

BRIEF REPORTS

Upper Extremity Deep Vein Thrombosis in Hospitalized Patients: A Descriptive Study

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Increasingly, there is a focus on the prevention of hospital-acquired conditions including venous thromboembolism. Many studies have evaluated pulmonary embolism and lower extremity deep vein thrombosis, but less is known about upper extremity deep vein thrombosis (UEDVT) in hospitalized patients. The objective of this study was to describe UEDVT incidence, associated risks, outcomes, and management in our institution. Using an information technology tool, we reviewed records of all symptomatic adult inpatients diagnosed with UEDVT at an academic tertiary center between September 2011 and November 2012. Fifty inpatients were diagnosed with 76 UEDVTs. Their mean age was 49 years; 70% were men. Sixteen percent had a history of venous thromboembolism; 20% had a history of malignancy. The mean length of stay (LOS) was 24.6 days (range, 2–91 days); 50% were transferred from outside

hospitals. Thirty-eight percent of UEDVTs were in internal jugular veins, 21% in axillary veins, and 25% in brachial veins. Forty-four percent of patients had UEDVT associated with central venous catheters (CVCs). During hospitalization, 78% were fully anticoagulated; 75% of survivors at discharge. Only 38% were discharged to self-care; 10% died during hospitalization. Patients with UEDVT were more likely to have CVCs, malignancy, and severe infection. Many patients were transferred critically ill with prolonged LOS and high in-hospital mortality. Most UEDVTs were treated even in the absence of concurrent lower extremity deep vein thrombosis or pulmonary embolism. Additional research is needed to modify risks and optimize outcomes. *Journal of Hospital Medicine* 2014;9:48–53. © 2013 Society of Hospital Medicine

Increasingly, there is a focus on prevention of hospital-acquired conditions including venous thromboembolism (VTE). Many studies have evaluated pulmonary embolism (PE) and lower extremity deep vein thrombosis (LEDVT), but despite increasing recognition of upper extremity deep vein thrombosis (UEDVT),^{1–4} less is known about this condition in hospitalized patients.

UEDVTs may be classified as primary, including disorders such as Paget-Schroetter syndrome or other structural abnormality, or may be idiopathic; the majority are secondary clots.⁵ Conventional risk factors for LEDVT including older age and obesity have been found to be less commonly associated,^{1,2,5–7} and patients with UEDVT are generally younger, leaner, and a higher proportion are men. They are more likely to have malignancy or history of VTE and have undergone recent surgery or intensive care unit stay.^{1,2,6} Central venous catheters (CVCs), often used in hospitalized patients, remain among the biggest

known risks for UEDVT^{1–3,7–10}; concomitant malignancy, VTE history, severe infection, surgery lasting >1 hour, and length of stay (LOS) >10 days confer additional risks with CVCs.^{6–8,11}

UEDVTs, once thought to be relatively benign, are now recognized to result in complications including PE, progression, recurrence, and post-thrombotic syndrome.^{2,4,12,13} Despite extensive efforts to increase appropriate VTE prophylaxis in inpatients,¹⁴ the role of chemoprophylaxis to prevent UEDVT remains undefined. Current guidelines recommend anticoagulation for treatment and complication prevention,^{13,15} but to date the evidence derives largely from observational studies or is extrapolated from the LEDVT literature.^{2,13}

To improve understanding of UEDVT at our institution, we set out to (1) determine UEDVT incidence in hospitalized patients, (2) describe associated risks and outcomes, and (3) assess management during hospitalization and at discharge.

METHODS

We identified all consecutive adult patients diagnosed with Doppler ultrasound-confirmed UEDVT during hospitalization at Harborview Medical Center between September 2011 and November 2012. For patients who were readmitted during the study period, the first of their hospitalizations was used to describe associated factors, management, and outcomes. We present characteristics of all other hospitalizations during this time period for comparison. Harborview is

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MRN	Name	Age	Admit Dt Tm	Disch Dt Tm	BMI	Notes	Central Line
XXX	TEST, PATIENT	XX	mm/dd/yy	mm/dd/yy	XX	Links to Admit Note/ Discharge	PICC: Day 7 R arm, Double Lumen, Power Injectable, Uter: Length 43cm ArmCirc26cm Tail 1cm At bedside

Observation Dt Tm	Source System	Pos Flag	POA?	Vasc Type
Hospital day 15	Radiology	+		
Hospital day 19	Vascular	-		LE
Hospital day 19	Vascular	+		UE

