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Upper-Extremity Deep-Vein Thrombosis: A Retrospective Cohort Evaluation of Thrombotic Risk Factors at a University Teaching Hospital Antithrombosis Clinic

Rebecca H. Stone, PharmD[1], Adam P. Bress, PharmD, MS[2], Edith A. Nutescu, PharmD, MS[1], and Nancy L. Shapiro, PharmD[1]

Abstract

Background: Upper-extremity deep-vein thrombosis (UEDVT) causes significant morbidity and mortality and is not well characterized in the existing literature, particularly in underrepresented minorities such as African Americans. **Objective:** To describe the characteristics of a cohort of patients with UEDVT seen at an urban academic medical center. **Methods:** This was a retrospective cohort study among patients with a confirmed UEDVT at the University of Illinois Hospital and Health Sciences System between 1996 and 2011. Patients were identified by ICD-9 code for UEDVT. Variables collected include thrombotic risk factors and outcomes, including recurrent thrombosis and bleeding. **Results:** We identified 229 patients with UEDVT; 71% were African American, and 11% were diagnosed with sickle cell disease. The average number of UEDVT risk factors was 4.40 ± 1.5, the most common being central venous catheter (CVC) use (178, 78%). In the year following UEDVT, 13% experienced recurrent thrombosis, and 6% experienced major bleeding. Of 181 patients receiving warfarin after an UEDVT, 36% of international normalized ratio (INR) values were therapeutic. Patients with sickle cell disease had a lower proportion of INRs within the target range (25% vs 38%, $P < 0.01$), and were more likely to be lost to follow-up (67% vs 46%, $P = 0.05$) and experience a recurrent thrombotic event (29% vs 11%, $P = 0.02$). **Conclusion:** A CVC is the most common risk factor for UEDVT; however, patients with sickle cell disease demonstrate additional unique demographics and risk factors. Patients included in this underrepresented demographic cohort had a low quality of anticoagulation control, particularly those with sickle cell disease.

Keywords

upper-extremity deep-vein thrombosis, anticoagulation, sickle cell disease

Background

Upper-extremity deep-vein thrombosis (UEDVT) is commonly defined as thrombosis of the brachial, axillary, and subclavian veins and may extend into the brachiocephalic vein, superior vena cava, or internal jugular vein.[1] It is thought that 2% to 14% of all venous thrombotic events (VTEs) involve the upper extremities.[1-5] Primary UEDVT is defined as thrombosis that is unprovoked or a result of structural anomalies and comprises 20% to 30% of UEDVT events.[1,6] Secondary UEDVT is frequently caused by central venous catheters (CVCs), pacemakers, malignancy, or pregnancy.[1,6,7] Secondary UEDVT incidence has increased, likely because of more widespread use of medical devices that may provoke this thrombotic event.[6,7] Although previously thought to be a benign process,[8] UEDVT negatively affects quality of life and commonly presents with edema, dilated collateral circulation, and pain.[1] Additionally, UEDVT may cause complications such as pulmonary embolism in approximately 5% of incident UEDVT patients,[1,3,5,9,10] recurrent UEDVT in 8%,[1,4,10] and postthrombotic syndrome of the arm in 20%.[1,9,11]

The strongest known risk factor for UEDVT is a CVC and is found in more than half of all cases.[2,3,10,12] CVCs precipitate thrombus formation via stasis, platelet adherence, and endothelial trauma.[7] Existing literature indicates that malignancy is present in about 12% to 33% of UEDVT cases.[5,10,13,14] The frequency of UEDVT caused by hereditary or acquired thrombophilia is unclear; other studies have found rates of thrombophilia ranging from 11% to 60% in patients with UEDVT.[7] There are no published data regarding the frequency of UEDVT in patients with sickle cell disease, but studies have demonstrated that sickle cell disease significantly increases the risk of thrombosis, particularly in the presence of a CVC.[15-17]

[1]University of Illinois at Chicago, IL, USA
[2]University of Utah, UT, USA

Corresponding Author:
Rebecca H. Stone, Department of Pharmacy Practice, College of Pharmacy, University of Illinois at Chicago, 833 S Wood St, Suite 164, Chicago, IL 60622, USA.
Email: Stonereb@uic.edu

Extensive literature exists regarding risk factors, prevention, and treatment of lower-extremity deep-venous thrombosis; however, these aspects of UEDVT are less clearly defined in the literature.[1] We, therefore, sought to identify associated risk factors for UEDVT, as defined by the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (ACCP), in an urban, majority African American patient population with a diagnosis of UEDVT, managed at the University of Illinois at Chicago (UIC) Antithrombosis Clinic.

