease patients were more likely to suffer in-hospital death (6.8% vs. 4%, $p=0.01$) and death within 30 days of venous thromboembolism diagnosis (12.6% vs. 6.5%, $p<0.0001$). Chronic obstructive pulmonary disease patients demonstrated increased mortality despite a higher frequency of venous thromboembolism prophylaxis. Immobility doubled the risk of in-hospital death (adjusted odds

Address for correspondence: Gregory Piazza, M.D., M.S. Cardiovascular Division Brigham and Women's Hospital 75 Francis St. Boston, MA 02115 Tel: (617) 732-6986 Fax: (617) 738-7652 gpiazza@partners.org.

All of he authors had access to the data and participated in the writing of the manuscript.
None of the authors have any conflicts of interest to disclose.

ratio 2.21; 95% confidence interval 1.35–3.62) and death within 30 days of venous thromboembolism diagnosis (adjusted odds ratio 2.04; 95% confidence interval 1.43–2.91).

Conclusion—Patients with chronic obstructive pulmonary disease have an increased risk of dying during hospitalization and within 30 days of venous thromboembolism diagnosis. Immobility in chronic obstructive pulmonary disease patients is an ominous risk factor for adverse outcomes.

Keywords

chronic obstructive pulmonary disease; deep vein thrombosis; prophylaxis; pulmonary embolism; venous thromboembolism

Patients with chronic obstructive pulmonary disease have an increased risk of venous thromboembolism, including pulmonary embolism, especially during acute exacerbations requiring hospitalization.[1, 2] Chronic obstructive pulmonary disease is associated with a procoagulant state marked by elevated circulating blood-borne tissue factor-procoagulant activity[3] and increased levels of fibrinogen and factor XIII.[4] The prevalence of pulmonary embolism ranges from 20% in outpatients with chronic obstructive pulmonary disease exacerbations to 25% in those requiring hospitalization.[2] However, based on autopsy studies, the frequency of pulmonary embolism may approach 30% in patients with chronic obstructive pulmonary disease exacerbation requiring hospitalization.[5] Concomitant pulmonary embolism may masquerade as an acute chronic obstructive pulmonary disease exacerbation.[5]

Chronic obstructive pulmonary disease is a particularly strong risk factor for PE among patients younger than 60 years.[6] One-year mortality for patients hospitalized for a chronic obstructive pulmonary disease exacerbation doubles for those who subsequently suffer venous thromboembolism compared with those who do not (61.9% vs. 31.8%, $p = 0.01$).[7] Venous thromboembolism in patients hospitalized for chronic obstructive pulmonary disease exacerbation portends a complicated clinical course, including longer length of stay and increased need for mechanical ventilation.[8]

While a large European registry has reported outcomes for chronic obstructive pulmonary disease patients with pulmonary embolism,[9] there is a paucity of data regarding the outcomes of patients with chronic obstructive pulmonary disease and concomitant venous thromboembolism in the United States. The Worcester Venous Thromboembolism Study is a population-based study of central Massachusetts residents with independently confirmed venous thromboembolism. In this analysis, we describe the clinical characteristics, use of prophylaxis, treatment strategies, and short-term outcomes of 484 venous thromboembolism patients with concomitant chronic obstructive pulmonary disease and 2,004 venous thromboembolism patients without chronic obstructive pulmonary disease.

Methods

Patient population

Lists of eligible patients were generated from health care system encounters in which any of 34 ICD-9 diagnosis codes consistent with venous thromboembolism were used in 1999, 2001, 2003, and 2005.[10] These lists were obtained from each of 11 medical centers serving residents of the Worcester, Massachusetts, metropolitan area.[10] Institutional Review Board (IRB) approval was obtained at all 11 study sites. Given the retrospective nature of this registry, informed consent was not required. Data queries included discharge diagnoses and outpatient, Emergency Department, radiology, and laboratory encounters. Medical records

of all potentially eligible patients were reviewed by dedicated nurse abstractors using pre-specified criteria to validate and characterize each case.[10] Each potentially eligible case of venous thromboembolism was independently validated by the study project coordinator using pre-specified diagnostic criteria. Each case of venous thromboembolism was classified as being either definite, probable, possible, or not acute or negative based on a modification of the classification used by Silverstein et al. (Appendix).[11, 12] Definite diagnosis of deep vein thrombosis required evidence for presumed acute thrombosis by compression ultrasonography, computed tomography, magnetic resonance imaging, or venography. Definite diagnosis of pulmonary embolism required evidence for presumed new thrombosis on computed tomography or pulmonary angiography. Probable pulmonary embolism required the presence of a high-probability ventilation-perfusion lung scan. Cases of venous thromboembolism were classified as possible if these confirmatory tests were not performed, or were indeterminate, and either the medical record indicated that the physician made a clinical diagnosis of deep vein thrombosis or pulmonary embolism, symptoms or signs of venous thromboembolism were documented, or the patient underwent therapy with anticoagulants or an inferior vena cava filter was inserted. If the classification of venous thromboembolism was not immediately clear using the specified criteria, the principal investigator (F.A.S.) reviewed the medical record. Only definite, probable, and possible cases were included in the analysis. There were no exclusion criteria for entry into the registry.

