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Authors

Fang, Margaret C
Fan, Dongjie
Sung, Sue Hee
et al.

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Treatment and Outcomes of Acute Pulmonary Embolism and Deep Venous Thrombosis: The Cardiovascular Research Network Venous Thromboembolism (CVRN VTE) Study

Margaret C. Fang, MD, MPH[1], **Dongjie Fan, MSPH**[2], **Sue Hee Sung, MPH**[2], **Daniel M. Witt, Pharm D**[3], **John R. Schmelzer, PhD**[4], **Marc S. Williams, MD**[5], **Steven H. Yale, MD**[6], **Christine Baumgartner, MD, MAS**[7], **Alan S. Go, MD**[2,8,9]

[1]Division of Hospital Medicine, University of California, San Francisco (San Francisco, CA) [2]Division of Research, Kaiser Permanente Northern California (Oakland, CA) [3]Department of Pharmacotherapy, University of Utah College of Pharmacy (Salt Lake City, UT) [4]Marshfield Clinic Research Institute (Marshfield, WI) [5]Genomic Medicine Institute, Geisinger (Danville, PA) [6]Department of Medicine, University of Central Florida College of Medicine (Orlando, FL) [7]Division of General Internal Medicine, Inselspital, Bern University Hospital, University of Bern (Bern, Switzerland) [8]Departments of Epidemiology, Biostatistics and Medicine, University of California, San Francisco (San Francisco, CA) [9]Departments of Medicine, Health Research and Policy, Stanford University School of Medicine (Palo Alto, CA)

Abstract

Background—Few studies describe both inpatient and outpatient treatment and outcomes of patients with acute venous thromboembolism in the US.

Methods—A multi-institutional cohort of patients diagnosed with confirmed pulmonary embolism and/or deep venous thrombosis during years 2004 through 2010 was established from four large, US-based integrated healthcare delivery systems. Computerized databases were accessed and medical records reviewed to collect information on patient demographics, clinical risk factors, initial antithrombotic treatment, and vital status. Multivariable Cox regression models were used to estimate the risk of death at 90 days.

Results—The cohort comprised 5,497 adults with acute venous thromboembolism. Pulmonary embolism was predominantly managed in the hospital setting (95.0%) while 54.5% of patients with lower extremity thrombosis were treated as outpatients. Anticoagulant treatment differed according to thromboembolism type: 2688 (92.8%) of patients with pulmonary embolism and

Corresponding author: Margaret C. Fang, MD, MPH, Associate Professor of Medicine, Division of Hospital Medicine, University of California, San Francisco, 533 Parnassus Ave., Box 0131, San Francisco, CA 94143, Margaret.Fang@ucsf.edu, Phone: (415) 502-7100.

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1625 (86.9%) of patients with lower extremity thrombosis were discharged on anticoagulants, compared to 286 (80.1%) patients with upper extremity thrombosis and 69 (54.8%) patients with other thrombosis. While 4.5% of patients died during the index episode, 15.4% died within 90 days. Pulmonary embolism was associated with a higher 90-day death risk than lower extremity thrombosis (adjusted hazard ratio [aHR] 1.23 [1.04-1.47]) as was not being discharged on anticoagulants (aHR 5.56 [4.76-6.67]).

Conclusions—In this multicenter, community-based study of patients with acute venous thromboembolism, anticoagulant treatment and outcomes varied by thromboembolism type. Although case-fatality during the acute episode was relatively low, 15.4% of people with thromboembolism died within 90 days of the index diagnosis.

Keywords

venous thromboembolism; anticoagulation; deep venous thrombosis; pulmonary embolism; mortality

Introduction

Venous thromboembolism, primarily pulmonary embolism and deep venous thrombosis, affects an estimated 750,000 people in the United States (US) each year and causes more than 100,000 deaths annually.[1-3] Yet there are relatively few large US-based studies that describe in detail the characteristics, treatment, and outcomes of venous thromboembolism. Many studies rely solely on diagnosis codes to identify thromboembolism, which may not accurately identify true thrombotic events[4-8]. Administrative databases also lack complete data on patient risk factors, acuity of illness, and treatment plan.[9] Most studies focus on hospitalized patients,[4-7, 10] despite acute management moving towards outpatient settings[11], or only include patients discharged on anticoagulants.

