Four-extremity venous duplex ultrasound for suspected deep venous thrombosis is an anachronism

Taehwan Yoo, MD, MS, Rishav Aggarwal, BS, Shayna Brathwaite, MD, MS, Bhagwan Satiani, MD, MBA, *and* Mounir J. Haurani, MD, *Columbus, Ohio*

ABSTRACT

Background: Duplex ultrasound is the "gold standard" for diagnosis of acute deep venous thrombosis (DVT) because of its high specificity, sensitivity, safety, and portability. However, unnecessary testing epitomizes inefficient use of scarce health care resources. Here we hypothesize that the majority of simultaneous four-extremity duplex ultrasound (FED) examinations are unnecessary. By analyzing clinical factors of patients with acute DVT found on FED, we aimed to identify a subset of high-risk patients who may have a valid indication for four-extremity testing.

Methods: We retrospectively reviewed all venous duplex ultrasound examinations performed in our Intersocietal Accreditation Commission-accredited vascular laboratory from January 1, 2009, to December 31, 2016. Patients with duplex ultrasound scans of all four limbs were included. DVT risk factors and indication for duplex ultrasound examination were recorded. The primary outcome was finding of acute DVT.

Results: There were 188 patients who met our search criteria, of whom 31 patients (16.5%) had acute DVT (11 upper extremity, 16 lower extremity, and 4 upper and lower extremity). Fever of unknown origin (FUO) was the main indication for requesting FED (53.7%). Patients who underwent FED for FUO had a significantly lower likelihood of DVT (odds ratio, 0.21; $P = .01$). DVT was rarely the proximate cause (<1% of all cases) as follow-up culture results and clinical course most often revealed other sources of fever. Only patients with an upper extremity central venous catheter (CVC; n = 103) with at least two associated risk factors had an upper extremity DVT, which was usually line associated (93%). Only patients with at least two associated risk factors had a lower extremity DVT.

Conclusions: FED for FUO is inefficient, given that DVT was rarely the proximate cause of fever. Acute upper extremity DVT was found only in patients with an upper extremity CVC, demonstrating that patients without upper extremity CVC do not benefit from upper extremity duplex ultrasound examination. Upper extremity DVT is usually line associated and dependent on the number of cumulative risk factors present, suggesting that only the extremity associated with the CVC in the right clinical context should be imaged. Lower extremity DVT is also dependent on the number of cumulative risk factors present, and testing should be reserved for patients according to the clinical context. Our results indicate that a restrictive strategy can reduce testing inefficiency and health care cost without compromising patients' safety. (J Vasc Surg: Venous and Lym Dis 2019;7:325-32.)

Keywords: Venous duplex; DVT; Vascular imaging lab

Increased pressure has been placed on imaging facilities to reduce unnecessary testing. The Medicare Payment Advisory Commission and private payers have discussed ways to reduce "low-value" service that has little or no clinical benefit or tests carrying risks that outweigh benefits.[1] Whereas reducing reimbursement as a primary means of cost savings may decrease cost in the short term, decreasing unnecessary testing by scrutinizing the indications for testing is an alternative approach that is more likely to improve efficiency without significantly detracting from the care of patients.

Venous duplex ultrasound is the imaging modality of choice when the diagnosis of acute deep venous thrombosis (DVT) is suspected.[2] It is safe, can be performed at the bedside, and in the hands of an experienced technologist has sensitivities and specificities consistently reported as high as 95%.[2,3] As a result, its availability and safety make it prone to overuse.

At our institution, we noted an increasing number of four-extremity duplex ultrasound (FED) tests ordered, especially in 2015 and 2016 (Fig 1, *a*). Interestingly, this increase was not department specific; rather, every department measured increased FED ordering in 2015 and 2016 (Fig 1, *b*). Based on these observations, we decided to study FED testing at our institution to determine the true incidence of DVT, with the secondary aim of determining whether FED is useful at determining the cause of fever of unknown origin (FUO). Our hypothesis was that FED is an inefficient and overused test for diagnosis

From the Division of Vascular Disease and Surgery, Department of Surgery, The Ohio State University.

Author conflict of interest: none.

Additional material for this article may be found online at www.jvsvenous.org.

Correspondence: Mounir J. Haurani, MD, Division of Vascular Disease and Surgery, Department of Surgery, The Ohio State University, 701 Prior Hall, 376 W 10th Ave, Columbus, OH 43210-1267 (e-mail: mounir.haurani@osumc.edu).

The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

2213-333X

https://doi.org/10.1016/j.jvsv.2018.11.004

of acute DVT. By investigating the necessity of FED, we aimed to establish data that can guide providers in making safe and cost-effective decisions.

METHODS

Data source and patient characteristics. After approval by The Ohio State University Institutional Review Board, including waiver of consent, and in accordance with the Declaration of Helsinki, we conducted a retrospective study of patients at our institution. Our cohort was composed of patients who within 48 hours underwent both bilateral lower and upper extremity duplex ultrasound examinations. Patients undergoing testing between January 1, 2009, and December 31, 2016, were included. We searched for patients by *Current Procedural Terminology* code for lower extremity ultrasound examination (93970). For each patient's record, detailed clinical variables were collected, including age, sex, ethnicity, body mass index (BMI), known provoking risk factors including recent trauma (within 3 months), recent surgery (within 3 months), pregnancy, oral contraceptive use, previous venous thromboembolism (VTE), presence and laterality of an upper central venous catheter (CVC), active malignant disease, current chemotherapy, and history of congenital or acquired thrombophilia (congenital: factor V Leiden gene mutation, prothrombin gene mutation, antithrombin III deficiency, protein C deficiency, or protein S deficiency; acquired: persistently positive lupus anticoagulant or elevated antiphospholipid antibodies, heparin-induced thrombocytopenia). We recorded the long-term use of therapeutic anticoagulation (warfarin, low-molecular-weight heparin, direct oral anticoagulants) and antiplatelet agents (aspirin, clopidogrel). A time frame of recent trauma and surgery of 3 months was chosen on the basis of previously published studies demonstrating this period as an antecedent risk factor for VTE.[4]