Incident cases of venous thromboembolism were defined as those occurring in patients without a prior history of deep vein thrombosis or pulmonary embolism. Recurrent venous thromboembolism was defined as a new occurrence of thrombosis in a previously uninvolved vein or pulmonary artery as confirmed by an imaging study.

Data collection

Data regarding demographic characteristics, comorbidities, risk factors, diagnosis, management, prior prophylaxis utilization, and outcomes were abstracted from the medical record. Based on information contained in hospital and ambulatory care records, patients with a clinical diagnosis of chronic obstructive pulmonary disease, chronic lung disease, emphysema, or chronic bronchitis were classified as chronic obstructive pulmonary disease patients. Surgery was defined as a major operation where general or epidural anesthesia lasted 30 minutes or longer. Immobility was defined as limited ambulation, restricted activity of bed-to-chair or bed-to-bathroom, or complete bed rest based on medical record documentation. Clinical characteristics were defined as “recent” if occurring or active within three months prior to venous thromboembolism diagnosis.

Major bleeding for study years 1999, 2001, and 2003 was defined as any episode of bleeding requiring transfusion or resulting in hospitalization (or prolongation of hospitalization), stroke, myocardial infarction, or death. In order to be consistent with International Society of Thrombosis and Hemostasis criteria,[13] our definition was revised for the 2005 patient cohort. Major bleeding was defined as clinically overt bleeding that: 1) resulted in death; 2) was at a critical site (intracranial, intraocular, retroperitoneal, interarticular, pericardial, muscular with compartment syndrome; 3) required transfusion of at least 2 units of packed red blood cells; or 4) resulted in a hemoglobin decrease of at least 20 gram/L.

Data regarding thromboprophylaxis utilization were obtained for patients hospitalized for any non-venous thromboembolism-related condition or for major surgery within the three months prior to diagnosis of deep vein thrombosis or pulmonary embolism. This information was abstracted from medical records at the same time as data regarding the incident venous thromboembolism event. Medical records from other Worcester area hospitals were reviewed in case prior hospitalization was at an institution other than that of the index

venous thromboembolism. First recurrence of venous thromboembolism or a major bleeding event was determined through review of medical records at the same hospital as the index event and screening of medical records from the other participating medical centers. Data regarding all-cause mortality were obtained through review of hospital records and death certificates at the Massachusetts Division of Vital Statistics. Median follow-up was 922 days for long-term outcomes.

Statistical methods

Means, medians, and frequency distributions were calculated for continuous variables. Differences in the distribution of demographic characteristics, comorbidities, risk factors, diagnosis, management strategies, prophylaxis, and outcomes between venous thromboembolism patients with and without chronic obstructive pulmonary disease were examined using the chi-square or Fisher's exact test for categorical variables and t-test for continuous variables. Cumulative incidence rates of venous thromboembolism recurrence, major bleeding, and all-cause mortality were estimated using the life-table method. All statistical tests were two-tailed, and a p-value of less than 0.05 was considered statistically significant.

Cox regression analysis was utilized to evaluate whether chronic obstructive pulmonary disease was associated with an increased risk of in-hospital death and death within 30 days of venous thromboembolism diagnosis while controlling for several potentially confounding prognostic factors. Variables included in the regression model were selected based on the results of univariate analyses and a priori knowledge. These variables included age, gender, immobility for greater than 48 hours, medical history (history of ischemic heart disease, indwelling central venous catheter, intensive care unit discharge within three months of venous thromboembolism diagnosis, chronic kidney disease, and heart failure), and use of thromboprophylaxis. All statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC).

