RESEARCH LETTER

Whole-Arm Ultrasound to Rule Out Suspected Upper-Extremity Deep Venous Thrombosis in Outpatients

Upper-extremity deep venous thrombosis (UE-DVT) accounts for approximately 14% of all cases of DVT.1 Because UE-DVT may provoke pulmonary embolism (PE), prompt diagnosis is necessary to select the patients who require anticoagulation. This study aimed to evaluate the failure rate of ultrasonographic screening for UE-DVT.

Methods | Study Design. A prospective management study was conducted from January 1, 2011, through December 31, 2013, in the Angiology and Blood Coagulation Unit, University Hospital, Bologna, Italy, a tertiary care teaching hospital, in outpatients referred by general practice physicians to the vascular emergency department for suspected symptomatic DVT or superficial venous thrombosis (SVT) of the upper extremities. Exclusion criteria were age younger than 18 years, pregnancy or puerperium, PE symptoms, life expectancy of less than 3 months, and a need for anticoagulant therapy or anticoagulation lasting more than 48 hours. We enrolled eligible consecutive patients during business days. Patients with DVT or SVT received anticoagulants while patients with either negative or initially inconclusive findings from the ultrasonographic screening were not treated and were followed up for 3 months. The outcome was the cumulative 3-month incidence of objectively confirmed symptomatic PE and/or UE-DVT. All events were adjudicated by one of us (B.C.) who was not involved in patient enrollment or follow-up. Patients who were lost to follow-up were removed a priori from the analysis. This study was approved by the local Ethics Committee of Bologna University Hospital, Italy. Written informed consent was obtained for all patients.

Ultrasonography. Ultrasonography was performed according to the methods of Chin et al2: radial, ulnar, and brachial veins were scanned transversally, whereas axillary, subclavian, and internal jugular veins were scanned both transversally and longitudinally. The diagnostic criteria were the presence of intraluminal thrombus combined with a lack of vein compression and/or with an abnormal flow pattern in the segment of the vein distal to the thrombosis. Superficial venous thrombosis was diagnosed as previously described.3 If technical problems or anatomical barriers hampered visualization, findings from the ultrasonographic screening were considered indeterminate and it was repeated after 5 to 7 days.

Results | The Table shows characteristics of the 483 study participants. The Figure shows the study flowchart. Findings from the ultrasonographic screening at enrollment were normal in 319 patients (66.0%) and inconclusive in 21 (4.3%), who repeated the test after 5 to 7 days. For those who repeated the test, findings from the ultrasonographic screening showed SVT in 1 patient (4.8%) and DVT in 2 patients (9.5%). Of the 337 patients with negative ultrasonographic findings, 5 were lost to follow-up, one 89-year-old man died of infection (the death was not related to PE), and 2 patients (0.60%; 95% CI, 0.16%-2.17%) developed DVT or SVT (1 ipsilateral DVT after 1 month and 1 SVT after peripheral vein infusion). No PE occurred (0.0%; 95% CI, 0.0%-1.0%). Overall, 1 diagnosis of DVT was missed, for a failure rate of 0.30% (95% CI, 0.05%-1.68%).

Discussion | Our study shows that, similar to that of the lower extremities, a completely normal ultrasound on ultrasonography of the upper extremity can safely exclude DVT.4 Venography is the criterion standard for diagnosis of UE-DVT,5 but it has been largely replaced by ultrasonography in clinical practice. No prospective management study for suspected UE-DVT is available in which anticoagulation is withheld only on the basis of ultrasound.6 The proposed diagnostic algorithm for suspected UE-DVT with D-dimer in a recent study7 was designed to limit ultrasonographies, but 373 were performed in 402 patients because 14.3% patients repeated the ultrasonographic screening. Repeated testing involves greater resource use and more discomfort for patients, some of whom are not willing to return for a second test. With our approach, more initial ultrasonographies were performed, but they were repeated in only 4.3% of patients.