Methods

This study was approved by the Institutional Review Board at the UIC.

Patient Population

The primary objective of this study is to characterize the risk factors associated with confirmed UEDVT. The secondary objective is to quantify the prophylaxis, treatment, and thrombotic or bleeding outcomes of this patient population. A subgroup analysis will compare differences in the primary and secondary objectives between patients with CVC versus those without a CVC, and those with sickle cell disease versus those without sickle cell disease.

This was a retrospective chart review of patients with UEDVT diagnosed between January 1, 1996, and October 1, 2011. Patients received a referral to the University of Illinois Antithrombosis clinic and were screened using existing antithrombosis clinic medical records with documentation of UEDVT or ICD-9 code for UEDVT (451.8X or 453.8X), as generated by a report query in the electronic medical record (EMR). To reduce misclassification, patients identified with UEDVT were confirmed via manual review of a positive ultrasound duplex, Doppler, computed tomography scan, venography, or other diagnostic method in the EMR. Patients <18 years of age were excluded.

Data Collection

Pertinent data collected included patient baseline characteristics (Table 1); risk factors for VTE in hospitalized patients as defined by ACCP 9th guidelines[18] and nonhospitalized patients as defined by ACCP 8th edition[19] (nonhospitalized patient risk factors were not quantified in list format in the updated ACCP 9th edition, Appendix Table A1); DVT prophylaxis utilized, if any; treatment received for UEDVT diagnosis; and clinical outcomes such as recurrent DVT, PE, and bleeding. Data were extracted by manual chart review, which was conducted by 2 pharmacists using a standardized data collection sheet.

Clinical Definitions

The first documented UEDVT in the EMR is defined as the index event. The presence of thrombotic risk factors for nonhospitalized patients and hospitalized patients, as defined by the 8th and 9th editions of the ACCP guidelines,[18,19] was confirmed via manual review of documentation within the EMR. Patients with a CVC at any point within the 30 days preceeding the index UEDVT diagnosis were classified as having a CVC-associated UEDVT; the remaining patients were classified as having a non–CVC-associated UEDVT. Sickle cell disease was defined by documentation of this condition on the patient's problem list in the EMR by a University of Illinois Health physician and does not include patients who only have sickle cell trait. Immobilized patients were defined as those with documentation of any of the following events within the 30 days prior to the index UEDVT diagnosis: residing in the hospital greater than 3 days, admission to the intensive care unit, or arm paralysis or immobilization. Acute medical illness was defined as any medical condition requiring hospitalization, excluding those related to the index UEDVT event and/or surgical intervention. Proportion of international normalized ratios (INRs) in the therapeutic range was calculated in patients who had 4 or more INR results and was calculated by the number of therapeutic INR values divided by the total number of INR values documented while the patient was managed by the UIC Antithrombosis Clinic.[20] A recurrent thrombotic event or bleeding event is any documented episode that occurred within 12 months after the index UEDVT. The International Society on Thrombosis and Haemostasis criteria for major bleeding were used, including a drop in hemoglobin of 2 g/dL or more, the need for 2 or more units of transfusion of whole blood or red cells, hospitalization for bleeding, or having a bleeding event that was retroperitoneal, intracranial, or spinal in nature.[21]

Statistical Analysis

We determined the frequency of occurrence for all primary and secondary data points in the total patient population, in addition to subgroup analysis, which compared patient characteristics in 2 ways: (1) those with and without a history of CVC and (2) those with and without sickle cell disease. We compared continuous data between groups using Student's *t*-test. The χ^2 test and Fisher's exact test were used to compare differences in categorical data for patient characteristics, treatment received, and outcomes. Statistical analyses were performed with the IBM SPSS Statistics for Windows software package, Version 23.0 (IBM, Armonk, NY).