Results

Baseline characteristics

Patients with chronic obstructive pulmonary disease who suffered venous thromboembolism were older than patients without chronic obstructive pulmonary disease (mean age 68.2 years vs. 62.7 years, $p<0.0001$) (Table 1). Patients with chronic obstructive pulmonary disease were more likely to have developed venous thromboembolism during hospitalization for a non-venous thromboembolism-related condition (35.7% vs. 26.3%, $p<0.0001$). Chronic obstructive pulmonary disease patients with venous thromboembolism had a longer mean duration of hospitalization than those without chronic obstructive pulmonary disease (12.4 days vs. 10.1 days, $p=0.01$). Venous thromboembolism diagnostic categories were similar in both groups, and more than 93% of venous thromboembolism diagnoses in each group were classified as definite.

Comorbidities and risk factors

Patients with chronic obstructive pulmonary disease and venous thromboembolism were more likely to have comorbid conditions of immobility, infectious illness, heart failure, ischemic heart disease, and chronic kidney disease than patients without chronic obstructive pulmonary disease who suffered venous thromboembolism (Table 2). Patients with chronic obstructive pulmonary disease and venous thromboembolism were also more likely to have indwelling central venous catheters and intensive care unit discharge and endotracheal intubation within three months of venous thromboembolism diagnosis.

Clinical presentation of venous thromboembolism

Patients with chronic obstructive pulmonary disease were less likely to have symptomatic venous thromboembolism. However, patients with venous thromboembolism and chronic obstructive pulmonary disease were more likely to report dyspnea and cough and more frequently presented with tachycardia, systemic arterial hypotension, and hypoxemia at the time of venous thromboembolism diagnosis (Table 3). There was no difference in the type of venous thromboembolism between patients with or without chronic obstructive pulmonary disease.

Prophylaxis of venous thromboembolism

Patients with chronic obstructive pulmonary disease who were hospitalized for any non-venous thromboembolism-related condition or had major surgery within the three months prior to diagnosis of deep vein thrombosis or pulmonary embolism were more likely to have received prophylactic measures than patients without chronic obstructive pulmonary disease (60% vs. 46.6%, $p<0.0001$) (Table 4). Patients with chronic obstructive pulmonary disease were more likely to have received subcutaneous unfractionated heparin or warfarin for venous thromboembolism prophylaxis.

Treatment of venous thromboembolism

Intravenous unfractionated heparin and low-molecular weight heparin were the most common parenteral anticoagulants used in the initial treatment of venous thromboembolism in patients with and without chronic obstructive pulmonary disease (Table 5). A high frequency of inferior vena cava filter insertion was observed in patients with venous thromboembolism and chronic obstructive pulmonary disease (14.1%) as well as in those without chronic obstructive pulmonary disease (11.3%) ($p=0.1$).

Outcomes

Patients with chronic obstructive pulmonary disease were more likely to have a complicated course after venous thromboembolism than those without chronic obstructive pulmonary disease (Table 6). Patients with chronic obstructive pulmonary disease were more likely to suffer in-hospital death (6.8% vs. 4%, $p=0.01$) and death within 30 days of venous thromboembolism diagnosis (12.6% vs. 6.5%, $p<0.0001$) compared with patients with venous thromboembolism who did not have chronic obstructive pulmonary disease. We observed no significant difference in the frequency of in-hospital mortality or 30-day mortality when comparing patients with and without chronic obstructive pulmonary disease who had a definite venous thromboembolism diagnostic category with patients with and without chronic obstructive pulmonary disease who had either a definite, probable, or possible venous thromboembolism diagnostic category.

Immobility (adjusted odds ratio [OR] 2.21; 95% confidence interval [CI] 1.35–3.62) and use of thromboprophylaxis (adjusted OR 2.12; 95% CI 1.27–3.55) were associated with a two-fold increase in the risk of in-hospital death (Table 7). Chronic obstructive pulmonary disease (adjusted OR 1.53; 95% CI 1.09–2.16), immobility (adjusted OR 2.04; 95% CI 1.43–2.91), indwelling central venous catheter (adjusted OR 1.65; 95% CI 1.08–2.53), and use of thromboprophylaxis (adjusted OR 1.59; 95% CI 1.1–2.3) were independently associated with death within 30 days of venous thromboembolism diagnosis.

Discussion

We observed that patients with chronic obstructive pulmonary disease who subsequently developed venous thromboembolism had a 70% higher rate of in-hospital death and twice the rate of dying within 30 days of venous thromboembolism diagnosis compared with

venous thromboembolism patients who did not have chronic obstructive pulmonary disease. Immobility in patients with chronic obstructive pulmonary disease is particularly ominous and is associated with a doubling in the rate of death during hospitalization and 30 days after venous thromboembolism diagnosis. A high frequency of comorbid conditions, such as heart failure, ischemic heart disease, and chronic kidney disease, not only increases the risk of venous thromboembolism but may complicate management and outcomes. Patients with chronic obstructive pulmonary disease and venous thromboembolism had an increased risk of death despite a higher frequency of venous thromboembolism prophylaxis prescription.