To more completely describe the treatment and outcomes of patients with venous thromboembolism, we conducted a multicenter observational cohort study of patients with acute thrombosis within the Cardiovascular Research Network Venous Thromboembolism (CVRN VTE) consortium. Our goal was to describe treatment strategies, morbidity, and mortality outcomes of both inpatients and outpatients with acute thromboembolism.

Materials and Methods

Cohort Assembly

The CVRN VTE study is a retrospective cohort of patients with venous thromboembolism enrolled in one of four integrated healthcare delivery systems in the US. The four systems represented diverse geographic patient sources, with service provided during the study period to the following populations: Kaiser Permanente Northern California (>3.2 million members in Northern California during the study period), Kaiser Permanente Colorado (>460,000 members in the Denver, Colorado metropolitan area), Geisinger Health System, now Geisinger (~2.5 million members in central and northwest Pennsylvania), and Marshfield Clinic (>550,000 members in central and northwest Wisconsin). All clinical sites used electronic health record systems during the time period of the study. The study was

approved by the institutional review board at each of the participating sites according to local policies and procedures. A waiver of informed consent was obtained due to the nature of the study.

The cohort was assembled by first searching computerized health plan databases for all individuals ⩾21 years of age with a clinical encounter (inpatient, emergency department [ED] or ambulatory) associated with either a primary or secondary *International Classification of Diseases, Ninth Revision* (ICD-9) diagnosis code of venous thromboembolism, between October 1, 2004 and December 31, 2010. Only the first encounter with a code for venous thromboembolism during the time period was reviewed. Because the focus of the study was on incident thrombosis, patients with a prior code for thrombosis while enrolled in the health plan, or prescribed anticoagulants within 4 years prior, were excluded. We included only subjects with continuous health plan and pharmacy benefits for at least 12 months prior to the index thrombotic encounter.

Events were categorized as *pulmonary embolism* (ICD-9 code 415.1x), *lower extremity deep venous thrombosis* (451.1x, 451.2, 451.81, 453.4x, 453.5x), *upper extremity deep venous thrombosis* (451.83, 451.84, 451.89, 453.72, 453.73, 453.74, 453.75, 453.76, 453.77, 453.82, 453.83, 453.84, 453.85, 453.86, 453.87), and *other venous thrombosis* (451, 451.9, 452, 453, 453.0, 453.1, 453.2, 453.3, 453.79, 453.8, 453.89, 453.9). We did not include pregnancy-related thromboembolism or superficial thrombophlebitis as part of this study.

Validation of Venous Thromboembolic Events

We identified 42,941 unique individuals with an incident clinical encounter assigned a diagnosis of thromboembolism meeting inclusion criteria. To attain a target sample size of ~5500 patients with valid, acute venous thrombosis, we initially selected 7,334 clinical encounters for review, comprising all available patients in two of the health systems and a random sample of patients from the other two systems. All available inpatient admission, transfer, discharge, ED, and outpatient encounter notes were redacted, as well as relevant radiology reports within 72 hours before and after the index venous thromboembolism date. Trained physician and pharmacist reviewers then reviewed medical records using a structured adjudication tool to determine whether the encounter represented a valid acute thromboembolism. Events were considered valid if there was radiographic, operative, or autopsy evidence of an acute thrombosis, or if a physician documented in the medical record that an acute venous thromboembolism had occurred during that episode of care. An encounter with a prior history of venous thromboembolism whose acute management was not contiguous with the current episode was not considered an acute event. Superficial venous thromboses/thrombophlebitis were not considered valid events.