Date	Time	Src	Event	Result
Hospital day 18	04:30	Event	SCD(s)	Pt non-compliant, won't wear
	06:25	Event	heparin	5 000 units
	07:27	Lab	Platelet Count	356
	13:00	Event	heparin	5 000 units
	21:00	Event	heparin	5 000 units
Hospital day 19	05:10	Event	heparin	5 000 units
	05:11	Lab	Platelet Count	415
	08:00	Event	SCD(s)	OFF Legs - Bilaterally
	11:09	Study	Vascular	-
	11:20	Study	Vascular	+
	13:00	Event	heparin	Not Given. Patient Refused
	18:30	Lab	Prothrombin INR	1.3
	21:00	Event	warfarin	2.5 mg
	21:15	Event	dalteparin	15 000 units
	21:15	Event		
Hospital day 19	06:39	Lab	Platelet Count	446
	08:44	Event	SCD(s)	OFF Legs - Bilaterally
	21:45	Event	dalteparin	15 000 units

Patient has a PICC line in the right upper extremity and presents with right upper extremity edema. Deep vein thrombosis (non-occlusive) in the right subclavian, axillary, brachial and basilic veins along the PICC line. Superficial thrombophlebitis is present in the left cephalic vein (occlusive) and median cubital veins (non-occlusive). No deep vein thrombosis in the right internal jugular, radial or ulnar veins. No deep vein thrombosis in the left internal jugular or axillary veins. Could not rule out non-occlusive thrombus in the bilateral innominate or left subclavian veins due to vessel death.

FIG. 1. The Harborview venous thromboembolism tool. Abbreviations: PICC, peripherally inserted central catheter; SCD, sequential compression device. R, Right; cm, centimeters; ArmCirc Arm circumference; Dt, Date; Tm, Time; Pos, Positive; POA, Present on Admission; Vasc Type, Type of Vascular Study; LE, lower extremity; UE, upper extremity; Src, Source; Pt, Patient.

a 413-bed academic tertiary referral center and the only level 1 trauma center in a 5-state area. Patients with UEDVT were identified using an information technology (IT) tool (the Harborview VTE tool) (Figure 1), which captures VTE events from vascular laboratory and radiology studies using natural language processing. Doppler ultrasound to assess for deep vein thrombosis (DVT) and computed tomographic scans to diagnose PE were ordered by inpatient physicians for symptomatic patients. The reason for obtaining the study is included in the ultrasound reports. We do not routinely screen for UEDVT at our institution. UEDVT included clots in the deep veins of the upper extremities including internal jugular, subclavian, axillary, and brachial veins. Superficial thrombosis and thrombophlebitis were excluded. We previously compared VTE events captured by this tool with administrative billing data and found that all VTE events that were coded were captured with the tool.

The VTE tool (Figure 1) displays imaging results together with demographic, clinical, and medication data and links this information with admission, discharge, and death summaries as well as CVC insertion procedure notes from the electronic health record (EHR). Additional data, including comorbid conditions, primary reason for hospitalization, past medical history such as prior VTE events, and cause of death (if not available in the admission note or discharge/death summaries), were obtained from EHR abstraction by 1 of the investigators. A 10% random sample

of charts was rereviewed by another investigator with complete concordance. Supplementary data about date of CVC insertion if placed at an outside facility, date of CVC removal if applicable, clinical assessments regarding whether a clot was CVC-associated, and contraindications to therapeutic anticoagulation were also abstracted directly from the EHR. Administrative data were used to identify the case mix index, an indicator of severity of illness.

Pharmacologic VTE prophylaxis included all chemical prophylaxis specified on our institutional guideline, most commonly subcutaneous unfractionated heparin 5000 units every 8 hours or low molecular weight heparin (LMWH), either enoxaparin 40 mg every 12 or 24 hours or dalteparin 5000 units every 24 hours. Mechanical prophylaxis was defined as use of sequential compression devices (SCDs) when pharmacologic prophylaxis was contraindicated. Prophylaxis was considered to be appropriate if it was applied according to our guideline for >90% of hospital days prior to UEDVT diagnosis. Therapeutic anticoagulation included heparin bridging (most commonly continuous heparin infusion, LMWH 1 mg/kg or dalteparin) as well as oral vitamin K antagonists. The VTE tool (Figure 1) allows identification of pharmacologic prophylaxis and therapy that is actually administered (not just ordered) directly from our pharmacy IT system. SCD application (not just ordered SCDs) is electronically integrated into the tool from nursing documentation.