Table 1. Baseline Characteristics of Patients With Upper-Extremity Deep-Vein Thrombosis (UEDVT).

	Total Cohort	CVC Within 30 Days			Sickle Cell Disease		
Baseline Characteristics	n = 229	No, n = 51	Yes, n = 178	*P* value	No, n = 205	Yes, n = 24	*P* value
Age (years) ± SD	49.68 ± 15.2	50.31 ± 14.95	49.49 ± 15.31	0.73	51.47 ± 14.37	34.38 ± 13.63	<0.01
BMI (kg/m^2) ± SD	28.83 ± 8.0	29.46 ± 8.07	28.66 ± 7.94	0.54	29.10 ± 8.07	26.63 ± 6.66	0.10
Men, n (%)	78 (34)	18 (35)	60 (34)	0.83	73 (36)	5 (21)	0.15
African American, n (%)	163 (71)	39 (76)	124 (70)	0.34	139 (68)	24 (100)	<0.01[a]
Hispanic, n (%)		9 (18)	27 (15)	0.67	36 (18)	0 (0)	0.02[a]
White, n (%)		3 (6)	21 (12)	0.23	24 (12)	0 (0)	0.09[a]
Other ethnicity, n (%)		0 (0)	6 (3)	0.34[a]	6 (3)	0 (0)	1.0[a]
Diagnosed as inpatient, n (%)	107 (47)	13 (25)	94 (53)	<0.01	89 (43)	18 (75)	<0.01
Symptomatic UEDVT, n (%)		42 (82)	147 (83)	0.97	168 (82)	21 (88)	0.76[a]
Symptom: pain, n (%)		20 (39)	87 (49)	0.22	93 (45)	14 (58)	0.23
Symptom: swelling, n (%)		28 (55)	110 (62)	0.38	125 (61)	13 (54)	0.52

Abbreviations: BMI, body mass index; CVC, central venous catheter.
[a] Fisher's exact *d.f.*, low frequency of event.

Results

Patient Demographics

A total of 229 patients met criteria for study inclusion. The majority were women (143, 63%) and African American (163, 71%); the average age was 49.7 ± 15 years; and the average body mass index was 28.8 ± 8.22 kg/m^2. Complete baseline characteristics are listed in Table 1. Patients were diagnosed with UEDVT in the inpatient (107, 47%) and outpatient (118, 52%) setting, and 4 patients (2%) were diagnosed in an unknown setting outside of UI Health. In all, 83% experienced symptoms (189, 83%) at UEDVT diagnosis, primarily pain and swelling.

Risk Factors

We were interested in a predetermined set of risk factors for thrombosis in nonhospitalized and hospitalized patients, as defined by the ACCP guidelines 8th and 9th editions; see Appendix Table A1.[18,19] The mean number of all thrombotic risk factors per patient was 4.4 ± 1.5; CVC use within the past 30 days (178, 77.7%) was the most common risk factor for the total cohort. A complete list of risk factors and frequency of occurrence is shown in Table 2.

Prophylaxis

There were 107 patients in the inpatient setting with an average length of stay of 11 days at the time of UEDVT diagnosis; of these patients, 30% (32) had a prior DVT or PE. Documented pharmacological VTE prophylaxis occurred in 59% (63) of the total inpatient group, of whom 17% (11) were on intended therapeutic anticoagulation, such as a heparin drip or warfarin because of a previous thrombotic event. Of these 11 on intended therapeutic anticoagulation, 10 had documentation of a previous history of DVT or PE. The average Padua prediction score, assessing VTE risk in the 107 hospitalized patients, was 4.3 ± 2.5; 64% (69) of the hospitalized patients scored ≥4, indicating high risk for VTE; however, only 60% (41) of those who were high risk received VTE prophylaxis.[18] See Appendix Table A1.