Of the initial 7,334 patients, 7,063 had medical records available for review. However, only 2,135 (30.2%) were determined upon review to represent valid thromboembolism events, with ambulatory encounters and those with thrombosis codes in the secondary position less likely to represent true acute events (results of the validation process described previously).[8] To enhance the likelihood of finding valid encounters, we then randomly selected an additional set of patients for review, restricting to hospital/ED encounters with a primary

diagnosis of thrombosis in years 2006 or later, until we reached a total of ~5500 valid events (Supplemental Figure).

Presentation, Treatment, and Outcomes of Acute Venous Thromboembolism

Clinical and demographic information were obtained from computerized health plan databases. Relevant medical conditions within 4 years prior to the index event were identified using inpatient or outpatient ICD-9 codes. Ascertainment of diabetes mellitus and malignant cancer was supplemented using regional diabetes and cancer registries from some of the health systems.[12], [13] ICD-9 codes were used to calculate a Charlson comorbidity index score for each patient.[14] Receipt of medications to manage chronic cardiovascular diseases were identified by searching health plan pharmacy dispensing databases within 30 days prior to the index thromboembolism date.

Clinician reviewers collected information on thromboembolism type, smoking history, and documented immobility or injury (such as surgery within 30 days, trauma or prolonged immobility within 7 days, indwelling venous catheters). Thromboembolic events were defined as “unprovoked” if they occurred in the absence of identifiable risk factors such as diagnosed cancer or documented history of recent surgery, immobility, or injury.

Reviewers assessed whether antithrombotic medications were prescribed at the end of the encounter and categorized as oral anticoagulants (specifically warfarin, as direct oral anticoagulants were not yet approved for use in thromboembolism), parenteral anticoagulants (e.g., low-molecular-weight heparins, fondaparinux), and antiplatelet agents (aspirin, clopidogrel, ticlopidine, dipyridimole, and cilostazol). For encounters without antithrombotic treatment at discharge, the encounter documentation was reviewed for potential reasons why treatment was not issued.

The primary outcome for the study was death from any cause within 90 days after the index thromboembolic event. Secondary outcomes included death during the index event, death within 30 days, and new functional impairment at discharge. Death was determined from medical record review, health plan databases, and the Social Security Index death files. Functional impairment was ascertained by review of the encounter documentation. Reviewers used their clinical judgement to determine whether the patient suffered functional consequences as a result of the thrombotic event and categorized as “at least some functional impairments related to the event”, “no functional impairments related to the event”, or “unknown”.

Statistical Analysis

The study objective was to compare anticoagulant treatment patterns and short-term outcomes by thromboembolism type (any pulmonary embolism, lower extremity thrombosis, upper extremity thrombosis, and other venous thromboses). We first used descriptive statistics to report clinical characteristics, treatment, and outcomes by event type, using ANOVA for continuous variables and χ^2 tests for categorical variables when comparing amongst thromboembolism types. We then modeled death within 90 days as a function of event type and anticoagulant treatment, developing a multivariable Cox regression model that incorporated variables that have been or could be plausibly be related to short-term

mortality, including risk factors for thrombosis, coexisting medical conditions, Charlson comorbidity risk score, and baseline use of medications to manage cardiovascular conditions. A two-sided p-value less than 0.05 was considered statistically significant. All analyses were performed using SAS version 9.1 (SAS Institute, Inc., Cary, NC).

Results

The cohort comprised 5,497 adults with confirmed acute incident venous thromboembolism. The mean age of the cohort was 65.7 years and 51.4% were women (Table 1). The majority of subjects (n=3,056) had pulmonary embolism with or without concomitant deep venous thrombosis, followed by patients with isolated lower extremity thrombosis (n=1,928). Relatively few patients had isolated upper extremity thrombosis (n=383) or other forms of thrombosis (n=130).

Cancer was a common comorbid condition, present in 2,022 (36.4%) of patients overall and with a particularly high prevalence among people with upper extremity thrombosis (44.9%). Recent immobility and/or injury was identified in 2,302 (41.9%) of the cohort. In 188 (49.1%) of the 383 patients with upper extremity thrombosis, an indwelling venous catheter was identified as a potential provoking event. For 1,254 (22.8%) of patients, the event was categorized as unprovoked (e.g., no history of immobility, injury, recent hospitalization, or known cancer).