The reason for testing was found by chart review of progress notes at the time the study was performed and the listed indication on the order. The ordering provider was cross-checked against clinical progress notes to correctly assess the department ordering the study. Indications were broken down into five main categories; fever, symptoms (swelling or limb pain), known pulmonary embolism diagnosed by computed tomography of the chest or ventilation-perfusion scan looking for the source of the embolus, acute hypoxic respiratory failure, and surveillance after previous acute DVT. Patients who had testing done for fever also had infectious disease culture results recorded. Ordering clinician specialties were grouped on the basis of our institution's organizational structure in regard to which intensive care units are shared among specialties and overall hospital department structure.

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center retrospective study
- **Key Findings:** In 188 patients with four-extremity venous duplex ultrasound (FED) examination, 31 (16.5%) had acute deep venous thrombosis (DVT; 11 upper extremity, 16 lower extremity, and 4 both upper and lower extremity). The indication for obtaining FED was fever of unknown origin in 53.7%, with very low likelihood of having a DVT (odds ratio, 0.21; $P = .01$). Only patients with central venous catheter had upper extremity DVT, usually line associated (93%).
- **Take Home Message:** For diagnosis of suspected DVT, FED is not routinely indicated, and it is an inefficient use of health care resources.

Duplex ultrasound analysis. A trained general surgery resident or vascular surgeon reviewed all duplex ultrasound study results with VascuPro vascular laboratory software (Consensus Medical Systems Inc, Richmond, BC, Canada). All studies were performed by registered sonographers with the Philips iU22 (Philips Healthcare, Bothell, Wash), General Electric Logiq E (GE Healthcare, Wauwatosa, Wisc), and Zonare Z (Zonare Medical Systems Inc, Mountain View, Calif) ultrasound machines, depending on whether the study was done in the laboratory or on a portable machine. The main outcome recorded was the presence of acute DVT. Secondary outcomes were the laterality and location of acute DVT.

Statistical analysis. Univariate comparisons between groups for discrete variables were made using Fisher exact test, χ^2 test, logistic regression, and multivariate analysis using Stata version 14.1 (StataCorp, College Station, Tex). Statistical significance was defined by α of .05. Sample size analysis was carried out using a one-proportion power analysis, assuming a historical positive DVT rate of 0.15 ($d = 0.10$, $\alpha = .05$), and was found to be 114.

RESULTS

Patient characteristics. We identified a total of 188 patients who underwent FED performed from January 1, 2009, to December 31, 2016 (Supplementary Table, online only). The mean age of patients was 55.0 years, and 55.9% (n = 105) were men; 16.5% of patients (n = 31) had acute DVT (11 upper extremity only, 16 lower extremity only, and 4 simultaneous upper and lower extremity).

Ordering indications for FED testing. The most common indication for FED testing (Fig 2) was fever (53.7%), followed by extremity symptoms (32.9%; 8.0% with unilateral extremity symptoms), acute respiratory failure (5.9%), pulmonary embolism (4.8%), and surveillance after previous acute DVT (2.8%).

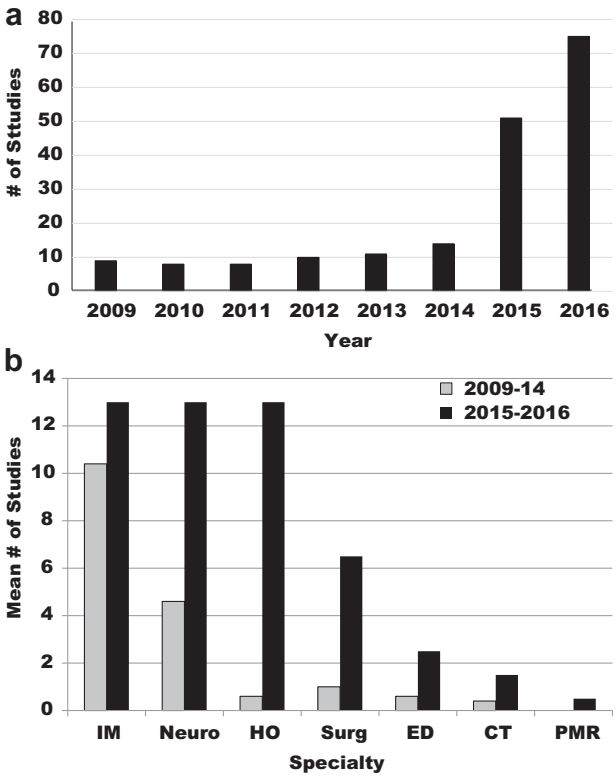

Fig 1. a, Number of four-extremity duplex ultrasound (FED) studies performed by year. From 2009 to 2014, FED testing was low, at approximately 10 studies per year. However, during the most recent years (2015-2016), there has been a large increase in testing. **b,** Mean number of studies by ordering provider specialty. When mean ordering patterns are broken down from 2009 to 2014 (*gray bars*) compared with 2015 to 2016 (*black bars*) by provider specialty, there is an increase in FED ordering across all providers during the more recent years, indicating that this increase is not a specific but rather an institution-wide pattern. *CT,* Cardiothoracic surgery; *ED,* emergency department; *HO,* hematology/oncology; *IM,* internal medicine; *Neuro,* neurology; *PMR,* physical medicine and rehabilitation; *Surg,* surgery.