Treatment

Most patients received warfarin (198, 87%) for their chronic UEDVT treatment, followed by chronic low-molecular-weight heparin (LMWH; 12, 5%), or both warfarin and LMWH at different points in treatment (19, 8%). Requirement of both warfarin and LMWH at different points in treatment, or chronic LMWH, was not a result of bridging, and these patients were selected because they were clinically preferred in the setting of other concurrent medical complications such as malignancy, altered gastrointestinal absorption, transplantation, pregnancy, or other unknown reasons. As shown in Table 3, 79% (n = 181) of patients receiving warfarin had 4 or more INR values to evaluate, with the average time in therapeutic range at 36% ± 18.8%. A high percentage of patients were lost to follow-up while on treatment (109, 48%), which included patients who transferred care elsewhere or were discharged from the antithrombosis clinic because of nonadherence to follow-up appointments.

Subsequent Thrombotic or Bleeding Events

A total of 29 patients (13%) experienced a recurrent thrombotic event, of which 69% (20) occurred while prescribed treatment dose anticoagulation (Table 4). There were 62 (27%) bleeding events; 14 (6%) patients had major bleeding, whereas 47 (21%) patients experienced a minor bleeding event only; there were no fatal bleeding events.

Table 2. Risk Factors for VTE in Hospitalized and Nonhospitalized patients, as Defined by the ACCP.[19]

		CVC Within 30 Days			Sickle Cell Disease		
Risk Factors	Total Cohort, n = 229	No, n = 51	Yes, n = 178	*P* Value	No, n = 205	Yes, n = 24	*P* Value
Total number of risk factors ± SD	4.40 ± 1.5	3.27 ± 1.4	4.72 ± 1.3	<0.01	4.46 ± 1.5	3.88 ± 1.2	0.03
Padua score (diagnosed while inpatient) ± SD	4.40 ± 2.6	4.0 ± 2.4	4.51 ± 2.7	0.19	4.56 ± 2.6	3.04 ± 2.1	<0.01
CVC, n (%)	178 (78)	0	178 (100)	<0.01	160 (78)	18 (75)	0.73
Major surgery, n (%)	45 (20)	8 (16)	37 (21)	0.42	42 (21)	3 (13)	0.43
Trauma, n (%)	6 (3)	2 (4)	4 (2)	0.62[a]	6 (3)	0 (0)	1.0[a]
Immobility in past 30 days, n (%)	116 (21)	18 (35)	98 (55)	0.01	100 (49)	16 (67)	0.10
Cancer (active or occult), n (%)	70 (31)	15 (29)	50 (31)	0.84	67 (33)	3 (13)	0.06[a]
Current cancer therapy, n (%)	33 (14)	3 (6)	30 (17)	0.05	32 (16)	1 (4)	0.22[a]
Previous VTE, n (%)	65 (28)	16 (31)	57 (32)	0.92	58 (28)	7 (29)	0.93
Age >40 years, n (%)	175 (76)	40 (78)	135 (76)	0.70	166 (81)	9 (38)	<0.01
Pregnant or postpartum, n (%)	6 (3)	1 (2)	5 (3)	1.0[a]	3 (2)	3 (13)	0.02[a]
Selective estrogen receptor modulators, n (%)	6 (3)	1 (2)	5 (3)	1.0[a]	6 (3)	0 (0)	1.0[a]
Oral contraceptives or hormone replacement therapy, n (%)	4 (2)	0 (0)	4 (2)	0.58[a]	3 (2)	1 (4)	0.36[a]
Acute medical illness, n (%)	122 (54)	17 (33)	105 (59)	<0.01	102 (50)	20 (83)	<0.01
Erythropoiesis-stimulating agents, n (%)	0 (0)	0 (0)	0 (0)	—	0 (0)	0 (0)	—
Inflammatory bowel disease, n (%)	0 (0)	0 (0)	0 (0)	—	0 (0)	0 (0)	—
Nephrotic syndrome, n (%)	66 (29)	17 (33)	49 (28)	0.42	61 (30)	5 (21)	0.36
Myeloproliferative disorder, n (%)	1 (0.5)	0 (0)	1 (1)	1.0	1 (1)	0 (0)	1.0[a]
Paroxysmal nocturnal hemoglobinuria, n (%)	2 (1)	0 (0)	2 (1)	1.0	2 (1)	0 (0)	1.0[a]
BMI ≥30 kg/m^2, n (%)	89 (39)	23 (44)	66 (37)	0.33	83 (41)	6 (25)	0.14
Inherited or acquired thrombophilia (excluding sickle cell disease), n (%)	24 (11)	7 (14)	17 (10)	0.39	23 (11)	1 (4)	0.48[a]

Abbreviations: ACCP, American College of Chest Physicians; BMI, body mass index; CVC, central venous catheter; VTE, venous thromboembolism.
[a] Fisher's exact *d.f.*, low freqency of event.