Our findings are consistent with the RIETE registry in which pulmonary embolism patients with chronic obstructive pulmonary disease demonstrated high overall mortality (12% over three months).[9] The combination of chronic obstructive pulmonary disease and a high frequency of comorbid conditions, including heart failure and ischemic heart disease, may limit the ability of these patients to tolerate the ventilatory and hemodynamic demands of acute PE. Therefore, these chronic obstructive pulmonary disease patients, many of whom have already developed chronic right ventricular dysfunction, are susceptible to cardiovascular collapse due to superimposed right ventricular failure due to acute pulmonary embolism.[14]

We speculate that clinicians were more likely to prescribe thromboprophylaxis for medically frail chronic obstructive pulmonary disease patients because of their high frequency of comorbid medical conditions. This hypothesis might explain the increased mortality associated with the use of venous thromboembolism prophylaxis. An alternative explanation is that venous thromboembolism prophylaxis, in particular prophylactic anticoagulation, may be detrimental in this subset of venous thromboembolism patients who are frequently critically ill and have multiple comorbid conditions that may predispose to bleeding. Finally, since the study is a retrospective analysis, hidden biases may account for this finding.

Similar to our findings among heart failure patients in the Worcester Venous Thromboembolism Study[15] and those in the RIETE registry,[9] we observed that patients with chronic obstructive pulmonary disease have a high frequency of immobility preceding the diagnosis of venous thromboembolism. Immobility was present in more than half of patients with chronic obstructive pulmonary disease who suffered venous thromboembolism and was associated with a doubling in the rate of in-hospital death and death within 30 days of venous thromboembolism diagnosis. Increased mortality may also be due to advanced chronic obstructive pulmonary disease, which often results in immobility. Our data suggest that efforts to reduce immobility during and after hospitalization should be pursued to help prevent venous thromboembolism in patients with chronic obstructive pulmonary disease.

Our findings must be interpreted in the context of the study design. The registry population was predominantly Caucasian, thereby limiting the ability to generalize these observations to other racial or ethnic groups. The registry did not require pulmonary function testing or documentation of inhaled bronchodilators to confirm the diagnosis of chronic obstructive pulmonary disease. Therefore, some patients may have been misclassified as having chronic obstructive pulmonary disease based on an incorrect clinical diagnosis, while others may have been misclassified as not having chronic obstructive pulmonary disease despite having obstruction on pulmonary function testing or requiring bronchodilators. Furthermore, because the Worcester Venous Thromboembolism study did not capture data regarding chronic obstructive pulmonary disease severity or type (emphysema or chronic bronchitis), no statements can be made regarding relationships between disease severity or type and our study findings. As in any registry, unrecognized confounding may be present despite extensive evaluation of patient characteristics.

Our study presents data from a large registry analysis evaluating outcomes in patients with the combination of venous thromboembolism and chronic obstructive pulmonary disease. The methodology utilized in this analysis is consistent with published criteria for evaluating the scientific value of clinical data registries.[16] Consecutive patients with objectively confirmed venous thromboembolism from urban, suburban, and rural communities were enrolled and represent a “real world” population.

In conclusion, patients with chronic obstructive pulmonary disease have a significantly increased risk of death during hospitalization and within 30 days of venous thromboembolism diagnosis. Immobility is especially ominous among patients with chronic obstructive pulmonary disease who subsequently develop venous thromboembolism and is associated with a doubling in mortality during and after hospitalization. Chronic obstructive pulmonary disease patients demonstrated an increased mortality despite receiving venous thromboembolism prophylaxis with greater frequency. Quality Improvement initiatives that extend beyond efforts to increase prescription of thromboprophylaxis, such as minimizing immobility, are warranted to prevent venous thromboembolism in the vulnerable chronic obstructive pulmonary disease population.

Acknowledgments

None.

This study was supported by grant R01-HL70283 (PI: Spencer) from the National Heart, Lung, and Blood Institute.

Dr. Spencer is supported by a Career Investigator Award from the Ontario Heart and Stroke Association.

Appendix

Criteria for classification of venous thromboembolic events*

Deep vein thrombosis

Definite- if confirmed by venography, compression ultrasonography, computed tomography, magnetic resonance imaging, or autopsy.

Probable- if the above tests were not performed, or were indeterminate, but impedence plethysmography, radionuclide venography, or radiolabeled fibrinogen scan test results were reported as positive.