Table. Characteristics of the 483 Study Participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Valuea</th>
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<tbody>
<tr>
<td>Age, mean (SD) (IQR), y</td>
<td>59.0 (18.7) (29.9)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>300 (62.1)</td>
</tr>
<tr>
<td>Male</td>
<td>183 (37.9)</td>
</tr>
<tr>
<td>Active cancer</td>
<td>82 (17.0)</td>
</tr>
<tr>
<td>CVC</td>
<td>36 (7.4)</td>
</tr>
<tr>
<td>PICC</td>
<td>14 (2.9)</td>
</tr>
<tr>
<td>PM</td>
<td>16 (3.3)</td>
</tr>
<tr>
<td>History of vein thrombosis</td>
<td>83 (17.2)</td>
</tr>
<tr>
<td>Estrogen-containing therapyb</td>
<td>12 (2.5)</td>
</tr>
<tr>
<td>Peripheral vein infusionc</td>
<td>102 (21.1)</td>
</tr>
<tr>
<td>Recent hospital dischargec</td>
<td>50 (10.4)</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>339 (70.2)</td>
</tr>
<tr>
<td>Edema</td>
<td>269 (55.7)</td>
</tr>
<tr>
<td>Redness or rash</td>
<td>137 (28.4)</td>
</tr>
</tbody>
</table>

Abbreviations: CVC, central venous catheter; IQR, interquartile range; PICC, peripheral inserted central venous catheter; PM, pacemaker.

a Values are presented as number (percentage) of patients unless otherwise indicated.
b Contraception or hormone therapy.
c Within 1 month.
Our study was performed in a single center, with enrollment limited to business hours, and 5 patients (1.5%) with normal ultrasonographic findings were lost to follow-up. The electronic medical record was consulted for these 5 patients at the end of the follow-up period and no hospitalizations for PE and/or DVT were found.

Our data suggest that anticoagulation can be safely withheld on the basis of ultrasonographic screening for suspected UE-DVT.

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Author Contributions: Drs Sartori and Cosmi had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Sartori, Favaretto, Cosmi.

Acquisition, analysis, or interpretation of data: Sartori, Migliaccio, Favaretto, Brusi, Conti, Rodorigo.

Drafting of the manuscript: Sartori, Favaretto, Cosmi.

Critical revision of the manuscript for important intellectual content: Sartori, Migliaccio, Brusi, Conti, Rodorigo.

Statistical analysis: Sartori.

Administrative, technical, or material support: Migliaccio, Rodorigo.

Study supervision: Sartori, Favaretto, Conti, Cosmi.

Conflict of Interest Disclosures: None reported.


Invited Commentary

Ultrasound of the Whole Arm to Manage Suspected Upper-Extremity Deep Venous Thrombosis

Venous thromboembolism, which most commonly manifests as deep venous thrombosis (DVT) of the extremities and pulmonary embolism, affects more than 500,000 Americans annually and is the third most common cause of cardiovascular mortality in the United States. Upper-extremity DVT (UE-DVT) accounts for about 10% of all DVT cases, yet there have been few studies, to our knowledge, that provide high-
level evidence of the best diagnostic strategy to confirm or refute this disorder.

In 2012, when the ninth edition of the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines included its first chapter on the diagnosis of DVT, all but 1 of the guidance statements were based on level C (low- or very-low-quality evidence) according to the Grades of Recommendations, Assessment, Development, and Evaluation system. The guideline panel concluded that there is a much lower quality of evidence available to guide diagnosis of UE-DVT compared with lower-extremity DVT (LE-DVT).

Research of diagnostic testing for UE-DVT consists almost exclusively of accuracy studies (which compare a diagnostic test against the presumed criterion standard—contrast venography). This method assumes that the criterion standard has perfect operating characteristics, and the sensitivity and specificity of the comparator test is calculated based on the degree to which its results are in concordance. However, this method has many limitations. The assumption that the criterion standard has 100% sensitivity and specificity is overly optimistic and patients in such studies are not assessed for important outcomes. Moreover, venography is technically challenging, invasive, and carries the risks of contrast dye and radiation exposure.