CVCs included internal jugular or subclavian triple lumen catheters, tunneled dialysis catheters, or peripherally inserted central catheters (PICCs), single or double lumen. Criteria used to identify that a UEDVT was CVC-associated included temporal relationship (CVC was placed prior to clot diagnosis), plausibility (ipsilateral clot), evidence of clot surrounding CVC on ultrasound, and physician designation of association (as documented in progress notes or discharge summary).

Simple percentages of patient characteristics, associated factors, management, and outcomes were calculated using counts as the numerator and number of patients as the denominator. For information about UEDVTs, we used total number of UEDVTs as the denominator. Line days were day counts from insertion until removal if applicable. The CVC placement date was available in our mandated central line placement procedure notes (directly accessed from the VTE tool) for all lines placed at our institution; date of removal (if applicable) was determined from chart abstraction. For the vast majority of patients whose CVCs were placed at outside facilities, date of placement was available in the EHR (often in the admission note or in the ultrasound report/reason for study). If date of line placement at an outside facility was not known, date of admission was used. The University of Washington Human Subjects Board approved this review.

RESULTS

General Characteristics

Fifty inpatients were diagnosed with 76 UEDVTs during 53 hospitalizations. Three patients were admitted twice during the study period. Their first admission is used for the purposes of this review. None of these 3 patients had new UEDVTs diagnosed during their second admission.

The patients' mean age was 49 years (standard deviation [SD] 15.6; range, 24–82 years) vs 50.9 years (SD 17.49; range, 18–112 years) among all other hospitalizations during this time (Table 1). Seventy percent (35) of patients with UEDVT were men. Sixteen percent (8) of patients with UEDVT had known VTE history, 20% (10) of patients had malignancy, and 22% (11) of patients had stage V chronic kidney disease or were hemodialysis dependent.

Patients diagnosed with UEDVT had complex illness, long LOS, and were often transferred from outside hospitals relative to other hospitalizations during this time period (Table 1). Slightly more required intensive care and underwent surgery. Eighty-four percent (42) of patients with UEDVT required CVCs during hospitalization. Among patients whose UEDVT was not present on admission, 94% received appropriate VTE prophylaxis prior to UEDVT diagnosis.

In patients with UEDVT, the most common reasons for hospitalization were sepsis/severe infection (43%),

TABLE 1. Characteristics of Patients Diagnosed With UEDVT Compared With Characteristics From All Hospitalizations, September 2011 to November 2012

Characteristic	Patients With UEDVT, N = 50	All Hospitalizations, N = 23,407*
Age, y, mean (range)	49 (24–82)	51 (18–112)
Sex, % male (no.)	70% (35)	63% (14,746)
Case mix index, mean (range)	4.78 (0.69–17.99)	1.87 (0.16–26.34)
Length of stay, d, mean (range)	24.6 (2–91)	7.2 (1–178)
Transfer from outside hospital (no.)	50% (25)	25% (5,866)
Intensive care unit stay (no.)	46% (23)	36% (8,356)
Operative procedure (no.)	46% (23)	41% (9,706)
In-hospital mortality (no.)	10% (5)	4% (842)
Discharge to skilled nursing facility or other hospital, n = 45 surviving patients (no.)	62% (28)	13% (3,095)
30-day readmission, n = 45 surviving patients (no.)	18% (8)	5% (1,167)

NOTE: Abbreviations: UEDVT, upper extremity deep vein thrombosis.

*These numbers represent data gleaned from all hospitalizations. Individuals may have had more than 1 hospitalization during the study period. We are not able to identify individual patients; therefore, the population data are presented at the level of hospitalization.

cerebral hemorrhage (16%), and trauma (8%). Primary service at diagnosis was medicine 56.9%, surgery 25.5%, and neurosciences 17.6%.

Upper Extremity Deep Vein Thromboses

Fifty patients were diagnosed with 76 UEDVTs during their hospitalizations. In 40% (20) of patients, UEDVTs were present in >1 upper extremity deep vein; concurrent LEDVT was present in 26% (13) and PE in 10% (5). The majority of UEDVTs were found in internal jugular veins, followed by brachial and axillary veins. Seventeen percent were present on admission. Upper extremity swelling was the most common sign/symptom and reason for study. Characteristics of UEDVTs diagnosed are listed in Table 2.