Treatment and outcomes of acute venous thromboembolism

The majority of patients received anticoagulants (oral and/or parenteral) at discharge, although treatment differed by thrombosis type (Table 2). Among survivors of the acute event, 92.8% of those with pulmonary embolism and 86.9% of those with lower extremity thrombosis were discharged on anticoagulants. Anticoagulant treatment was less common among patients with thromboses in other locations: 80.1% of patients with upper extremity thrombosis and 54.8% of patients with other thrombosis. Few patients (2.9%) were discharged on antiplatelet agents only. Among the 430 patients who survived the acute episode and were not prescribed antithrombotic therapy at discharge, bleeding risk and/or poor prognosis were identified by reviewers as a rationale to avoid anticoagulants in 75.3% and 61.2% of patients, respectively.

Death during the index thrombotic episode occurred in 5.2% of patients with pulmonary embolism and 3.1% of patients with lower extremity thrombosis (Table 2). Among patients who survived the index event, reviewers noted “at least some functional impairments related to the event” more commonly among patients with pulmonary embolism (26.1%) than patients with isolated lower extremity thrombosis (15.6%. $p<0.01$). The proportion of patients who died after the index event continued to rise after discharge: all-cause mortality was 8.0% at 30 days and 15.4% at 90 days (Table 2). Among all inpatients, 9.8% died within 30 days and 17.9% died within 90 days. In contrast, 2.5% and 7.7% of ED/ambulatory patients died within 30 and 90 days, respectively. Crude mortality at 90 days was highest in patients with other thrombosis (25.4%), followed by isolated upper extremity thrombosis (20.9%) and then pulmonary embolism (15.5%). However, after multivariable adjustment, no significant differences in 90-day death rates persisted between these three groups (Table

3). In a multivariable Cox regression model, patients with pulmonary emboli had a higher 90-day mortality risk compared to patients with lower extremity thrombosis, with an adjusted hazard ratio [aHR] of 1.2 (95% confidence interval [CI] 1.04-1.5). Not being discharged on anticoagulants was associated with significantly higher mortality risk, aHR 5.6 (95% CI: 4.8-6.7). Other clinical factors associated with a higher risk of death at 90 days included older age, current smoking, a diagnosis of cancer, and higher Charlson comorbidity scores (Table 3).

Discussion

Our study provides a unique examination of the acute presentation, treatment, and outcomes of inpatients and outpatients with venous thromboembolism across four geographically diverse US-based health systems. Although most patients with thromboembolism were treated with anticoagulants, 1 in 10 people were not, frequently due to concerns for bleeding risk or poor clinical prognosis. The short-term outcomes after a diagnosis of thromboembolism are consequential, with 15.4% of patients dying within 90 days after initial diagnosis.

Strengths of our study include its diverse source population, inclusion of events from both inpatient and outpatient settings, and validation of index thromboembolic events and collection of data through review of medical records. These methods were then facilitated with additional data from comprehensive electronic medical records at each study site. We were able to identify health care utilization even if patients presented to facilities outside of the healthcare system, as all patients were enrolled in integrated healthcare delivery systems. In contrast, most large, contemporary studies addressing acute venous thromboembolism in the US have relied on administrative data obtained from hospital settings, providing an incomplete perspective.[4, 5, 15, 16] Our prior work found that only 30.9% of ambulatory encounters with a thrombosis diagnosis actually represented an acute thrombotic event .[8] With the advent of direct oral anticoagulants, it is likely that the outpatient treatment of thromboembolism will become even more prevalent.