A better standard of evidence on which to base practice is the diagnostic management study. Using this method, a diagnostic strategy is used in a patient population with suspected disease, a treatment decision is made based on the diagnostic result, and patients are followed up for important clinical outcomes for a predefined period. In diagnostic management studies of LE-DVT, an acceptable diagnostic strategy results in a “miss rate” (the percentage of patients who are diagnosed with venous thromboembolism during 3 months of follow-up after a normal test result) of approximately less than 2%. This standard is based on a management study of contrast venography. A number of diagnostic management studies that used ultrasonography for diagnosis of suspected LE-DVT have been published and meet this standard. While it would be tempting to assume that ultrasonographic findings are similarly accurate in the upper and lower extremities, applying evidence from management trials of LE-DVT is problematic. All the deep vessels of the lower extremity are accessible to compression (the principal method by which thrombosis is identified), but in the upper extremity, the clavicle prevents compression of much of the subclavian vein, limiting evaluation to Doppler flow analysis.

In this issue, Sartori and colleagues present a high-quality management study evaluating the ability of a single whole-arm ultrasonogram to exclude suspected UE-DVT (a second ultrasonogram was obtained 5-7 days later if the initial findings were inconclusive). The failure rate of the strategy was low, with the upper boundary of the 95% CI for missed DVT diagnosis being 1.68%, below the traditional standard for LE-DVT management studies and comparable with similar studies for LE-DVT.

Important strengths of the study include sequential enrollment of patients with suspected DVT during predefined hours, a well-delineated ultrasound protocol, management decisions made on the basis of the ultrasonogram without additional testing, low loss to follow-up, and the independent adjudication of outcomes. The principal limitations of the study are the relatively small sample size and the single-center design. Also, the protocol was not limited to the proximal deep veins but assessed the superficial and distal deep veins of the arm. Anticoagulation treatment was given regardless of thrombus location. However, the clinical importance and need for treatment of superficial venous thrombosis and distal-arm DVT is uncertain.

This work joins a recent diagnostic management study by Kleinjan et al, which used a multistep algorithm that included a clinical prediction score plus D-dimer, reserving ultrasonography for those with high pretest probability or abnormal D-dimer findings (similar to strategies previously validated for suspected LE-DVT). There was a similar overall rate of symptomatic venous thromboembolism during follow-up after application of this strategy (0.4%; 95% CI, 0.0%-2.2% for the full algorithm). Kleinjan et al’s strategy resulted in lower overall use of ultrasonography but more instances of a repeated ultrasonographic screening (14.3% of enrolled patients). The simpler strategy used by Sartori and colleagues required initial imaging in all cases, with a second ultrasonographic screening in 4.3% of patients.

Is ultrasonography, with or without the use of a clinical score and D-dimer, now the standard of care for suspected UE-DVT? External validation and impact analysis have been suggested as important elements to determine if a diagnostic strategy is ready for widespread adoption, so ideally a larger multicenter trial should confirm these findings. However, there are no such data available, to our knowledge, for a venogram-based strategy either. Many institutions use ultrasonography for diagnosis of suspected UE-DVT, given the risk associated with and pragmatic difficulty of venography. This trial provides reassurance that ultrasonography is a reasonable strategy. As advocated by the American College of Chest Physicians’ guidelines, venography can be reserved for patients in whom ultrasonographic findings are inconclusive or suspicion of thrombosis remains high despite a normal finding.

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Medicare Fee Cuts and Cardiologist-Hospital Integration

Physician practices are increasingly integrating with hospitals.1 For physicians, the expansion of accountable care organization contracts, centered on clinicians taking responsibility for population spending and quality, makes independent practice more challenging. For hospitals and health systems, acquiring practices helps them control referral patterns, coordinate care, and improve their bargaining power with payers.