Possible- if all of these confirmatory tests were not performed, or were indeterminate, and two of the following criteria were satisfied: the medical record indicated that the physician made a clinical diagnosis of deep vein thrombosis, symptoms or signs of deep vein thrombosis were documented, and the patient underwent therapy with anticoagulants or inferior vena cava filter insertion.

Pulmonary embolism

Definite- if confirmed by pulmonary angiography, spiral chest computed tomography, magnetic resonance imaging, or autopsy.

Probable- if the tests above were not performed, or were indeterminate, but ventilation-perfusion lung scan findings were high probability.

Possible- if all of the above confirmatory tests were not performed, or were indeterminate, and two of the following criteria were satisfied: the medical record indicated that the physician made a clinical diagnosis of pulmonary embolism, symptoms or signs of

pulmonary embolism were documented, and the patient underwent therapy with anticoagulants or inferior vena cava filter insertion.

*Modified from criteria previously utilized by Silverstein et al. in the Olmstead County study of venous thromboembolism.[12] Given increasing acceptance over the last decade of compression ultrasonography as a single diagnostic modality for deep vein thrombosis, we have classified patients with deep vein thrombosis confirmed by compression ultrasonography as definite, whereas these patients would have been categorized as probably by Silverstein's criteria.

Abbreviation list

CI	confidence interval
OR	odds ratio

References

1. Shetty R, Seddighzadeh A, Piazza G, Goldhaber SZ. Chronic obstructive pulmonary disease and deep vein thrombosis: a prevalent combination. J Thromb Thrombolysis. 2008; 26:35–40. [PubMed: 17940729]
2. Rizkallah J, Man SF, Sin DD. Prevalence of pulmonary embolism in acute exacerbations of COPD: a systematic review and metaanalysis. Chest. 2009; 135:786–793. [PubMed: 18812453]
3. Vaidyula VR, Criner GJ, Grabianowski C, Rao AK. Circulating tissue factor procoagulant activity is elevated in stable moderate to severe chronic obstructive pulmonary disease. Thromb Res. 2009; 124:259–261. [PubMed: 19162305]
4. Tapson VF. The role of smoking in coagulation and thromboembolism in chronic obstructive pulmonary disease. Proc Am Thorac Soc. 2005; 2:71–77. [PubMed: 16113472]
5. Ambrosetti M, Ageno W, Spanevello A, et al. Prevalence and prevention of venous thromboembolism in patients with acute exacerbations of COPD. Thromb Res. 2003; 112:203–207. [PubMed: 14987912]
6. Stein PD, Beemath A, Meyers FA, Olson RE. Pulmonary embolism and deep venous thrombosis in hospitalized adults with chronic obstructive pulmonary disease. J Cardiovasc Med (Hagerstown). 2007; 8:253–257. [PubMed: 17413301]
7. Gunen H, Gulbas G, In E, et al. Venous thromboemboli and exacerbations of COPD. Eur Respir J. 2010; 35:1243–1248. [PubMed: 19926740]
8. Akgun M, Meral M, Onbas O, et al. Comparison of clinical characteristics and outcomes of patients with COPD exacerbation with or without venous thromboembolism. Respiration. 2006; 73:428–433. [PubMed: 16636527]
9. Monreal M, Munoz-Torrero JF, Naraine VS, et al. Pulmonary embolism in patients with chronic obstructive pulmonary disease or congestive heart failure. Am J Med. 2006; 119:851–858. [PubMed: 17000216]
10. Spencer FA, Emery C, Lessard D, et al. The Worcester Venous Thromboembolism study: a population-based study of the clinical epidemiology of venous thromboembolism. J Gen Intern Med. 2006; 21:722–727. [PubMed: 16808773]
11. Spencer FA, Emery C, Lessard D, Goldberg RJ. Upper extremity deep vein thrombosis: a community-based perspective. Am J Med. 2007; 120:678–684. [PubMed: 17679126]
12. Silverstein MD, Heit JA, Mohr DN, et al. Trends in the incidence of deep vein thrombosis and pulmonary embolism: a 25-year population-based study. Arch Intern Med. 1998; 158:585–593. [PubMed: 9521222]
13. Schulman S, Kearon C. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. J Thromb Haemost. 2005; 3:692–694. [PubMed: 15842354]

14. Piazza G, Goldhaber SZ. The acutely decompensated right ventricle: pathways for diagnosis and management. Chest. 2005; 128:1836–1852. [PubMed: 16162794]

15. Piazza G, Goldhaber SZ, Lessard DM, et al. Venous thromboembolism in heart failure: preventable deaths during and after hospitalization. Am J Med. 2011; 124:252–259. [PubMed: 21396509]

16. Alpert JS. Are data from clinical registries of any value? Eur Heart J. 2000; 21:1399–1401. [PubMed: 10952831]

Table 1

Baseline characteristics of patients with venous thromboembolism.