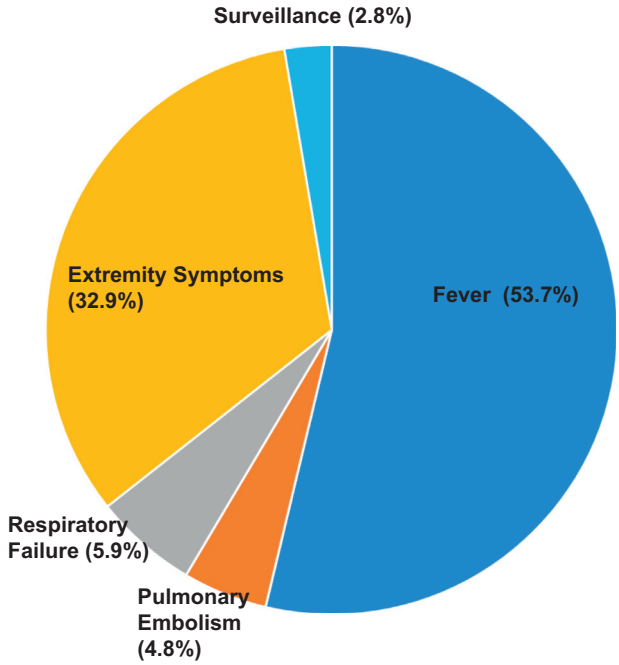

Fig 2. Ordering indication for four-extremity duplex ultrasound (FED) examination. Workup of fever was the most common reason for ordering FED.

Factors associated with acute DVT. Univariate comparison was performed on collected variables stratified by the outcome of DVT (Table I). Factors that were significant for increased association with DVT were major surgery in the past 3 months (24.3% vs 11.4%; $P = .02$), hospitalization ≥7 days (25.3% vs 6.7%; $P < .01$), immobility ≥7 days (22.0% vs 7.1%; $P < .01$), current malignant disease (27.1% vs 12.9%; $P = .02$), and presence of CVC (23.3% vs 8.2%; $P < .01$). DVT prophylaxis was protective, with a decreased overall risk of DVT (10.7% vs 26.9%; $P < .01$). Receiving therapeutic anticoagulation was nearly associated with a protective effect (4.2% vs 18.3%; $P = .06$). Not receiving anticoagulation or prophylaxis was significantly associated with acute DVT (37.8% vs 9.8%; $P < .01$).

The indication for which FED was ordered was associated with acute DVT risk. The most common reason for FED was for fever workup (53.7% of all tests; n = 101). This indication was associated with a decreased risk of acute DVT (10.9% vs 23.0%; $P = .02$). When imaging positively confirmed diagnosis of pulmonary embolism, there was a significant increased risk of having an acute DVT (77.8% vs 13.4%; $P < .01$). Having extremity symptoms was not associated with DVT; however, having unilateral symptoms was associated with acute DVT (40.0% vs 14.5%; $P = .02$). Ordering clinician specialty was also associated with acute DVT risk. If a general surgery, urology, obstetrics/gynecology (OBGYN), or surgical intensive care unit (SICU) provider ordered the FED study, there was an overall increased risk of having acute DVT (33.3% vs 14.7%; $P = .04$). In addition, there was an increased likelihood of finding acute DVT if any intensive care clinician ordered FED examination (22.0% vs 10.2%; $P = .03$).

Using multivariate logistic regression for all variables that were significant on univariate analysis, we found several risks that defined our model ($\alpha = .05$; Table II): BMI <25 kg/m^2 (odds ratio [OR], 4.69; $P < .01$), hospitalization ≥7 days (OR, 4.64; $P = .01$), current malignant disease (OR, 8.17; $P < .01$), and CVC (OR, 5.32; $P = .01$). The biggest risk factor for acute DVT was not receiving DVT prophylaxis or anticoagulation (OR, 14.23; $P < .01$). General surgery, urology, OBGYN, or SICU specialty (OR, 9.05; $P = .01$) was significant for increased risk of acute DVT. Of all possible indications for FED, fever was associated with decreased risk on multivariate analysis (OR, 0.21; $P = .01$). Intensive care specialty was significant (OR, 4.06; $P = .04$). Pregnancy and pulmonary embolism were not included, given their relatively small numbers, which would cause instability in the model.

Table I. Significant univariate characteristics associated with acute deep venous thrombosis (*DVT*)

Variable	Risk factor, No. (%)	DVT with risk factor, No. (%)	DVT without risk factor, No. (%)	*P* value
Patient characteristics				
BMI <25 kg/m^2	55 (29.3)	14 (25.5)	17 (12.8)	.03
Risk factors				
Major surgery ≤3 months	74 (39.4)	18 (24.3)	13 (11.4)	.02
Hospitalization ≥7 days	99 (52.7)	25 (25.3)	6 (6.7)	<.01
Immobility ≥7 days	118 (62.8)	26 (22.0)	5 (7.1)	<.01
Current malignant disease	48 (25.5)	13 (27.1)	18 (12.9)	.02
CVC	103 (54.8)	24 (23.3)	7 (8.2)	<.01
Medications				
DVT prophylaxis	121 (64.4)	13 (10.7)	18 (26.9)	<.01
Anticoagulation	24 (12.8)	1 (4.2)	30 (18.3)	.06
No prophylaxis or anticoagulation	45 (23.9)	17 (37.8)	14 (9.8)	<.01
Indication				
Fever	101 (53.7)	11 (10.9)	20 (23.0)	.02
Pulmonary embolism	9 (4.8)	7 (77.8)	24 (13.4)	<.01
Unilateral extremity symptoms	15 (8.0)	6 (40.0)	25 (14.5)	.02
Ordering clinician specialty				
General surgery, urology, OBGYN, or SICU	18 (9.6)	6 (33.3)	25 (14.7)	.04
Intensive care (any type)	100 (53.1)	22 (22.0)	9 (10.2)	.03

BMI, Body mass index; *CVC,* central venous catheter; *OBGYN,* obstetrics/gynecology; *SICU,* surgical intensive care unit.

