Improvements in the Diagnostic Approach for Patients with Suspected Deep Vein Thrombosis or Pulmonary Embolism

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Introduction

Deep vein thrombosis (DVT) and pulmonary embolism (PE), collectively known as venous thromboembolism (VTE), are common medical disorders that cause considerable morbidity and may result in fatalities if not promptly diagnosed and appropriately treated. In recent years there have been several important advances that have improved the diagnostic testing strategies for patients with suspected VTE. First, the accuracy and utility of the clinical diagnosis has been reevaluated and found to be a valuable adjunct to objective testing. Second, the fibrin degradation product, D-dimer, has been shown to be a sensitive and potentially useful test to exclude the diagnosis of VTE. Third, newer imaging modalities, such as spiral computerized tomographic angiography (spiral CT), have become available for the investigation of patients with suspected PE. Finally, diagnostic testing algorithms that rely primarily on non-invasive imaging procedures have been validated for the investigation of patients with suspected DVT and PE.

The purpose of this chapter is to update the reader about recent advances and current strategies for the investigation of patients with suspected VTE. As a result of clinical trials, safe and feasible approaches for the management of patients with suspected VTE have been validated that minimize the need for invasive testing and are practical even for small centers with limited radiologic facilities.

The Clinical Diagnosis of Venous Thromboembolism

Deep Vein Thrombosis

Prior to the 1970s, the diagnosis of DVT was usually made on clinical grounds. With the availability of venography, physicians began to recognize that errors were frequently made when the diagnosis of DVT was based on the clinical examination alone. Subsequently, the clinical diagnosis fell into such disfavor that its utility was felt only to trigger the consideration that objective testing may be required.

Studies in recent years have revisited the accuracy of the clinical diagnosis for DVT. Landefeld and associates found that five clinical findings were independently associated with the development of proximal DVT. Subsequently, it was demonstrated that explicit clinical criteria could reliably separate patients with suspected DVT into high, moderate, and low pre-test probability categories. These criteria combined consideration of the patients clinical presentation, associated risk factors, and the possible presence of an alternative diagnosis that would account for patient symptoms. Using such criteria, patients considered at high clinical pre-test probability had over a 75% incidence of DVT confirmed by objective testing. Conversely, patients considered at low pre-test probability, but in whom the diagnosis could not be excluded on clinical grounds alone, had less than a 5% incidence of DVT. A simple nine-point clinical criteria scoring system was subsequently developed to determine a patient’s pre-test probability for DVT. This scoring system was proven to have similar accuracy and be a useful adjunct to noninvasive testing for the management of patients with suspected DVT (Table 1).

Pulmonary Embolism

Until recently, the clinical diagnosis of PE was also felt to be inaccurate and of little value. In a multicenter study in which the diagnosis of PE was confirmed by pulmonary angiography, the PIOPED investigators demonstrated that experienced clinicians were able to separate cohorts of patients with suspected PE into high, moderate, and low probability groups using the clinical assessment alone. More recently, Perrier and colleagues were also able to stratify patients with suspected PE into probability categories using clinical criteria alone. In both of these studies, separation of the patients into low, moderate, and high pre-test probability categories was made using only the clinical judgement of the individual clinicians.

These findings were recently extended by Wells and colleagues, who developed an explicit model to determine pre-test probability for PE using clinical findings and chest x-ray results. This model (Fig. 1) combined consideration of whether the patient’s clinical presentation based on symptoms, signs, and risk factors, was typical for PE and whether there
was an alternative diagnosis at least as likely as PE to account for their symptoms. In a study evaluating over 1,200 inpatients and outpatients with suspected PE, clinicians using this clinical model were able to distinguish low, moderate, and high pre-test probability cohorts in whom the prevalence rates of PE were 3%, 28%, and 78%, respectively. In addition to demonstrating the accuracy of the clinical diagnosis, each of the above three studies found that consideration of clinical probability was a useful adjunct to imaging procedures in the evaluation of patients with suspected PE.

### D-Dimer for Diagnosis of Venous Thromboembolism

Markers of thrombosis have been evaluated for their predictive value for the diagnosis of VTE. The test that has been studied most extensively and shown to be the most useful is the D-Dimer assay. D-Dimer is a degradation product of the cross-linked fibrin blood clot. Levels of D-dimer are typically elevated in patients with acute VTE. D-dimer levels may also be increased in a variety of nonthrombotic disorders, including recent major surgery, hemorrhage, trauma, malignancy, or sepsis. Therefore, in general, D-dimer assays are sensitive, but nonspecific, markers for VTE.