	Total (n=2488)	Chronic obstructive pulmonary disease		p-value
		Yes (n =484)	No (n = 2004)	
Age, years (mean±SD)	63.8 ± 18.1	68.2 ± 15.2	62.7 ± 18.6	<0.0001
Age > 65 years, n (%)	1332 (53.5)	308 (63.6)	1,024 (51.1)	<0.0001
Body mass index, kg/m^2 (mean±SD)	28.7 ± 7.7	28.6 ± 8.9	28.7 ±7.3	0.86
Male, n (%)	1104 (44.5)	215 (44.5)	889 (44.5)	0.98
Ethnicity, n (%)				
Caucasian	2231 (89.7)	439 (90.7)	1,792 (89.4)	0.4
African-American	81 (3.3)	13 (2.7)	68 (3.4)	0.42
Asian	11 (0.4)	0 (0)	11 (0.6)	0.03
Hispanic	43 (1.7)	9 (1.9)	34 (1.7)	0.81
Other	21 (0.8)	7 (1.5)	14 (0.7)	0.13
Developed venous thromboembolism during hospitalization for another condition, n (%)	700 (28.1)	173 (35.7)	527 (26.3)	<0.0001
Length of stay, days (mean±SD)	10.6 ± 16.1	12.4 ± 16.3	10.1 ± 16	0.01
Venous thromboembolism diagnostic category, n (%)				
Definite	2320 (93.8)	454 (94.6)	1866 (93.4)	0.42
Probable	80 (3.2)	15 (3.1)	65 (3.1)	0.89
Possible	74 (3.0)	11 (2.3)	63 (3.2)	0.32

SD, standard deviation.

Table 2

Comorbid conditions in patients with venous thromboembolism.

	Total (n=2488)	Chronic obstructive pulmonary disease		p-value
		Yes (n =484)	No (n = 2004)	
Immobility > 48 hours, n (%)	1127 (45.3)	259 (53.5)	868 (43.3)	<0.0001
Infectious illness, n (%)	626 (25.2)	186 (38.4)	440 (22)	<0.0001
Smoking history, n (%) *				
Current smoker	345 (18.9)	84 (25.2)	261 (17.5)	0.002
Former smoker	600 (32.9)	161 (48.2)	439 (29.5)	<0.0001
Never smoker	754 (41.4)	79 (23.7)	675 (45.4)	<0.0001
Heart failure, n (%)	431 (17.3)	172 (35.5)	259 (12.9)	<0.0001
Cancer, n (%)	654 (26.3)	123 (25.4)	531 (26.5)	0.63
Major surgery within the previous 3 months, n (%)	685 (27.5)	122 (25.2)	563 (28.1)	0.2
Central venous catheter, n (%)	460 (18.5)	122 (25.2)	338 (16.9)	<0.0001
Diabetes, n (%)	476 (19.1)	120 (24.8)	356 (17.8)	0.0006
Intensive care unit discharge within the previous 3 months,n (%)	406 (16.3)	115 (23.8)	291 (14.5)	<0.0001
Endotracheal intubation with the previous 3 months, n (%)	389 (15.6)	103 (21.3)	286 (14.3)	0.0002
Ischemic heart disease, n (%)	324 (13.0)	99 (20.5)	225 (11.2)	<0.0001
ST-elevation MI	23 (0.9)	6 (1.2)	17 (0.9)	0.44
Non ST-elevation MI	50 (2.0)	15 (3.1)	35 (1.8)	0.07
Unspecified MI	226 (9.1)	70 (14.5)	156 (7.8)	<0.0001
Any MI	288 (11.6)	85 (17.6)	203 (10.1)	<0.0001
Unstable angina *	77 (4.2)	25 (7.5)	52 (3.5)	0.002
Stable angina *	118 (6.5)	34 (11.4)	84 (5.7)	0.004
Prior venous thromboembolism, n (%)	450 (18.1)	88 (18.2)	362 (18.1)	0.95
Cardiac procedure during admission, n (%)	249 (10.0)	67 (13.8)	182 (9.1)	0.003
Catheterization or EP study	180 (7.2)	57 (11.8)	123 (6.1)	<0.0001
PCI and stent	73 (2.9)	18 (3.7)	55 (2.7)	0.27
Pacemaker	66 (2.7)	12 (2.5)	54 (2.7)	0.79
ICD implantation	21 (0.8)	8 (1.7)	13 (0.7)	0.05
Chronic kidney disease, n (%)	196 (7.9)	58 (12)	138 (6.9)	<0.001
Dialysis dependent	63 (2.5)	14 (2.9)	49 (2.5)	0.58
Pulmonary hypertension, n (%)	93 (3.7)	36 (7.4)	57 (2.8)	<0.0001

MI, myocardial infarction; EP, electrophysiology study; ICD, implantable cardiac defibrillator; PCI, percutaneous coronary intervention.