Factors associated with upper extremity DVT. To determine the characteristics that were specifically associated with upper extremity DVT on FED, we examined our cohort by our secondary outcome of upper extremity DVT (Table III). Significant and nearly significant risk factors included BMI <25 kg/m^2 (relative risk [RR], 9.67; $P < .01$), recent surgery (RR, 2.31; $P = .10$), prolonged hospitalization (RR, 2.52; $P = .10$), and prolonged immobility (RR, 3.86; $P = .07$). Not receiving DVT prophylaxis or anticoagulation was significantly associated with increased risk (RR, 2.86; $P = .03$). Of unilateral extremity symptoms associated with increased risk (RR, 5.33; $P < .01$), DVT was always present on the symptomatic side. Of all patients with an acute upper extremity acute DVT (8.0%; n = 15), every patient had an upper extremity CVC. Of these patients, the majority of DVT was catheter associated, with clot forming on the same side as the catheter (93.3% of all upper extremity acute DVTs; n = 14). One patient had an upper extremity DVT on the side contralateral to the catheter. Further chart review found that this patient was recently postoperative from a heart transplantation, likely making the proximate cause a result of direct trauma (mobilization and suturing) to the deep veins during surgery. Conversely, there were no patients who had an acute upper extremity DVT without a CVC.

To ascertain whether the number of risk factors cumulatively increased risk of having an upper extremity DVT, we compiled associated factors only in patients who had an upper extremity CVC (n = 103) as a cumulative score and compared this with upper extremity DVT risk (Fig 3). Patients with no or one risk factor had no incidence of upper extremity DVT. Only patients with two or more risk factors had upper extremity DVT. Similar to lower extremity DVT, there was an increased risk of upper extremity DVT with increasing number of risk factors.

Factors associated with lower extremity DVT. To determine what characteristics were specifically associated with lower extremity DVT on the FED study, we examined our total cohort by our secondary outcome of lower extremity DVT (Table IV). Significant and nearly significant risk factors included recent surgery (RR, 2.31; $P = .05$), prolonged hospitalization (RR, 2.75; $P = .04$), prolonged immobility (RR, 3.36; $P = .04$), and active malignant disease (RR, 2.39; $P = .04$). Not receiving DVT prophylaxis or anticoagulation was significantly associated with increased risk (RR, 6.08; $P < .01$). Fever was associated with decreased risk (RR, 0.29; $P = .01$). Known acute pulmonary embolism was associated with increased risk (RR, 8.52; $P < .01$). Given the small number of patients who had FED performed for unilateral lower extremity symptoms (n = 11, with 2 lower extremity DVTs, not shown in Table IV), this indication was not associated with lower extremity DVT.

To ascertain whether the number of risk factors cumulatively increased risk of having a lower extremity DVT, we compiled associated factors as a cumulative score and compared this with lower extremity DVT risk (Fig 4). Pulmonary embolism was excluded as a predictive factor in

Table II. Multivariate comparisons of characteristics associated with acute deep venous thrombosis (*DVT*)

Characteristic	OR (CI)	*P* value
Patient characteristics		
BMI <25 kg/m^2	4.69 (1.47-14.99)	<.01
Risk factors		
Hospitalization ≥7 days	4.64 (1.36-15.84)	.01
Current malignant disease	8.17 (2.12-31.57)	<.01
CVC	5.32 (1.43-19.82)	.01
Medications		
No DVT prophylaxis or anticoagulation	14.23 (3.66-55.30)	<.01
Indication		
Fever	0.21 (0.06-0.69)	.01
Ordering clinician specialty		
General surgery, urology, OBGYN, or SICU	9.05 (1.49-55.06)	.01
Intensive care	4.06 (1.04-15.91)	.04

BMI, Body mass index; *CI*, confidence interval; *CVC*, central venous catheter; *OBGYN*, obstetrics/gynecology; *OR*, odds ratio; *SICU*, surgical intensive care unit.
Controlling for BMI <25 kg/m^2, major surgery ≤3 months, hospitalization ≥7 days, immobility ≥7 days, current malignant disease, CVC, no DVT prophylaxis or anticoagulation, fever, unilateral extremity symptoms, general surgery/urology/OBGYN/SICU, and intensive care provider.

this model as patients with known pulmonary embolism should have a DVT source that is able to be found by FED, as our results suggest. We do not believe that FED is clinically indicated in patients with pulmonary embolism as these patients should be treated with anticoagulation regardless of a positive or negative result. Patients with no or one risk factor had no incidence of lower extremity DVT. Only patients with two or more risk factors had lower extremity DVT. Interestingly, the risk of having a lower extremity DVT increased cumulatively with the number of risk factors.