As a result of these diagnostic characteristics, a positive D-dimer result is not useful to include the diagnosis of VTE, rather its potential value is as an exclusionary tool. The negative predictive value of the D-dimer increases proportionately, depending upon the sensitivity of the assay, and is inversely related to the prevalence of VTE in the study population. The specificity of a particular D-dimer assay and the characteristics of the particular study population influence the utility of the assay to exclude the diagnosis of VTE. For instance, use of a very nonspecific D-dimer assay or the testing of hospitalized patients would be predicted to be of limited value, due to the expected very high false positive rates that would be observed.

Several different D-dimer assays have been evaluated for the diagnosis of VTE and their accuracy varies. The most sensitive D-dimer tests are the enzyme-linked immunosorbent assays (ELISA). Bounameaux and colleagues reported that ELISA D-dimers had a mean sensitivity of 97% and specificity of 35% for the diagnosis of DVT. Until recently, ELISA D-dimer assays were performed on microplate readers, making them expensive, time consuming, and impractical to be performed in most centers as urgent diagnostic tests. However, semi-quantitative and rapid fluorescence quantitative ELISA D-dimer assays have been developed that remain highly sensitive. These newer assays have lowered the test turnaround time to less than 1 hour.

Two other D-dimer assay methods that have been evaluated as diagnostic markers for VTE are the whole blood agglutination assay (SimpliRED) and latex agglutination plasma assays. These assays are advantageous in that they are simple to perform, have a rapid turnaround time, and are inexpensive. These D-dimer tests are less sensitive but more specific than the ELISA assays. The sensitivity of the SimpliRED D-dimer assay in clinical trials has varied between 84% and 94%, whereas the latex agglutination plasma assays are less than 80% sensitive.

Prospective studies have reported that the negative predictive values of the ELISA and SimpliRED D-Dimer assays exceed 95%, making them potentially useful markers to exclude the diagnosis of DVT or PE. Due to its higher sensitivity, a negative ELISA D-dimer assay alone may be used to exclude the diagnosis of VTE, as demonstrated by Perrier and colleagues, who reported no thromboembolic complications were observed in the 3 month follow-up period in 159 patients with suspected PE who had a negative ELISA D-dimer (95% CI, 0%-2.3%).

The SimpliRED D-dimer, with its lower sensitivity, should only be considered as an exclusionary test in patient populations identified to have a lower prevalence of VTE. This was demonstrated in a recent study by Ginsberg and colleagues, who evaluated the SimpliRED D-dimer assay in a cohort of 1,177 inpatients and outpatients with suspected PE. The D-dimer assay had a sensitivity of 85%, a specificity of 68%, and a negative predictive value of 96%. The negative predictive value of the D-dimer test varied depending upon clinical pre-test probability from 99.0% (95% CI, 97.8%-99.7%) in patients at low pre-test probability to 87.9% (95% CI, 81.9%-92.4%).

### Table 1: Clinical Model to Determine Pre-test Probability for Deep Vein Thrombosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active cancer (treatment ongoing or within previous 6 months or palliative)</td>
<td>1</td>
</tr>
<tr>
<td>Paralysis, paresis or recent plaster immobilization of the lower extremities</td>
<td>1</td>
</tr>
<tr>
<td>Recent immobilization &gt; 3 days or major surgery within 12 weeks requiring general or regional anesthesia</td>
<td>1</td>
</tr>
<tr>
<td>Localized tenderness along the distribution of the deep venous system</td>
<td>1</td>
</tr>
<tr>
<td>Entire leg swollen</td>
<td>1</td>
</tr>
<tr>
<td>Calf swelling 3 cm &gt; asymptomatic side (measured 10 cm below tibial tuberosity)</td>
<td>1</td>
</tr>
<tr>
<td>Pitting edema confined to the symptomatic leg</td>
<td>1</td>
</tr>
<tr>
<td>Collateral superficial veins (non-varicose)</td>
<td>1</td>
</tr>
<tr>
<td>Alternative diagnosis as likely or greater than that of DVT</td>
<td>-2</td>
</tr>
</tbody>
</table>

Clinical Probability calculated as follows: HIGH (3); MODERATE 1 or 2; LOW (0)
Imaging Procedures for Deep Vein Thrombosis

Real-time, B-mode venous ultrasonography has become established as the imaging procedure of choice for the investigation of patients with a suspected first episode of DVT.21-23 This technique provides direct visualization of the deep venous structures and may be used to determine alternative causes of leg pain and swelling. Venous ultrasound imaging of the proximal venous system can be performed rapidly and without the need for extensive technologist training. It is also a portable technique, which allows for the assessment of critically ill patients at the bedside.