Table 3. Upper-Extremity Deep-Vein Thrombosis (UEDVT) Prophylaxis and Chronic Treatment.

	Total Cohort,	CVC Within 30 days			Sickle Cell Disease		
Treatment	n = 107	No, n = 13 (%)	Yes, n = 94 (%)	*P* Value	No, n = 89 (%)	Yes, n = 18 (%)	*P* Value
Pharmacological prophylaxis in the inpatient setting prior to UEDVT, n (%)	64 (49)	10 (85)	53 (56)	0.03	54 (61)	9 (50)	0.39
	n = 229	No, n = 51 (%)	Yes, n = 178 (%)	*P* Value	No, n = 205 (%)	Yes, n = 24 (%)	*P* Value
Warfarin, n (%)	198 (87)	47 (92)	151 (85)	0.18	178 (87)	20 (83)	0.54
LMWH, n (%)	12 (5)	2 (0.5)	10 (56)	1.0[a]	11 (5)	1 (4)	1.0[a]
LMWH + warfarin at different times in therapy, n (%)	19 (8)	2 (0.5)	17 (10)	0.26[a]	16 (8)	3 (13)	0.43[a]
Treated 0 to 3 months,[b] n (%)	64 (28)	16 (31)	48 (27)	0.54	56 (27)	8 (33)	0.53
Treated >3 to 6 months, n (%)	81 (35)	14 (27)	67 (38)	0.18	71 (35)	10 (42)	0.50
Treated >6 months, n (%)	84 (37)	21 (41)	63 (35)	0.45	78 (38)	6 (25)	0.21
Lost to follow-up while on treatment, n (%)	109 (48)	27 (53)	82 (46)	0.39	93 (46)	16 (67)	0.05
Patients with ≥4 INR values, n (%)	181 (79)	40 (78)	141 (79)	0.58	164 (85)	17 (74)	0.22[a]
Proportion of INRs in therapeutic range, n (%)	36% ± 18.7%	38%	36%	0.58	38%	25%	0.02

Abbreviations: CVC, central venous catheter; INR, international normalized ratio; LMWH, low-molecular-weight heparin.
[a] Fisher's exact *d.f.*, low freqency of event.
[b] Of patients who received <3 months of therapy, 51 were lost to follow-up, and 2 died.

Subgroup Analysis

Sickle Cell Disease Versus No Sickle Cell Disease. A total of 24 African American patients with sickle cell disease were identified, which is 15% of the African American patient population and 10% of the total patient population included in this study. They were younger (mean = 34.4 ± 13.6 vs 51.5 ± 14.4 years, $P < 0.001$) and were more likely to be diagnosed with UEDVT in the inpatient setting than those without sickle cell disease (43% vs 18%, $P < 0.01$). Regarding thrombotic risk factors, patients with sickle cell disease had significantly less cumulative VTE risk factors (3.88 ± 1.2 vs 4.46 ± 1.5, $P = 0.03$), were more likely to have an acute medical illness (83% vs 50%, $P < 0.01$), and be pregnant when diagnosed (13% vs 2%, $P = 0.02$). There was no difference in occurrence of other VTE risk factors between patients with sickle cell disease and those without, including CVC frequency. Although not statistically significant, a larger percentage of patients with

Table 4. Treatment Outcomes Within 1 Year of the Upper-Extremity Deep-Vein Thrombosis Event.