Table III. Factors associated with upper extremity deep venous thrombosis (*DVT*)

Characteristic	RR (CI)	*P* value
Risk factors		
BMI <25 kg/m^2	9.67 (2.84-32.94)	<.01
Surgery ≤3 months	2.31 (0.86-6.22)	.10
Hospitalization ≥7 days	2.52 (0.83-7.64)	.10
Immobility ≥7 days	3.86 (0.90-16.59)	.07
CVC	–	–
Medications		
No DVT prophylaxis or anticoagulation	2.86 (1.10-7.45)	.03
Indication		
Unilateral symptoms	5.33 (1.99-14.26)	<.01

BMI, Body mass index; *CI*, confidence interval; *CVC*, central venous catheter; *RR*, relative risk.

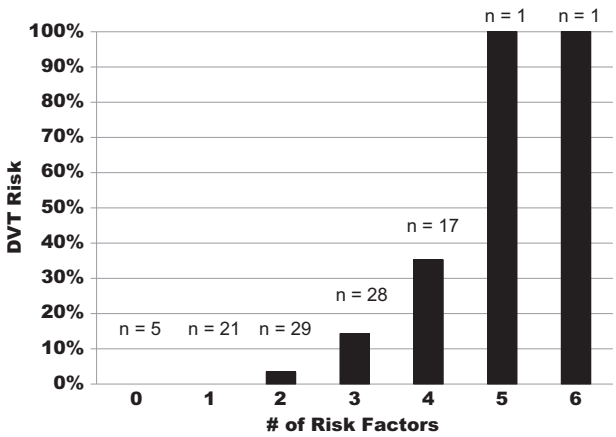

Fig 3. Risk of upper extremity deep venous thrombosis (*DVT*) by number of associated risk factors. Upper extremity DVT risk factors are taken from Table III (body mass index [BMI] <25 kg/m^2, surgery ≤3 months, hospitalization ≥7 days, immobility ≥7 days, no DVT prophylaxis or anticoagulation, unilateral symptoms). The *n above bars* marks the number of patients corresponding to the number of risk factors. In patients with an upper extremity central venous catheter (CVC), those with minimal risk (no or one associated risk factor, n = 26) had no DVT. As risk factors increased cumulatively, upper extremity DVT risk increased.

DVT as a cause of fever. To determine how often DVT was the cause of fever, we examined the cohort of patients with fever as the indication for FED. The patients' infectious disease culture results and service notes (Table V) were reviewed. Of the 101 patients with fever as the indication for FED, 11 were positive for acute DVT (10.8%). Of these, 10 patients had positive culture results that could explain fever symptoms. Only one patient with fever had an acute DVT (1.0%) without positive culture results or other abnormalities, making this the only case in which fever could be attributed to acute DVT. Seventeen other patients had fever without acute DVT and negative culture results. Six patients had a limited fever course, and a proximate cause was never found. Three patients had drug-induced fever that resolved after the offending agent was stopped. Three patients had neutropenic fever after chemotherapy. Two patients suffered recent neurologic insult and were diagnosed with autonomic instability as the proximate cause. One patient was found to have graft-versus-host disease. Another patient was found to have autoimmune hepatitis. One patient was eventually diagnosed with Q fever. Interestingly, most patients undergoing FED for fever (77.2%; n = 78) already had positive culture results and were being treated with antibiotics at the time FED was performed.

DISCUSSION

Here we demonstrate that FED represents an inefficient use of health care resources. The most common indication for testing, fever, was associated with a lower likelihood of

Table IV. Factors associated with lower extremity deep venous thrombosis (*DVT*)

Characteristic	RR (CI)	*P* value
Risk factors		
Surgery ≤3 months	2.31 (0.99-5.38)	.05
Hospitalization ≥7 days	2.75 (1.04-7.27)	.04
Immobility ≥7 days	3.36 (1.02-11.06)	.04
Active malignant disease	2.39 (1.05-5.41)	.04
Medications		
No DVT prophylaxis or anticoagulation	6.08 (2.59-14.30)	<.01
Indication		
Fever	0.29 (0.11-0.76)	.01
Pulmonary embolism	8.52 (14.31-16.87)	<.01

CI, Confidence interval; *RR*, relative risk.

acute DVT. Although elevated temperatures may be associated with acute DVT, most patients with DVT have slight or no increase in temperature, and it rarely causes true fever, making it an overall poor indicator.[5] DVT as the cause of fever has been described in case reports and case series.[6] However, our data show that DVT as the cause of FUO is a rare phenomenon, with only one patient in our 7-year experience qualifying. Many patients with fever also often had positive culture data, for which they were already receiving antibiotic therapy, which does not truly fit the definition of FUO (narrowly defined by fever of at least 38.3°C that is persistent for at least 3 weeks and defies diagnosis with at least 1 week of workup).[7]

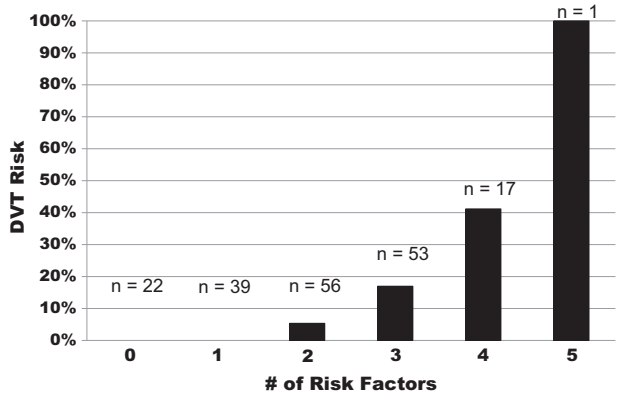

Fig 4. Risk of lower extremity deep venous thrombosis (*DVT*) by number of associated risk factors. Lower extremity DVT risk factors are taken from Table IV (surgery ≤3 months, hospitalization ≥7 days, immobility ≥7 days, active malignant disease, no DVT prophylaxis or anticoagulation, fever). The *n above bars* marks the number of patients corresponding to the number of risk factors. Patients with minimal risk (no or one associated risk factor, n = 61) had no DVT. As risk factors increased cumulatively, lower extremity DVT risk increased.