The inability to completely compress the vein lumen is the principal criteria for the diagnosis of deep venous thrombosis.21-23 There are several adjunctive ultrasonographic findings that may be observed in patients with DVT, such as vein distension, absence of flow by Doppler, echoic signals within the vessel lumen, and visualization of filling defects by color Doppler. However, these findings do not increase the sensitivity of ultrasound imaging beyond the parameter of vein compressibility.22

Other Diagnostic Tests for Deep Vein Thrombosis

In most centers, venous ultrasound imaging has replaced venography for the investigation of patients with suspected DVT, although the latter is still regarded as the “gold standard” technique.25 Venography remains the only diagnostic test that can reliably detect DVT isolated to the calf veins, the iliac veins, or the inferior vena cava. Venography is also the most accurate method for the diagnosis of asymptomatic thrombi that
May develop following high-risk surgical procedures. However, venous ultrasound imaging has a number of limitations, including the risk of allergic and non-allergic side effects, the requirement for contrast use, and greater technical demands, which make it less practical than venous ultrasound imaging.

Venous ultrasound imaging has also proven more sensitive and specific than other non-invasive tests that use indirect techniques to detect DVT, such as changes in venous hemodynamics (Doppler ultrasound, impedance plethysmography) or the presence or absence of fibrin accretion (\textsuperscript{125}I fibrinogen scanning).

### Accuracy of Ultrasound for the Diagnosis of Deep Vein Thrombosis

#### Symptomatic Patients

Venous ultrasound imaging is a very accurate test for patients presenting with symptoms suspected to be caused by their first episode of DVT. A meta-analysis of studies in symptomatic patients, using venography as the gold standard, reported that the sensitivity of ultrasound imaging was 97\% (95\% CI, 96\%--98\%) for the diagnosis of DVT involving the proximal leg veins. The specificity was 94\% (95\% CI, 90\%--98\%) for all deep vein thrombi. Similar accuracy rates for venous ultrasound imaging were reported in studies in which the entire proximal venous system was examined and those in which the examination was limited to the deep veins in the common femoral and the popliteal regions extending distally to the trifurcation of the popliteal vein were examined.

Studies evaluating the accuracy of compression ultrasonography for the diagnosis of calf DVT have been relatively small, and the results have been highly variable. A meta-analysis reported the sensitivity of ultrasonography for isolated calf vein thrombosis to be 73\% (95\%, CI 54\%--93\%). In addition, the rates of technically inadequate studies, up to 40\% in one study, were higher for calf than proximal vein evaluation.

#### Asymptomatic Patients

Venous ultrasound imaging has been extensively evaluated as a screening test performed on asymptomatic patients in high-risk settings for DVT. A meta-analysis showed that the sensitivity of ultrasound imaging for proximal DVT was only 62\% following total hip or knee arthroplasty and that somewhat lower sensitivity rates were observed for isolated calf vein thrombosis. The sensitivity of postoperative ultrasound screening was not increased with the addition of Doppler or color Doppler. Likely explanations for the low sensitivity include small size and unpredictable location of DVT in the postoperative setting.

In addition to its low sensitivity, a recent, randomized study demonstrated that performance of screening venous ultrasound imaging of the proximal venous system prior to hospital discharge did not reduce the rate of subsequent symptomatic venous thromboembolic complications in patients who received warfarin prophylaxis following total hip or knee arthroplasty. Based on this study, routine ultrasound screening cannot be recommended following joint arthroplasty, at least in patients receiving DVT prophylaxis.
Imaging Procedures for Pulmonary Embolism

Ventilation-Perfusion Lung Scanning

For many years ventilation perfusion (V/Q) lung scanning has been used as the imaging procedure of choice for the evaluation of patients with suspected PE. This radionuclide test is non-invasive with minimal side effects and at least the perfusion portion of the study may be performed in critically ill patients.