Patient Outcome, n (%)	Total Cohort, n = 229	CVC Within 30 Days			Sickle Cell Disease		
		No, n = 51 (%)	Yes, n = 178 (%)	*P* Value	No, n = 205 (%)	Yes, n = 24 (%)	*P* Value
Any recurrent VTE	29 (13)	5 (10)	24 (14)	0.49	22 (11)	7 (29)	0.02[a]
Recurrent DVT while on treatment	16 (7)	5 (10)	11 (6)	0.37	11 (5)	5 (21)	0.02[a]
Recurrent DVT posttreatment	10 (4)	0 (0)	10 (6)	0.12[a]	8 (4)	2 (8)	0.28[a]
Recurrent PE while on treatment	4 (2)	1 (2)	3 (2)	1.0[a]	4 (2)	0 (0)	1.0[a]
Recurrent PE posttreatment	1 (0.5)	0 (0)	1 (0.5)	1.0[a]	1 (0.5)	0 (0)	1.0[a]
Any bleeding	62 (27)	21 (41)	41 (23)	0.01	58 (28)	4 (17)	0.23
Minor bleeding only	47 (21)	16 (31)	31 (17)	0.03	43 (21)	4 (17)	0.79[a]
Major bleeding	14 (6)	5 (10)	9 (5)	0.32[a]	14 (7)	0 (0)	0.37[a]
Bleeding with hospitalization	14 (6)	5 (10)	9 (5)	0.32[a]	14 (7)	0 (0)	0.37[a]
Bleeding with transfusion	8 (4)	3 (6)	5 (3)	0.38[a]	8 (4)	0 (0)	1.0[a]
Intracranial bleeding	1 (0.5)	0 (0)	1 (0.5)	1.0[a]	1 (0.5)	0 (0)	1.0[a]
Leads to death	0 (0)	0 (0)	0 (0)	—	0 (0)	0 (0)	—

Abbreviations: CVC, central venous catheter; DVT, deep-vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism.
[a] Fisher's exact *d.f.*, low freqency of event.

sickle cell disease were started on pharmacological anticoagulation prophylaxis than those without sickle cell diease (38% vs 27%, $P = 0.27$). There was no difference in chronic treatmeat type following UEDVT, or treatment duration. However, while on treatment with warfarin, patients with sickle cell disease had a lower mean percentage of INR values within the target range (25% vs 38%, $P = 0.02$). Following treatment initiation, patients with sickle cell disease were more likely to be lost to follow-up (67% vs 46%, $P = 0.05$), to have any recurrent thrombotic event (29% vs 11%, $P = 0.02$), or have a recurrent DVT while on anticoagulation treatment (21% vs 5%, $P < 0.02$). There were no significant differences in bleeding events

Central Venous Catheter. A total of 178 (78%) patients had UEDVT associated with a CVC. There were no significant differences in age, sex, or race in patients with a CVC versus no CVC, and patients with a CVC were more likely to be diagnosed in the inpatient setting (53% vs 25%, $P < 0.01$). Patients with a CVC had a higher mean number of total risk factors (4.72 ± 1.3 vs 3.27 ± 1.4, $P < 0.01$) and were more likely to have an acute medical illness (59% vs 33%, $P < 0.01$), immobility within the past 30 days (55% vs 35%, $P = 0.01$), or undergo current cancer treatment (17% vs 6%, $P = 0.05$).

No significant difference was seen between initiation of prophylactic anticoagulation in hospitalized patients prior to the UEDVT, long-term treatment agent, duration of anticoagulation, INR control, or percentage of patients lost to follow-up in the CVC versus the non-CVC group (see Table 3). Regarding patient outcomes, there were no significant differences in recurrent thrombosis, either on or off pharmacological anticoagulation treatment. Patients without a CVC were more likely to experience any bleeding (41% vs 23%, $P = 0.01$) and minor bleeding (31% vs 17%, $P = 0.03$), but there was no statistically significant difference in major bleeding between groups (10% vs 5%, $P = 0.32$).

Discussion

This retrospective review provides a profile of a previously uncharacterized patient population diagnosed with UEDVT in an underrepresented African American population. This study found that the most common risk factors for UEDVT in the total cohort were CVC use within the past 30 days, patient age >40 years, immobilization, history of thromboembolism, and cancer. However, there were differences between associated risk factors in CVC versus non-CVC patients, and those with and without sickle cell disease.