We confirm that upper extremity acute DVT is rarely spontaneous and required a causative event, such as mechanical trauma or partial obstruction from cardiothoracic surgery or presence of a CVC. Spontaneous upper extremity DVT that occurs without an iatrogenic cause is rare, with an incidence of 2 per 100,000 people per annum, of which two-thirds are caused by effort-induced thrombosis and mechanical thoracic outlet obstruction known as the Paget-von Schroetter syndrome, which typically occurs in younger, healthier, nonhospitalized patients.[8] Comparatively, secondary upper extremity DVT from a central venous device, spurred by the ever-increasing use of central access and implantable cardiac devices, is significantly more common and is the major risk factor for development of DVT.[9,10] Overall, catheter-associated upper extremity DVT makes up an estimated 80% of cases, which are likely much more common in our inpatient cohort in which FED is ordered.[3,11]

Interestingly, BMI <25 kg/m^2 was a risk factor for upper but not lower extremity DVT. This has been previously documented; however, the cause remains unclear.[12] Just as leaner patients are at increased risk of spontaneous upper extremity DVT from increased extrinsic compression, we conjecture that leaner patients in general may have relatively increased extrinsic compression and endothelial damage in the presence of a CVC, leading to an increased predisposition toward upper extremity DVT.

Given that almost all upper extremity DVTs in our cohort were line associated, our results suggest that patients without an upper extremity CVC do not need upper extremity DVT testing. Patients who have an upper extremity CVC may need duplex ultrasound imaging on the ipsilateral side of the CVC, as most acute DVT is line associated. Therefore, a simple algorithm considering the presence and laterality of an upper extremity CVC can be used to safely decrease unnecessary testing for most patients (Fig 5, *a*). Our results suggest that patients who have a CVC but without other significant risk factors or unilateral symptoms do not require testing. Conversely, patients with significant risk and presence of a CVC should consider being testing on the ipsilateral side of the CVC. Using this algorithm, there would be no patients who require bilateral upper extremity testing. Of the 103 patients with upper extremity CVC, 26 patients (25.2%) would not need any upper extremity testing, given a lack of significant risk factors or symptoms.

Clinical diagnosis appears significantly more reliable for upper extremity DVT suspected on the basis of a CVC than that of lower extremity DVT.[3,13] In contrast, lower extremity acute DVT does not present with reliable clinical symptoms and can happen spontaneously in any immobilized patient because of relative immobility with stasis compared with the upper extremities. Thus, lower extremity testing requires a lower threshold of suspicion.[14]

It is well known that lower extremity DVT is associated with many risk factors. In our cohort, patients with two

Table V. Causes of fever in four-extremity venous duplex ultrasound (*FED*) cohort

Proximate cause	Total cohort, No. (%)
Infection	83 (82.2)
Cultures positive before FED	78 (77.2)
Cultures positive after FED	5 (5.0)
Unknown	6 (5.9)
Drug reaction	3 (3.0)
Neutropenic fever	3 (3.0)
Autonomic instability from CNS injury	2 (2.0)
Graft-versus-host disease	1 (1.0)
Autoimmune hepatitis	1 (1.0)
Q fever	1 (1.0)
Acute DVT	1 (1.0)

CNS, Central nervous system; *DVT,* deep venous thrombosis.

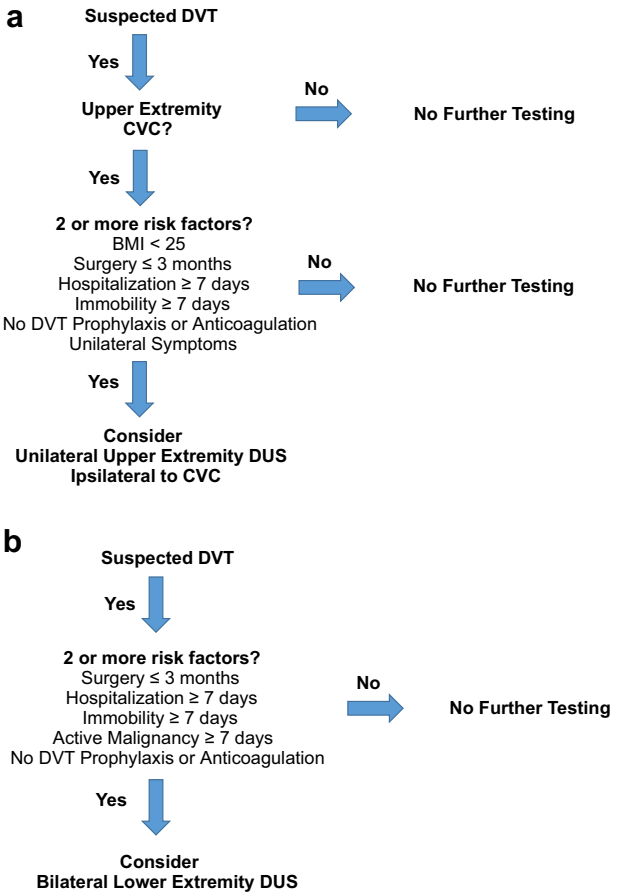

Fig 5. a, Algorithm to decrease unnecessary upper extremity testing. An algorithm requiring an upper extremity central venous catheter (*CVC*) and the presence of at least two upper extremity deep venous thrombosis (*DVT*) risk factors could significantly reduce testing without compromising patients' safety. **b,** Algorithm to decrease unnecessary lower extremity testing. An algorithm based on the presence of at least two lower extremity risk factors could significantly reduce testing without compromising patients' safety. *BMI,* Body mass index; *DUS,* duplex ultrasound.