*Data not collected for this variable in 2005.

Table 3

Clinical presentation of venous thromboembolism.

		Chronic obstructive pulmonary disease		
	Total (n=2488)	**Yes (n =484)**	**No (n = 2004)**	**p-value**
Any symptoms, n (%)	1989 (82.6)	372 (79.3)	1,617 (83.4)	0.006
Extremity swelling, n (%)	1163 (46.7)	233 (48.1)	930 (46.4)	0.49
Dyspnea, n (%)	563 (22.6)	154 (31.8)	409 (20.4)	<0.0001
Extremity pain, n (%)	756 (30.4)	126 (26)	630 (31.4)	0.02
Heart rate > 100 bpm, n (%)	256 (11.7)	65 (13.4)	191 (9.5)	0.02
Chest pain, n (%)	250 (10.1)	60 (12.4)	190 (9.5)	0.06
Cough, n (%)	191 (7.7)	60 (12.4)	131 (6.5)	<0.0001
Systolic blood pressure < 100 mmHg, n (%)	153 (7.0)	42 (8.7)	111 (5.5)	0.02
Fever, n (%)	156 (6.3)	41 (8.5)	115 (5.7)	0.03
Oxygen saturation < 90%, n (%)	55 (15.6)	29 (6)	26 (1.3)	0.002
Dizziness, n (%)	69 (2.8)	9 (1.9)	60 (3)	0.15
Hemoptysis, n (%)	22 (0.9)	7 (1.5)	15 (0.8)	0.17
Loss of consciousness, n (%)	36 (1.5)	7 (1.5)	29 (1.5)	0.99
Any deep vein thrombosis, n (%)	2132 (85.7)	405 (83.7)	1,727 (86.2)	0.16
Proximal lower extremity with calf deep vein thrombosis, n (%)	309 (12.4)	64 (13.2)	245 (12.2)	0.55
Proximal lower extremity without calf deep vein thrombosis, n (%)	1050 (42.2)	187 (38.6)	863 (43.1)	0.08
Calf deep vein thrombosis, n (%)	193 (7.8)	39 (8.1)	154 (7.7)	0.78
Upper extremity deep vein thrombosis, n (%)	294 (11.8)	65 (13.4)	229 (11.4)	0.23
Pulmonary embolism, n (%)	704 (28.3)	153 (31.7)	551 (27.5)	0.07
Both pulmonary embolism and deep vein thrombosis present, n (%)	350 (14.1)	75 (15.5)	275 (13.7)	0.32

Table 4

Characteristics of prophylaxis in patients with hospitalization or major surgery within three months of subsequently developing venous thromboembolism.*

		Chronic obstructive pulmonary disease		
	Total (n=2488)	**Yes (n = 435)**	**No (n = 1644)**	**p-value**
Receiving any prophylaxis, n (%)	1027 (49.4)	261 (60)	766 (46.6)	<0.0001
Pneumatic compression devices, n (%)	564 (27.1)	115 (26.4)	449 (27.3)	0.71
Subcutaneous unfractionated heparin, n (%)	454 (21.8)	132 (30.3)	322 (19.6)	<0.0001
Intravenous unfractionated heparin, n (%)	128 (6.2)	31 (7.1)	97 (5.9)	0.35
Low-molecular weight heparin, n (%)	188 (9.0)	47 (10.8)	141 (8.6)	0.16
Warfarin, n (%)	99 (4.8)	32 (7.4)	67 (4.1)	0.01

*Patients could have received more than one prophylactic modality.