Descriptions of short-term outcomes following acute pulmonary embolism vary across different studies. The Multicenter Emergency Medicine Pulmonary Embolism in the Real World Registry (EMPEROR) study reported a relatively low 30-day mortality rate (5.4%) in patients with pulmonary embolism presenting to US-based emergency departments between 2005-2008[17], comparable to the international Registro Informatizado de la Enfermedad TromboEmbólica (RIETE) registry (5.9% mortality).[18] In contrast, a Canadian study found a substantially higher (16.9%) 30-day mortality rate among hospitalized and ambulatory patients[19] as did a Danish nationwide registry (19.9% 30-day mortality after hospitalization).[20] The Nationwide Inpatient Sample, a nationally representative sample of US-hospital admissions, reported a declining risk of inpatient death after pulmonary embolism (7.1% in 1993 and 3.2% in 2012).[21] Our study found that 5.2% of patients with pulmonary embolism died during the index event and 8.7% at 30 days.

Variation in short-term outcomes observed across studies may have several possible explanations. One possibility may be differences in anticoagulation management and

delivery; for example, the four health systems in our study were all integrated healthcare delivery models of care. Our study included patients treated in outpatient settings, who may have less severe disease and better functional status. Previous studies have shown that selective outpatient treatment of acute pulmonary embolism is feasible and effective.[22-25] Despite this, outpatient management of pulmonary embolism is still limited in clinical practice [18, 26-28] Different follow-up periods could account for differences in case-fatality rates, given secular trends of lower mortality from pulmonary embolism within the last two decades.[4, 18, 21] Finally, the introduction and increased use of multidetector computed tomography may have contributed to including less severe or even clinically unimportant pulmonary emboli.[7, 29]

In contrast to pulmonary embolism, we observed less discrepancy in 30-day mortality after deep venous thrombosis in our cohort compared to findings from the Worcester VTE study (5.4%),[30] a Canadian study (7%),[19] and a Danish registry (4.5%).[20] Our results are consistent with other studies that show pulmonary embolism as an independent predictor of short-term death compared to deep venous thrombosis alone.[30-32]

Most patients in our study were prescribed anticoagulants and anticoagulant treatment was associated with a significantly lower risk for 90-day death. Causality between treatment and mortality cannot be inferred, as it is highly likely there was channeling bias, where patients with limited life expectancy or at higher risk for adverse outcomes from anticoagulants were less likely to be prescribed treatment. Indeed, poor prognosis was commonly cited as a reason for avoiding therapy. Anticoagulation treatment varied by event type, with upper extremity thrombosis and thrombosis in unusual sites less likely to be treated with anticoagulants.

Our results have several implications for practitioners, policy makers, and researchers. Our results underline the persistent public health importance of venous thromboembolism and highlight the substantial short-term mortality after incident thrombosis. Efforts to prevent thromboembolism and ensure timely diagnosis and treatment should be undertaken. Given that more than 19 billion dollars annually are spent for the treatment of thromboembolism in the US,[33] with a substantial amount accounting from in-hospital care,[34] better education of clinicians about the appropriate risk stratification and the possibility of home treatment of patients could help to reduce costs.[26]

There are also several limitations to this study. We oversampled for hospitalized patients, so preferentially captured more pulmonary embolism events and our findings might have been slightly biased towards patients with more severe disease. As a retrospective and observational study of clinical care, variation in documentation could have contributed to misclassification of certain variables, such as prior injury or immobility. Our study specifically addressed incident thrombosis and did not include recurrent thromboembolic events, which have different risk factors and outcomes. Finally, our study did not include the experience of patients with thrombosis who were treated with the direct oral anticoagulants, which were not yet in widespread use during the study period.[35] Nevertheless, VKAs remain commonly prescribed in the US and worldwide.[36, 37]

Conclusions

This large, multicenter cohort of patients with acute venous thromboembolism provides unique insights into treatment and outcomes of thromboembolism and demonstrated that anticoagulant treatment patterns and short-term mortality varied by event-type. Although case-fatality during the acute episode was relatively low, 15.4% of affected patients with acute thromboembolism died within 90 days of the incident event, highlighting the need for effective strategies to improve outcomes in this population. As treatment options continue to expand beyond warfarin to include direct oral anticoagulants, it is important to document how treatment and outcomes of thromboembolism evolves over time.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Characteristics of 5,497 Patients with Acute Venous Thromboembolism