or more associated risk factors had a cumulatively increasing risk of lower extremity DVT. However, patients with one or no risk factor had no incidence of DVT. Therefore, our results argue that lower extremity testing should be reserved for patients with multiple significant risk factors (Fig 5, *b*). By scanning only patients with two or more risk factors, the number of bilateral lower extremity studies could be reduced by 61 patients (32.4%) without missing a single diagnosis of lower extremity DVT.

Using a simple algorithm based on the laterality and presence of an upper extremity CVC and cumulative risk score, we demonstrate that the use of FED to diagnose DVT can be avoided in most cases. There are circumstances in which FED may be considered. Patients with cardiothoracic surgery who have direct manipulation of the great vessels may warrant FED as the relative postoperative immobility and direct surgical trauma involving the central venous system may predispose to formation of thrombus in either extremity and is a known complication of open heart surgery.[15] Certain patients may have bilateral upper extremity CVCs or other partially obstructing lines, such as intravenous shunts or pacemaker leads, in addition to multiple significant clinical risk factors that may warrant FED.

It is unknown why providers began ordering FED with greater frequency from 2015. Interestingly, it was not a matter of a few departments driving up the number of tests. Rather, every department to different degrees increased testing in this 2-year period, suggesting that a decreased reliance on risk factor assessment to guide testing has overall decreased the threshold for ordering studies. We conjecture that the favorable portability and safety of ultrasound make this test particularly prone to overuse. Unlike other diagnostic modalities, such as computed tomography and magnetic resonance imaging, there is no additional risk from ultrasound; there is no radiation exposure, tenuous patients do not need to be moved, it remains comparatively less expensive, and it does not need contrast agents that may cause allergic or nephrotoxic reactions.[2] Given that ultrasound is a risk-free test, we believe that providers do not adequately assess other associated costs, such as financial cost to the patient and insurer, additional time of the technologist, and the physician's interpretation time.

General surgery, urology, OBGYN, or SICU ordering providers had an overall increased rate of detecting DVT by FED compared with other departments, even after controlling for associated risk factors. We hypothesize that this may be due to additional variables that are not well accounted for in our study. For example, these services perform large pelvic operations that carry an overall increased risk of DVT, perhaps making the overall incidence of DVT higher.

Our study has noted limitations. Our data came from a cohort of 188 patients spanning our 7-year experience from a single institution, which may not reflect the population of patients or outcomes at other centers. Depending on different rates of malignant disease, CVC, and traumatic injury, the potential value of FED may be different. In some categories, known risk factors for DVT (such as previous VTE, male sex, pregnancy, thrombophilia, unilateral extremity symptoms) failed to reach our cutoffs for significance after controlling for other factors, probably because of the overall low numbers of patients with these risk factors, making our study underpowered to include these in our model. In addition, FED makes up an overall small number of total venous duplex ultrasound tests ordered, for which the exact indications for testing as well as patients' characteristics are likely to differ from those of patients who are receiving just upper or lower extremity testing. Therefore, our results may not be generalizable to all patients for whom venous duplex ultrasound is requested. Also, the granularity of the data is dependent on the specificity of the ordering provider in charting and listing the indication for FED. For example, several studies were ordered for "edema" but failed to specify laterality, making this difficult to truly ascertain. Last, as with any retrospective review, our study is vulnerable to selection bias.

CONCLUSIONS

In our single-center retrospective cohort of patients who underwent FED, we demonstrate that this test is not indicated for most patients. Overall, FUO is associated with a decreased likelihood of finding a DVT, for which FED is not recommended. By following a simple algorithm based on the location of upper CVC or recent cardiothoracic surgery and number of cumulative risk factors, unnecessary testing and cost can be significantly reduced without affecting patients' care.

AUTHOR CONTRIBUTIONS

Conception and design: TY, RA, BS, MH
Analysis and interpretation: TY, BS, MH
Data collection: TY, RA, SB
Writing the article: TY, RA, SB, BS, MH
Critical revision of the article: TY, BS, MH
Final approval of the article: TY, RA, SB, BS, MH
Statistical analysis: TY, MH
Obtained funding: Not applicable
Overall responsibility: MH