Of the 50 patients diagnosed with UEDVT during hospitalization, 44% (22) were found to have UEDVTs directly associated with a CVC. Forty-two of the 50 patients had a CVC; 52% (22 of 42) had CVC-associated UEDVTs. Fifty percent (11) of these CVCs were triple lumen catheters, 32% (7) were PICCs, and 18% (4) were tunneled dialysis lines. Three of 42 patients with CVCs and line-associated clots were had a malignancy. For patients with CVC-associated clot, lines were in place for an average of 14.3 days (range, 2–73 days) prior to UEDVT diagnosis.

Treatment and Management

Seventy-eight percent (39) of patients with UEDVT received in-hospital treatment with heparin/LMWH bridging and oral anticoagulation. Of the 45 patients who survived hospitalization, 75% (34) were prescribed anticoagulation for 3+ months at discharge;

TABLE 2. Characteristics of UEDVTs

Characteristic	% UEDVTs (No.), n = 76
Anatomic site	
Internal jugular	38% (29)
Axillary	21% (16)
Subclavian/axillary	9% (7)
Subclavian	7% (5)
Brachial	25% (19)
Hospital day of diagnosis, d, mean (range)	
Present on admission	17% (13)
Diagnosed at outside hospital or within 24 hours of transfer	54% (7)
Diagnosed during prior hospitalization at our institution	15% (2)
Diagnosed within 24 hours of admission via our emergency department	23% (3)
Patient-reported chronic UEDVT	8% (1)
Primary UEDVT/anatomic anomaly	
Signs and symptoms (reasons for obtaining study)	0% (0)
Upper extremity swelling	71% (54)
Presence of clot elsewhere (eg, pulmonary embolism)	9% (7)
Inability to place central venous access	8% (6)
Assessment of clot propagation (known clot)	8% (6)
Pain	3% (2)
Patient-reported history	1% (1)

NOTE: Abbreviations: UEDVT, upper extremity deep vein thrombosis.

23% (10) had documented contraindications to anticoagulation, most commonly recent gastrointestinal or intracranial bleeding. Two percent of patients (1) was not prescribed pharmacologic treatment at discharge and had no contraindications documented. No patients underwent thrombolysis or had superior vena cava filters placed. Sixty-four percent (14 of 22) of CVCs that were thought to be directly associated with UEDVT were removed at diagnosis.

Outcomes

Five patients (10%) died during hospitalization, none because of VTE or complications thereof. Cause of death included septic shock, cancer, intracranial hemorrhage, heart failure, and recurrent gastrointestinal bleeding. Of the 45 surviving patients, only 38% (17) were discharged to self-care; more than half (62% [28]) were discharged to skilled nursing facilities, other hospitals, or rehabilitation centers. Eight patients (18%) were readmitted to our institution within 30 days; none for recurrent or new DVT or PE. No additional patients died at our medical center within 30 days of discharge.

DISCUSSION

UEDVT is increasingly recognized in hospitalized patients.^{3,9} At our medical center, ~0.2% of symptomatic inpatients were diagnosed with UEDVT over 14 months. These patients were predominantly men with high rates of CVCs, malignancy, VTE history, severe infection, and renal disease. Interestingly, although the literature suggests that some proportion of patients with UEDVT have anatomic abnormalities, such as

Paget-Schroetter syndrome,¹⁵ none of the patients in our study were found to have these anomalies. In our review, hospitalized patients with UEDVT were critically ill, with a long LOS and high morbidity and mortality, suggesting that in addition to just being a complication of hospitalization,^{1,6} UEDVT may be a marker of severe illness.

In our institution, clinical presentation was consistent with what has been described with the majority of patients presenting with upper extremity swelling.^{1,3} The internal jugular veins were the most common anatomic UEDVT site, followed by brachial then axillary veins. In other series including both in- and outpatients, subclavian clots were most commonly diagnosed, reflecting in part higher rates of CVC association and CVC location in those studies.^{3,9} Concurrent DVT and PE rates were similar to those reported.^{1,3,10}

Although many studies have focused on prevention of LEDVT and PE, few trials have specifically targeted UEDVT. Among our patients with UEDVTs that were not present on admission, VTE prophylaxis rates were considerably higher than what has been reported,^{1,6} suggesting that in these critically ill patients' prophylaxis may not prevent symptomatic UEDVT. It is unknown how many UEDVTs were prevented with prophylaxis, as only patients with symptomatic UEDVT were included. Adequacy of prophylaxis at outside hospitals for patients transferred in could not be assessed. Nonetheless, low numbers of UEDVT at a trauma referral center with many high-risk patients raise the question of whether prophylaxis makes a difference. Additional study is needed to further define the role of chemoprophylaxis to prevent UEDVT in hospitalized patients.