In 2010, based on recommendations from the American Medical Association and a national practice expense survey of physicians, the Centers for Medicare & Medicaid Services reduced fees for cardiovascular services, focusing on those delivered in the office setting.2 For example, payment for a myocardial perfusion image in the office was cut 26%, compared with 5% in the hospital outpatient department (HOPD). Payment for an echocardiogram was cut 16% in the office, compared with a 3% increase in the HOPD setting. This widened the already existing payment gap favoring HOPDs—by 2013, an echocardiogram cost Medicare 141% more in HOPDs than in the office.3

The American College of Cardiology (ACC) projected a surge of integration in response to physician office fee reductions, with cardiologists exchanging practice ownership for more predictable salaries as hospital employees.4 We analyzed trends in cardiologist-hospital integration.

Methods | We analyzed 2007-2012 medical claims in a continuously enrolled national sample of traditional Medicare beneficiaries and commercially insured individuals from Truven Medicare and Commercial databases. We measured cardiologist-hospital integration by calculating the share of volume billed in HOPDs. This captures both shifts in care to HOPDs and changes in practice patterns induced by physician-hospital integration. We focused on 3 affected services—myocardial perfusion imaging (MPI), echocardiograms, and electrocardiograms.3 We expected shares of HOPD volume to increase.

We used segmented regression to assess changes in integration growth after the physician office fee cut. Independent variables included beneficiary age and sex, time trend, a postintervention indicator, and the interaction between post-intervention and trend. We also included quarter and metropolitan statistical area fixed effects. Standard errors were clustered by metropolitan statistical area.

This research was approved by the Harvard Medical School Institutional Review Board.

Results | Our sample included 806 266 Medicare beneficiaries with a mean age of 75.7 years, who were 53.3% female, and represented all states, and 12 567 069 commercially insured individuals aged 55 to 64 years who were 52.8% female with a similar geographic distribution.

Across all services, prices favored the HOPD setting after 2010 (Table). The shares of volume in the HOPD setting also increased after 2010 (Figure). Growth in the HOPD share was 5.9, 3.9, and 2.7 percentage points per year (P < .001) faster after 2010 compared with before 2010 for MPI, echocardiograms, and electrocardiograms, respectively. The overall volume of echocardiograms and electrocardiograms per beneficiary continued to increase after the fee cut, while that for MPI decreased slightly (Table).

Aggregate analyses of all cardiovascular imaging and cardiovascular medicine services produced qualitatively similar results. Similar results were also found in commercial populations, suggesting that integration was associated with comparable effects across payers (Table).

Discussion | Integration accelerated after the fee cuts. This is consistent with the 2010 ACC Practice Census, which found that 40% of cardiologists planned to integrate with hospitals due to the fee cuts and 13% were considering it.5 The Medicare Payment Advisory Commission estimated that if cardiology imaging alone continued to migrate to HOPDs, nearly all would be provided there by 2021, costing an additional $1.1 billion per year to Medicare and $290 million per year in beneficiary cost sharing because of higher prices for facility-based services.3

Hospital outpatient departments may be more expensive than office settings because of the costs of licensing requirements, ancillary services, maintaining standby capacity, and treating more complex patients.3 However, if equivalent quality care could be delivered in the office, the case for paying the higher fee may be more difficult to justify. Moreover, while higher HOPD payments may be covering higher hospital costs, they may also be passed on to physicians through higher salaries. Ultimately, integration may offset savings that fee cuts were intended to achieve, both because facility-based fees are higher and because of higher prices due to market power.

Our results may not be causal or generalizable. Other market forces could have also encouraged integration, such as hospitals acquiring practices to preserve their referral base under new payment models and the rising costs of independent practice, including malpractice premiums, infrastructure costs (eg, electronic medical records), and costs of meeting new quality reporting or performance goals. Moreover, integration has not been limited to cardiology, supporting the potential effect of broader secular factors. At the service level, the effect of any fee cut depends on its magnitude, the previous fees in each setting, and changes in the volume of affected and substitute services across different sites of care.

Amidst growing recognition of payment disparities across sites of care, policies that aim to equalize payments across settings have received increasing attention. The president’s fiscal year 2016 budget proposes site-neutral payments, estimated to save nearly $29.5 billion over 10 years. If fee cuts did indeed lead to hospital acquisition of physician practices, then...