The accuracy of lung scanning has been evaluated in two studies that used pulmonary angiography as the gold standard. A normal perfusion lung scan essentially excludes the diagnosis of PE. A high-probability lung scan has an 85% to 90% predictive value for PE. Unfortunately, most lung scans fit into a non-diagnostic category (neither normal nor high probability), in which the incidence of PE varies from 10% to 30%. Criteria have been developed by the PIOPED investigators to distinguish moderate probability (termed intermediate, prevalence of PE about 30%) from lower probability (termed low, prevalence of PE about 15%) lung scans. However, the designation of a low probability lung scan has been criticized because of the interpretation by some clinicians that low probability means no probability, and on that basis, anticoagulant therapy has been withheld inappropriately in some patients. Hull and colleagues developed the term “non-high probability” to account for lung scan results in the low and moderate probability categories and to indicate that further testing was required to exclude the diagnosis of PE in these patients.

Assessment of clinical probability has unearthed a further problem with the accuracy of lung scanning. Using pulmonary angiography as the gold standard, two studies have demonstrated that between 45% and 66% of high probability lung scans were falsely positive when a skilled clinician deemed the patients pre-test probability for PE was low. Therefore, patients with non-high probability lung scans or those with high-probability scans, in whom the clinical pre-test probability is low, require further investigation to exclude or confirm the diagnosis of PE.

Other Imaging Techniques for the Diagnosis of Pulmonary Embolism

Pulmonary angiography has been regarded as the gold standard test for PE, and for many years, it had been recommended as the test of choice to confirm or exclude this diagnosis in patients with non-high probability lung scans. However, pulmonary angiography is an invasive procedure that may result in arrhythmias, hypotension, and other adverse reactions to contrast dye. For many centers, pulmonary angiography is unavailable, and in others, it is simply not practical to use this procedure routinely to exclude PE. In addition, a negative pulmonary angiogram does not preclude the development of thromboembolic complications. In the PIOPED study, 1.6% of patients with normal pulmonary angiograms developed PE in a 1-year follow-up period. Most of these events occurred within 1 month of the procedure.

Over the past decade contrast enhanced spiral CT has emerged as a new non-invasive imaging modality for the investigation of patients with suspected PE. Spiral CT has made it possible to directly visualize segmental and some subsegmental arteries using a single bolus of contrast while advancing the patient through the x-ray beam. Spiral CT images must be obtained while patients are holding their breath or breathing shallowly for 15 to 25 seconds. Spiral CT may identify alternative causes for symptoms in patients with suspected PE.

A pooled analysis of five comparative studies, using pulmonary angiography as the gold standard, determined the overall sensitivity and specificity of spiral CT for the diagnosis of PE to be 72% (95% CI, 59%-83%) and 95% (95% CI, 89%-98%), respectively. However, for central PE, those involving the main pulmonary arteries and their segmental branches, the sensitivity of CT increased to 94% (95% CI, 86%-98%) and the specificity remained high (94%; 95% CI, 88%-98%).

Mayo and colleagues directly compared the accuracy of spiral CT with lung scanning in 139 patients with suspected PE. They demonstrated that, when there was discordance between the spiral CT and the lung scan result, spiral CT demonstrated the correct diagnosis in 92% of cases. Also, in the 20 patients with intermediate probability lung scans, spiral CT made the correct diagnosis in 16 (80%).

The clinical significance of pulmonary emboli not detected by spiral CT is uncertain. Pulmonary angiography studies indicate that from 6% to 36% of pulmonary emboli may be limited to the subsegmental arteries. Although such small emboli in themselves may carry a low risk of serious complications, they may be a harbinger for subsequent thromboembolic complications.

Magnetic resonance imaging (MRI) has also been evaluated for the diagnosis of PE. Although this technique appears promising, further research is required to compare the utility of this test with other pulmonary imaging modalities.

Approach to Patients for the Diagnosis of the First Episode of Deep Vein Thrombosis

Patients presenting with symptoms of a suspected first episode of DVT should undergo venous ultrasound imaging of the proximal venous system. Due to the very high specificity of this test, a positive compression ultrasound result is sufficiently predictive that treatment can be initiated in patients who have no previous history of DVT. The dilemma is how to manage patients who have a negative initial ultrasound, since about 10% to 20% of patients presenting with symptomatic DVT will have thrombosis isolated to the veins of the calf and at least 20% to 30% of calf vein thrombi will eventually extend to the proximal venous system, at which point the likelihood of developing clinically important pulmonary embolic complications is much greater.