In our inpatient group, 84% required CVCs; 44% of patients were thought to have CVC-associated UEDVTs. Careful patient selection and attention to potentially modifiable risks, such as insertion site, catheter type, and tip position, may need further examination in this population.^{3,11,16} Catheter duration was long; focus on removing CVCs when no longer necessary is important. Interestingly, almost 10% in our study underwent diagnostic ultrasound because a new CVC could not be successfully placed suggesting that UEDVT may develop in critically ill patients regardless of CVCs.

In our study, there were high rates of guideline-recommended pharmacologic treatment; surprisingly the majority of CVCs with associated clot were removed. Guidelines currently support 3 months of anticoagulation for treatment of UEDVT^{2,13,17}; evidence derives from observational trials or is largely extrapolated from LEDVT literature.^{2,13} Routine CVC removal is not specifically recommended for CVC-associated UEDVT, particularly if lines remain functional and medically necessary; systemic anticoagulation should be provided.¹³

In our review, no hospitalized patients with UEDVT developed complications or were readmitted to our medical center within 30 days for clot progression, new PE, or post-thrombotic syndrome, which is lower than rates reported over longer time periods.^{2,6,10,12} Ten percent died during hospitalization, all from their primary disease rather than from complications of VTE or VTE treatment, and no additional patients died at our institution within 30 days. Although these rates are lower than have been otherwise reported,^{2,10} the inpatient mortality rate is similar to a recent study that included inpatients; however, all patients who died in that study had cancer and CVCs.³ In the latter study, 6.4% died within 30 days of discharge.

Limitations

There are several limitations to this study. It was conducted at a single academic referral center with a large and critically ill trauma and neurosciences population, thereby limiting generalizability. This study describes hospitalized patients at a tertiary care center who were diagnosed with UEDVT. For comparison, we obtained information regarding characteristics of hospitalization for all other inpatients during this time frame. Individuals may have had multiple hospitalizations during the study period, but because we were unable to identify information about individuals, direct statistical comparisons could not be made. However, in general, inpatients with UEDVT appeared to be sicker, with prolonged LOS and high in-hospital mortality relative to other hospitalized patients.

Only symptomatic UEDVT events were captured, likely underestimating true UEDVT incidence. In addition, we defined UEDVTs as those diagnosed by Doppler ultrasound; therefore theoretically, UEDVTs that were more centrally located or diagnosed using another modality would not be represented here. However, in a prior internal review we found that all VTE events coded in billing data during this time period were identified using our operational definition.

In our study, VTE prophylaxis was administered in accordance with an institutional guideline. We did not have information regarding adequacy of prophylaxis at outside institutions for patients transferred in, and patients admitted through the emergency department likely were not on prophylaxis. Therefore, information about prophylaxis is limited to prophylaxis administered at our medical center for hospitalized patients who had UEDVTs not present on admission.

Information regarding CVC insertion date and CVC type for CVCs placed in our institution is accurate based on our internal reviews. Although we had reasonable capture of information about CVC placement at outside facilities, these data may be incomplete, thereby underestimating potential association of CVCs with UEDVTs identified in our hospitalized patients. Additionally, criteria used to assess association of a

CVC with UEDVT may have led to underrepresentation of CVC-associated UEDVT.

Management of UEDVT in this study was determined by the treating physicians, and patients were only followed for 30 days after discharge. Information about readmission or death within 30 days of discharge was limited to patient contact with our medical center only. Treatment at discharge was determined from the discharge summary. Therefore, compliance with treatment cannot be assessed. Although these factors may limit the nature of the conclusions, data reflect actual practice and experience in hospitalized patients with UEDVT and may be hypothesis generating.

CONCLUSIONS

Among hospitalized patients, UEDVT is increasingly recognized. In our medical center, hospitalized patients diagnosed with UEDVT were more likely to have CVCs, malignancy, renal disease, and severe infection. Many of these patients were transferred critically ill, had prolonged LOS, and had high in-hospital mortality. Most developed UEDVT despite prophylaxis, and the majority of UEDVTs were treated even in the absence of concurrent LEDVT or PE. As we move toward an era of increasing accountability, with a focus on preventing hospital-acquired conditions including VTE, additional research is needed to identify modifiable risks, explore opportunities for effective prevention, and optimize outcomes such as prevention of complications or readmissions, particularly in critically ill patients with UEDVT.

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