	TOTAL	Pulmonary embolism (with or without deep venous thrombosis) N=3056	Lower extremity thrombosis N=1928	Isolated upper extremity thrombosis N=383	Isolated other thrombosis N=130	P-Value[17]
Age, mean years (SD)	65.7 (15.8)	65.7 (15.6)	66.5 (16.1)	62.8 (15.8)	61.1 (15.0)	<0.001
Women, n (%)	2824 (51.4)	1565 (51.2)	991 (51.4)	209 (54.6)	59 (45.4)	0.33
Race, n (%)						<0.001
White	4375 (79.6)	2437 (79.7)	1546 (80.2)	302 (78.9)	90 (69.2)	
Black	436 (7.9)	260 (8.5)	135 (7.0)	28 (7.3)	13 (10.0)	
Asian	161 (2.9)	85 (2.8)	46 (2.4)	19 (5.0)	11 (8.5)	
American/Pacific Islander						
Other/unknown	525 (9.6)	274 (9.0)	201 (10.4)	34 (8.9)	16 (12.3)	
Hispanic ethnicity, n (%)	391 (7.1)	200 (6.5)	138 (7.2)	40 (10.4)	13 (10.0)	0.02
Treatment setting, n (%)						<0.001
Hospital	4155 (75.6)	2902 (95.0)	878 (45.5)	267 (69.7)	108 (83.1)	
Emergency department or ambulatory clinic only	1342 (24.4)	154 (5.0)	1050 (54.5)	116 (30.3)	22 (16.9)	
Baseline medical history, n (%)						
Hypertension	3165 (57.6)	1748 (57.2)	1118 (58.0)	225 (58.7)	74 (56.9)	0.91
Diabetes mellitus	1178 (21.4)	624 (20.4)	416 (21.6)	108 (28.2)	30 (23.1)	0.006
Cancer	2002 (36.4)	1115 (36.5)	665 (34.5)	172 (44.9)	50 (38.5)	<0.001
Prior ischemic stroke	125 (2.3)	70 (2.3)	43 (2.2)	9 (2.3)	3 (2.3)	1.0
Ischemic heart disease[18]	558 (10.2)	312 (10.2)	208 (10.8)	35 (9.1)	3 (2.3)	0.02
Heart failure	514 (9.4)	280 (9.2)	171 (8.9)	55 (14.4)	8 (6.2)	0.004
Atrial fibrillation or flutter	504 (9.2)	271 (8.9)	175 (9.1)	52 (13.6)	6 (4.6)	0.006
Valvular heart disease	320 (5.8)	162 (5.3)	120 (6.2)	32 (8.4)	6 (4.6)	0.07
Chronic pulmonary disease[19]	1065 (19.4)	623 (20.4)	325 (16.9)	104 (27.2)	13 (10.0)	<0.001
Chronic liver disease	181 (3.3)	75 (2.5)	63 (3.3)	19 (5.0)	24 (18.5)	<0.001
Hospitalization for sepsis	195 (3.5)	90 (2.9)	74 (3.8)	29 (7.6)	2 (1.5)	<0.001
Inflammatory bowel disease	98 (1.8)	50 (1.6)	35 (1.8)	9 (2.3)	4 (3.1)	0.51
Hypercoagulable hematologic conditions[20]	124 (2.3)	55 (1.8)	49 (2.5)	15 (3.9)	5 (3.8)	0.01
Thrombophilia[21]	22 (0.4)	8 (0.3)	9 (0.5)	3 (0.8)	2 (1.5)	0.06
Prior hospitalization for intracranial hemorrhage	103 (1.9)	46 (1.5)	48 (2.5)	8 (2.1)	1 (0.8)	0.07
Prior hospitalization for gastrointestinal hemorrhage	161 (2.9)	82 (2.7)	57 (3.0)	16 (4.2)	6 (4.6)	0.26
Prior hospitalization for other hemorrhage	41 (0.7)	19 (0.6)	19 (1.0)	2 (0.5)	1 (0.8)	0.50
Prior hospitalization for mechanical fall	32 (0.6)	17 (0.6)	14 (0.7)	1 (0.3)	0 (0.0)	0.54
Baseline medication use, n (%)						
Angiotensin converting enzyme inhibitor	1106 (20.1)	626 (20.5)	371 (19.2)	86 (22.5)	23 (17.7)	0.40
Angiotensin II receptor blocker	324 (5.9)	193 (6.3)	99 (5.1)	25 (6.5)	7 (5.4)	0.34
Beta blocker	1730 (31.5)	978 (32.0)	603 (31.3)	118 (30.8)	31 (23.8)	0.26