CVC patients were more likely to have a recent history of immobility, be undergoing current cancer treatment, and have an acute medical illness. Joffe et al[2] published a large UEDVT registry evaluating risk factors for VTE, which was similarly stratified by CVC versus non-CVC groups.[2] This registry evaluated 592 patients with UEDVT in a majority white population. The aforementioned study and this study had similar findings despite differences in patient population; both identified that patients with CVC were more likely to be diagnosed in the inpatient setting, have had immobility in the past 30 days and be undergoing current cancer treatment. It is likely that inpatients are at higher risk for UEDVT than outpatients because of the decrease in mobility associated with hospitalization and the almost universal use of peripheral venous catheters and CVCs during hospitalization, which may predispose them to thrombosis. Patients with conditions causing frequent hospitalization, such as those with sickle cell disease, may have more frequent and longer hospitalizations during flares of their disease, adding to the importance of adequate DVT prophylaxis. DVT prophylaxis has increased in clinical practice; however, rates of DVT prophylaxis were poor in this cohort as well as the Joffe et al[2] cohort: 49% versus 33%, respectively. Since the data collection period for this study, the 9th edition of the ACCP guidelines incorporated the Padua prediction score risk assessment model, defining high risk of VTE

as a patient risk factor score of ≥4 points. Identified risk factors such as active cancer, previous VTE, reduced mobility, and an already known thrombophilic condition are scored at 3 points, whereas elderly status, heart or respiratory failure, acute myocardial infarction or stroke, infection, obesity, and ongoing hormonal treatment are scored at 1 point each.[18] The majority of patients hospitalized in this study had a Padua score of 4 or more and may have benefited from prophylaxis. There were no differences between CVC and non-CVC patients in treatment type following UEDVT or INR control. Recurrent thrombosis did not differ between patients with or without CVC. There were no differences in rates of major bleeding between groups; however, rates of any bleeding and minor bleeding occurred more frequently in patients without CVC.

Patients with sickle cell disease had a lower total number of thrombotic risk factors; however, recent studies demonstrated that VTE incidence is higher in the African American race, and sickle cell disease is an independent risk factor for thrombosis.[15,17,22] Understanding thrombosis risk in this high-risk patient population is important. Naik et al[15] found that patients with sickle cell disease and VTE had a higher mortality rate than those without VTE. Of the African American patients in this study, 15% had sickle cell disease; however, the overall percentage of African Americans in this study (~70%) is roughly comparable to the total percentage of African Americans managed in the UIC Antithrombosis Clinic (~60%).[23] Of note, although the overwhelming majority of patients with sickle cell disease are African American, this condition can be found in certain populations of Hispanics, Asians, Indians, and those of Mediterranean descent. Patients with sickle cell disease in this study were younger, and more likely to be pregnant and have an acute medical illness at the time of diagnosis; hospitalized patients had a lower mean Padua prediction score than patients without sickle cell disease. The frequency of CVC use was the same in the sickle cell and non–sickle cell disease patient population, although other studies have noted that patients with sickle cell disease often have a high frequency of catheter-related VTE, likely reflecting the frequent catheter use in this patient population.[17]

There were no differences in treatment type between the sickle cell and non–sickle cell disease patient populations, but those with sickle cell disease had higher rates of any recurrent thrombotic event, recurrent thrombotic event while prescribed therapeutic anticoagulation, lower frequency of therapeutic INRs, and increased loss to follow-up. Of note, the low proportion of INRs in therapeutic range may be related to the large percentage of patients who were lost to follow-up before reaching a stable therapeutic dose. Racial differences in metabolism or other implicit racial disparities could potentially affect the proportion of INRs in therapeutic range; however, this study was not designed to evaluate these variables, nor has this been confirmed in other published research. There were no differences in rates of any, major, or minor bleeding between those with sickle cell disease and those without.