Table 5

Therapy in patients with venous thromboembolism.*

		Chronic obstructive pulmonary disease		
	Total (n=2488)	**Yes (n =484)**	**No (n = 2004)**	**p-value**
Initial Therapy				
Warfarin, n (%)	1591 (64.0)	313 (64.7)	1,278 (63.8)	0.71
IV unfractionated heparin, n (%)	1179 (47.4)	261 (53.9)	918 (45.8)	0.001
Low-molecular weight heparin, n (%)	1262 (50.7)	238 (49.2)	1,024 (51.1)	0.45
Inferior vena cava filter, n (%)	294 (11.8)	68 (14.1)	226 (11.3)	0.1
SC unfractionated heparin, n (%)	94 (3.8)	26 (5.4)	68 (3.4)	0.05
Hirudin,n (%)	4 (0.2)	1 (0.2)	3 (0.2)	0.79
Discharge Therapy				
Warfarin alone, n (%)	934 (39.3)	189 (41.9)	745 (38.7)	0.21
Low-molecular weight heparin and warfarin, n (%)	772 (32.5)	130 (28.8)	642 (33.4)	0.06
Low-molecular weight heparin alone, n (%)	206 (8.7)	43 (9.5)	163 (8.5)	0.48
Neither, n (%)	463 (19.5)	89 (19.7)	374 (19.4)	0.89

IV, intravenous; SC, subcutaneous.

* Patients could have received more than one therapeutic modality.

Table 6

Outcomes of patients with venous thromboembolism.*

		Chronic obstructive pulmonary disease		
	Total (n=2488)	**Yes (n =484)**	**No (n = 2004)**	**p-value**
No complications, n (%)	1766 (71.0)	307 (63.4)	1,459 (72.8)	<0.0001
Recurrent pulmonary embolism, n (%)	38 (1.5)	6 (1.2)	32 (1.6)	0.56
Recurrent deep vein thrombosis, n (%)	287 (11.5)	65 (13.4)	222 (11.1)	0.15
Long-term major bleeding, n (%)	313 (12.6)	70 (14.5)	243 (12.1)	0.17
In-hospital major bleeding, n (%)	103 (4.1)	25 (5.2)	78 (3.9)	0.22
Hep arin-induced thrombocytopenia, n (%)	25 (1.6)	9 (1.9)	16 (0.8)	0.1
In-hospital death, n (%)	113 (4.5)	33 (6.8)	80 (4)	0.01
Death within 30 days of venous thromboembolism diagnosis, n (%)	191 (8.0)	61 (12.6)	130 (6.5)	<0.0001

* Long-term outcomes data encompassed a median follow-up period of 992 days.

Table 7

Univanate and multivanate results for variables in the multivanable model for in-hospital death and death within 30 days of venous thromboembolism diagnosis.

In-hospital death		
Variable	**Univariate Model OR (95% CI)**	**Multivariate Model Adjusted OR (Adjusted 95% CI)**
Chronic obstructive pulmonary disease	1.76 (1.16–2.67)	1.19 (0.76–1.86)
Age	1.02 (1.01–1.03)	1.02 (1.00–1.03)
Sex (male vs. female)	1.24 (0.85–1.81)	1.30 (0.88–1.94)
Immobility > 48 hours	4.30 (2.75–6.71)	2.21 (1.35–3.62)
Ischemic heart disease	1.66 (1.03–2.69)	0.89 (0.53–1.51)
Central venous catheter	3.80 (2.59–5.60)	1.41 (0.85–2.34)
Intensive care unit discharge within the previous 3 months	5.06 (3.44–7.45)	1.97 (1.18–3.30)
Chronic kidney disease	2.17 (1.27–3.72)	1.18 (0.66–2.12)
Heart failure	3.02 (2.03–4.49)	1.41 (0.89–2.24)
Receiving any thromboprophylaxis	4.85 (3.13–7.54)	2.12 (1.27–3.55)

Death and death within 30 days of venous thromboembolism diagnosis		
Variable	**Univariate Model OR (95% CI)**	**Multivariate Model Adjusted OR (Adjusted 95% CI)**
Chronic obstructive pulmonary disease	2.09 (1.52–2.89)	1.53 (1.09–2.16)
Age	1.04 (1.03–1.05)	1.04 (1.03–1.05)
Sex (male vs. female)	1.12 (0.83–1.50)	1.31 (0.95–1.79)
Immobility > 48 hours	3.17 (2.30–4.38)	2.04 (1.43–2.91)
Ischemic heart disease	1.62 (1.10–2.38)	0.90 (0.59–1.36)
Central venous catheter	2.65 (1.94–3.64)	1.65 (1.08–2.53)
Intensive care unit discharge within the previous 3 months	2.86 (2.07–3.95)	1.21 (0.78–1.87)
Chronic kidney disease	2.14 (1.39–3.30)	1.29 (0.80–2.06)
Heart failure	2.69 (1.95–3.71)	1.18 (0.81–1.71)
Receiving any thromboprophylaxis	3.08 (2.25–4.21)	1.59 (1.10–2.30)