	TOTAL	Pulmonary embolism (with or without deep venous thrombosis) N=3056	Lower extremity thrombosis N=1928	Isolated upper extremity thrombosis N=383	Isolated other thrombosis N=130	P-Value[17]
Calcium channel blocker	807 (14.7)	470 (15.4)	262 (13.6)	59 (15.4)	16 (12.3)	0.29
Diuretic	1615 (29.4)	924 (30.2)	540 (28.0)	112 (29.2)	39 (30.0)	0.41
Aldosterone receptor antagonist	152 (2.8)	81 (2.7)	42 (2.2)	18 (4.7)	11 (8.5)	<0.001
Alpha blocker	416 (7.6)	224 (7.3)	152 (7.9)	34 (8.9)	6 (4.6)	0.38
Statin	1586 (28.9)	941 (30.8)	515 (26.7)	110 (28.7)	20 (15.4)	<0.001
Other lipid-lowering agent	136 (2.5)	72 (2.4)	54 (2.8)	9 (2.3)	1 (0.8)	0.45
Non-aspirin antiplatelet agent	290 (5.3)	152 (5.0)	117 (6.1)	19 (5.0)	2 (1.5)	0.08
Antidiabetic treatment	736 (13.4)	411 (13.4)	240 (12.4)	66 (17.2)	19 (14.6)	0.09
Non-steroidal anti-inflammatory drugs	588 (10.7)	353 (11.6)	192 (10.0)	34 (8.9)	9 (6.9)	0.08
Current smoker, n (%)	438 (8.0)	228 (7.5)	147 (7.6)	43 (11.2)	20 (15.4)	<0.001
Hospitalization within 30 days prior to index thrombotic event	1045 (19.0)	580 (19.0)	349 (18.1)	94 (24.5)	22 (16.9)	0.03
Recent immobility/injury, n (%)	2302 (41.9)	1230 (40.2)	794 (41.2)	252 (65.8)	26 (20.0)	<0.001
Indwelling venous catheter	301 (5.5)	76 (2.5)	32 (1.7)	188 (49.1)	5 (3.8)	
Prolonged immobility	977 (17.8)	557 (18.2)	363 (18.8)	47 (12.3)	10 (7.7)	
Trauma/surgery within 30 days	1172 (21.3)	621 (20.3)	446 (23.1)	94 (24.5)	11 (8.5)	
Charlson comorbidity index, n(%)						<0.001
<1	1550 (28.2)	878 (28.7%)	568 (29.5)	64 (16.7)	40 (30.8)	
1-2 (mild)	1664 (30.3)	947 (31.0)	586 (30.5)	90 (23.5)	41 (31.5)	
3-4 (moderate)	910 (16.6)	505 (16.5)	317 (16.4)	72 (18.8)	16 (12.3)	
≥ 5 (severe)	1373 (25.0)	726 (23.8)	457 (23.7)	157 (41.0)	33 (25.4)	

[17] Comparison by thrombosis types

[18] Defined as acute myocardial infarction, unstable angina, percutaneous coronary intervention, or coronary artery bypass grafting

[19] Defined as chronic obstructive pulmonary disease, emphysema, chronic bronchitis, chronic obstructive asthma, bronchiectasis, interstitial lung disease, pulmonary hypertension

[20] Defined as polycythemia vera, paroxysmal nocturnal hemoglobinuria, homocystinuria, congenital deficiency of other clotting factors, defibrination syndrome, essential thrombocythemia, myelofibrosis with myeloid metaplasia, monoclonal paraproteinemia.