The entire UEDVT cohort demonstrated poor quality of control of their anticoagulation in the outpatient setting as compared with the total patient population managed in this clinic, with a proportion of INR in therapeutic range of 36% as compared with 62% (unpublished clinic-specific quality data). This significant difference is likely related to a short duration of therapy because of loss to follow-up, multiple comorbidities, inability to keep appointments for INR monitoring, and missed doses of warfarin; however, the sickle cell population demonstrated exceptionally poor control (25%). Patients with sickle cell disease may represent an area of opportunity for the use of direct oral anticoagulants (DOACs) for treatment, which require less laboratory monitoring and fewer blood draws and inconveniences for the patient. However, further studies are required to determine if DOAC use can lead to better therapeutic outcomes in this specific patient population. Patient self-testing of warfarin may also be an option for this population to overcome the barriers of coming to clinic appointments, provided that their hematocrit levels are above the minimum recommended threshold of 25% for the CoaguChek XS Plus meter.[24]

As with other studies, this study has limitations. This is a retrospective study that must rely on information documented in the medical record, which may not always be complete. The use of pharmacological DVT prophylaxis in this population was low. Since the start of this study, clinic practice has increased recommendations for VTE prophylaxis, and hospital-wide DVT prophylaxis guidelines have been implemented since the time peroid of data collection; therefore, this low rate of prophylaxis may not be an accurate reflection of current clinical practice. INR values were counted from the initiation of warfarin and may include the titration period, further contributing to this low rate of INR control. In this retrospective study, many patients were lost to follow-up while on treatment, and this likely underreports all recurrent thrombotic and bleeding outcomes.

In conclusion, CVC use, age, immobilization or hospitalization, and cancer are the most common risk factors of UEDVT in this majority African American population. Poor quality of anticoagulation control with warfarin contributed to high rates of VTE recurrence despite referral to an established anticoagulation clinic, which may create opportunities for alternate chronic anticoagulation strategies. In particular, patients diagnosed with sickle cell disease exhibited poor quality of anticoagulation control, and it may be beneficial to conduct further studies to determine if this population may benefit from alternative therapies such as the DOACs for UEDVT treatment. These results provide new information regarding risk factors, treatment, and outcomes of UEDVT in this underrepresented patient population.

Appendix A

Table A1. Risk Factors for Venous Thromboembolism.[a]

8th Edition ACCP Guidelines (2008)[19]	9th Edition ACCP Guidelines (2012)[18]	
Risk Factors for VTE	Risk Factors for VTE in Hospitalized Medical Patients	Padua Scoring
Surgery	Recent surgery (≤1 month)	2
Trauma (major or lower extremity)	Recent (≤1 month) trauma	2
Immobility, lower-extremity paresis	Reduced mobility[b]	3
Cancer (active or occult)	Active cancer[c]	3
Cancer therapy (hormonal, chemotherapy, angiogenesis inhibitors, or radiotherapy	Chemotherapy or radiation in last 6 months	1
Venous compression (tumor, hematoma, arterial abnormality)		
Previous VTE	Previous VTE (with exclusion of superficial vein thrombosis)	3
Increasing age	Elderly age (≥70 years)	1
Pregnancy and the postpartum period		
Estrogen-containing oral contraceptives or hormone replacement therapy	Ongoing hormonal treatment	1
Selective estrogen receptor modulators		
Erythropoiesis-stimulating agents		
Acute medical illness	Active infection and/or rheumatological disorder	1
	Acute MI or ischemic stroke	1
	Heart and or respiratory failure	1
Inflammatory bowel disease		
Nephrotic syndrome		
Myeloproliferative disorders		
Paroxysmal nocturnal hemoglobinuria		
Obesity	Obesity (BMI ≥ 30 kg/m^2)	1
Central venous catheterization		
Inherited or acquired thrombophilia	Already known thrombotic condition[d]	3

Abbreviations: ACCP, American College of Chest Physicians; BMI, body mass index; MI, myocardial infarction; VTE, venous thromboembolism.

[a] In the Padua prediction score risk assessment model, high risk of VTE is defined by a cumulative score ≥4 points. In a prospective observational study of 1180 medical inpatients, 60.3% of patients were low risk, and 39.7% were high risk. Among patients who did not receive prophylaxis, VTE occurred in 11.0% of high-risk patients versus 0.3% of low-risk patients (HR = 32.0; 95% CI = 4.1-251.0).[AQ1]

[b] Anticipated bed rest with bathroom privileges (either because of patient's limitations or on physician's order) for at least 3 days.

[c] Patients with local or distant metastases and/or in whom chemotherapy or radiotherapy had been performed in the previous 6 months.

[d] Carriage of defects of antithrombin, protein C or S, factor V Leiden, G20210A prothrombin mutation, and antiphospholipid syndrome.

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