REFERENCES

1. Schwartz AL, Landon BE, Elshaug AG, Chernew ME, McWilliams JM. Measuring low-value care in Medicare. JAMA Intern Med 2014;174:1067-76.
2. Lewis BD, James EM, Welch TJ, Joyce JW, Hallett JW, Weaver AL. Diagnosis of acute deep venous thrombosis of the lower extremities: prospective evaluation of color Doppler flow imaging versus venography. Radiology 1994;192:651-5.
3. Kucher N. Deep-vein thrombosis of the upper extremities. N Engl J Med 2011;364:861-9.
4. Spencer FA, Emery C, Lessard D, Anderson F, Emani S, Aragam J, et al. The Worcester Venous Thromboembolism study: a population-based study of the clinical epidemiology of venous thromboembolism. J Gen Intern Med 2006;21:722-7.
5. Kazmers A. Do patients with acute deep vein thrombosis have fever? Am Surg 2000;66:598-601.
6. AbuRahma AF, Saiedy S, Robinson PA, Boland JP, Cottrell DJ, Stuart C. Role of venous duplex imaging of the lower extremities in patients with fever of unknown origin. Surgery 1997;121:366-71.
7. Petersdorf RG, Beeson PB. Fever of unknown origin: report on 100 cases. Medicine (Baltimore) 1961;40:1-30.
8. Joffe HV. Upper-extremity deep vein thrombosis. Circulation 2002;106:1874-80.
9. Winters JP, Callas PW, Cushman M, Repp AB, Zakai NA. Central venous catheters and upper extremity deep vein thrombosis in medical inpatients: the Medical Inpatients and Thrombosis (MITH) Study. J Thromb Haemost 2015;13:2155-60.
10. Hamada SR, Espina C, Guedj T, Buaron R, Harrois A, Figueiredo S, et al. High level of venous thromboembolism in critically ill trauma patients despite early and well-driven thromboprophylaxis protocol. Ann Intensive Care 2017;7:97.
11. Sajid MS, Ahmed N, Desai M, Baker D, Hamilton G. Upper limb deep vein thrombosis: a literature review to streamline the protocol for management. Acta Haematol 2007;118:10-8.
12. Joffe HV, Kucher N, Tapson VF, Goldhaber SZ. Deep Vein Thrombosis FREE Steering Committee. Upper-extremity deep vein thrombosis: a prospective registry of 592 patients. Circulation 2004;110:1605-11.
13. Constans J, Salmi LR, Sevestre-Pietri MA, Perusat S, Nguon M, Degeilh M, et al. A clinical prediction score for upper extremity deep venous thrombosis. Thromb Haemost 2008;99:202-7.
14. Criado E, Burnham CE. Predictive value of clinical criteria for the diagnosis of deep vein thrombosis. Surgery 1997;122:578-83.
15. Elboudwarej O, Patel JK, Liou F, Rafiei M, Osborne A, Chai W, et al. Risk of deep vein thrombosis and pulmonary embolism after heart transplantation: clinical outcomes comparing upper extremity deep vein thrombosis and lower extremity deep vein thrombosis. Clin Transplant 2015;29:629-35.

Submitted Jun 14, 2018; accepted Nov 2, 2018.

Additional material for this article may be found online at www.jvsvenous.org.

Supplementary Table (online only). Characteristics of four-extremity venous duplex ultrasound (FED) cohort

Variable	Total cohort	No DVT	DVT
Patient characteristics			
Patients	188 (100)	157 (83.5)	31 (16.5)
Age, years	55.0 (16.3)	54.7 (16.1)	56.5 (17.6)
Male	105 (55.9)	88 (56.1)	17 (54.8)
BMI, kg/m^2	30.7 (9.8)	30.9 (9.5)	29.5 (11.4)
Risk factors			
Trauma ≤3 months	16 (8.5)	14 (8.9)	2 (6.5)
Major surgery ≤3 months	74 (39.4)	56 (35.7)	18 (58.1)
Hospitalization ≥7 days	98 (52.1)	74 (47.1)	24 (77.4)
Immobility ≥7 days	118 (62.8)	92 (58.6)	26 (83.9)
Pregnancy	3 (1.6)	1 (0.6)	2 (6.5)
Previous VTE	30 (16.0)	25 (15.9)	5 (16.1)
Current malignant disease	48 (25.5)	35 (22.2)	13 (41.9)
CVC	103 (54.8)	79 (50.3)	24 (77.4)
Thrombophilia	6 (3.2)	5 (3.2)	1 (3.2)
Medications			
Antiplatelet	67 (35.6)	59 (37.6)	8 (25.8)
DVT prophylaxis	121 (64.4)	108 (68.8)	13 (41.9)
Anticoagulation	24 (12.8)	23 (14.6)	1 (3.2)
No prophylaxis or anticoagulation	45 (23.9)	28 (17.8)	17 (54.8)
Statin	57 (30.3)	50 (31.8)	7 (22.6)
Indication			
Fever	101 (53.7)	90 (57.3)	11 (35.5)
Pulmonary embolism	9 (4.8)	2 (1.3)	7 (22.6)
Acute respiratory failure	11 (5.9)	10 (3.2)	1 (6.3)
Extremity symptoms	62 (32.9)	50 (31.8)	12 (38.7)
Unilateral extremity symptoms	15 (8.0)	9 (5.7)	6 (19.3)
Surveillance	5 (2.7)	5 (3.2)	0 (0.0)
Ordering clinician specialty			
Internal medicine or MICU	78 (41.5)	67 (42.6)	11 (35.4)
Neurology, neurosurgery, or NCCU	49 (26.1)	40 (25.5)	9 (29.0)
Hematology/oncology	29 (15.4)	26 (16.6)	3 (9.7)
General surgery, urology, OBGYN, or SICU	18 (9.6)	12 (7.6)	6 (19.4)
Emergency medicine	8 (4.2)	8 (5.1)	0 (0.0)
Cardiothoracic surgery	5 (2.7)	3 (1.9)	2 (6.5)
PMR	1 (0.5)	1 (0.6)	0 (0.0)
Intensive care (any type)	100 (53.1)	9 (5.7)	22 (71.0)

BMI, Body mass index; *CVC,* central venous catheter; *DVT,* deep venous thrombosis; *MICU,* medical intensive care unit; *NCCU,* neurocritical care unit; *OBGYN,* obstetrics/gynecology; *PMR,* physical medicine and rehabilitation; *SICU,* surgical intensive care unit; *VTE,* venous thromboembolism. Categorical variables are presented as number (%). Continuous variables are presented as mean (standard deviation).