[21] Defined as ICD-9 codes 289.81 (primary hypercoagulable state) and 289.82 (secondary hypercoagulable state)

Table 2.

Short-term Outcomes of 5,497 Adults with Acute Venous Thromboembolism

	TOTAL N=5497	Pulmonary embolism (with or without lower extremity thrombosis) N=3056	Lower extremity thrombosis N=1928	Isolated upper extremity thrombosis N=383	Isolated other thrombosis N=130	P-value
Disposition at discharge *						<0.05
In-hospital death	247 (4.5%)	158 (5.2%)	59 (3.1%)	26 (6.8%)	4 (3.1%)	
Alive, no functional impairment	3746(68.1%)	1953 (63.9%)	1422 (73.8%)	276 (72.1%)	95 (73.1%)	
Alive, with at least some functional impairment	1185 (21.6%)	797 (26.1%)	301 (15.6%)	61 (15.9%)	26 (20.0%)	
Alive, unknown functional status	319 (5.8%)	148 (4.8%)	146 (7.6%)	20 (5.2%)	5 (3.8%)	
Death within 30 days	439 (8.0%)	267 (8.7%)	112 (5.8%)	43 (11.2%)	18 (13.9%)	<0.05
Death within 90 days	846 (15.4%)	475 (15.5%)	258 (13.4%)	80 (20.9%)	33 (25.4%)	<0.05
Antithrombotic treatment among survivors of acute thromboembolism	N=5250	N=2898	N=1869	N=357	N=126	<0.05
Anticoagulant	4668 (88.9%)	2688 (92.8%)	1625 (86.9%)	286 (80.1%)	69 (54.8%)	
Aspirin/other antiplatelet only	152 (2.9%)	32 (1.1%)	94 (5.0%)	20 (5.6%)	6 (4.8%)	

* Functional impairment ascertained by review of encounter documentation. Reviewers asked to determine whether the patient suffered functional consequences as a result of the thrombotic event

Table 3.

Significant predictors of death within 90 days in 5,497 adults with acute venous thromboembolism

Variable	Adjusted Hazard Ratio* (95% CI)
Venous thromboembolism type	
Pulmonary embolism	ref
Lower extremity thrombosis	0.81 (0.68-0.96)
Upper extremity thrombosis	0.82 (0.64-1.05)
Other thrombosis	0.85 (0.57-1.26)
No anticoagulant treatment at discharge	5.6 [4.8-6.7]
Age (years)	
<60	ref
60-69	1.49 (1.18-1.89)
70-79	1.56 (1.24-1.97)
≥80	2.39 (1.89-3.02)
Current smoker	1.34 (1.03-1.75)
Unprovoked thrombosis	0.70 (0.57-0.87)
Treatment setting	
Inpatient	ref
Emergency department or outpatient	0.50 (0.40-0.62)
Malignant cancer	1.38 (1.16-1.63)
Charlson comorbidity index category	
<1 normal	ref
1-2 mild	1.42 (1.07-1.87)
3-4 moderate	1.79 (1.32-2.41)
≥ 5 severe	3.78 (2.81-5.09)

* Multivariable models also adjusted for: gender, race, Hispanic ethnicity, hospitalization in the prior 30 days, specific medical conditions (unstable angina, acute myocardial infarction, stroke/transient ischemic attack, peripheral arterial disease, chronic lung disease, chronic liver disease, diabetes mellitus, heart failure, dementia, inflammatory bowel disease, thrombophilia, sepsis, hypercoagulable hematologic conditions, intracranial hemorrhage, extracranial bleeding) and baseline medication use (ACE inhibitor, angiotensin receptor blocker, beta blocker, calcium channel blocker, diuretic, aldosterone receptor antagonist, alpha blockers, statin, non-aspirin antiplatelet agent, diabetic therapy).