To detect the proximal extension of calf vein thrombosis the approach of serial testing has evolved. This technique was originally validated by Hull and colleagues with impedance plethysmography (IPG) and has been extended for use with ultrasonography. Patients with an initial negative study have antithrombotic therapy withheld and then undergo follow-up venous ultrasound imaging over a 1-week period. Patients in which proximal extension of DVT is detected may have
antithrombotic treatment initiated, whereas leg symptoms are attributed to other causes in those patients with negative serial ultrasound. Recent large management studies by Cogo and associates and Bidwell and colleagues have demonstrated that serial ultrasound testing with a single follow-up study is a safe strategy for managing patients with suspected DVT since those with negative serial ultrasounds have a less than 1% risk of developing symptomatic proximal DVT or PE in a 3-month follow-up period.50,51

The drawback of the serial ultrasound testing approach is that very few patients (1% to 2% in two recent studies) with suspected DVT who have a negative initial ultrasound test will be confirmed to have proximal DVT upon serial testing. As a result, serial testing is not cost-effective.52,53 Performing calf imaging in all patients with negative proximal exams is likewise not desirable because it is time consuming, and the rate of inadequate scans would result in the need for additional testing in many patients. In addition, the sensitivity and specificity of venous ultrasound imaging is lower for calf than proximal DVT, resulting in increased numbers of false positive and negative studies. No prospective study has evaluated the safety of withholding anticoagulants solely on the basis of a single negative ultrasound assessment of either the proximal, alone, or both the proximal and calf venous systems.

It would be desirable to identify patients in whom the diagnosis of DVT could be safely excluded on the basis of a single negative ultrasonography study of the proximal venous system. A recent management study demonstrated that patients at low clinical pre-test probability, as determined by explicit clinical criteria, had DVT safely excluded on the basis of a single negative ultrasound test.7 Only 0.6% (95% CI, 0.1% to 1.8%) of patients in this subgroup developed venous thromboembolic complications in a 3-month follow-up period.

The D-dimer may also be used to limit the need for serial testing in patients with suspected DVT. Bernardi and colleagues reported that in 598 outpatients with suspected DVT, patients with a single normal ultrasound and a negative ELISA D-dimer, had a very low rate of venous thromboembolic complications over a 3-month follow-up period (0.4%; 95% CI, 0% to 0.9%).54 The safety of this approach was subsequently confirmed in a study of Perrier and colleagues, who reported no complications in a cohort of 125 patients with suspected DVT who had a normal ultrasound and a negative ELISA D-dimer study.16 Ginsberg and colleagues reported that, among 273 outpatients who had a single normal IPG and a negative SimpliRED D-dimer result, only 4 (1.5%; 95% CI 0, 4%-3.7%) had venous thromboembolic complications in a 3-month follow-up period.55 When this cohort was restricted to patients at low pre-test probability for DVT, the thromboembolic complication rate in patients with a negative D-dimer and a normal IPG was only 0.6%.55 Management algorithms for patients with suspected DVT are presented in Figure 2.

Is Urgent Diagnostic Imaging Required for Patients with Suspected Deep Vein Thrombosis?

Until recently, the options were limited for managing patients coming into Emergency Departments with suspected DVT. Physicians could either arrange for urgent imaging procedures to confirm or exclude the diagnosis of DVT or initiate intravenous unfractionated heparin therapy until appropriate diagnostic testing could be performed. Currently, there is more flexibility in managing patients presenting with suspected DVT at times when diagnostic imaging is not available. Patients in whom there is a moderate or high clinical suspicion of DVT may receive an injection of unfractionated or low molecular weight heparin in doses designed to treat an acute DVT.56 Diagnostic imaging can then be arranged on a more elective basis the following day. Since unfractionated or low molecular weight heparin are safe and effective for patients with proven DVT, they would provide adequate therapy for patients with suspected DVT.57-59 Patients at low pre-test probability by clinical assessment or a negative D-Dimer test may have diagnostic imaging safely delayed for a 12 to 24 hour period without the need for anticoagulant coverage.11,56

Investigation of Patients with Suspected Pulmonary Embolism

Patients with suspected PE should undergo either lung scanning or spiral CT imaging, depending upon the availability of these tests and the radiological expertise at a given center.60,61 Although there are much more data on the use of diagnostic algorithms with lung scanning, spiral CT appears to be both a more sensitive and specific test (at least for central PE), and, thus, it is likely that similar principles for the investigation of patients with suspected embolism may be applied for this latter technique. It remains to be proven whether the use of spiral CT may enable further simplification of the management of patients with suspected PE beyond approaches used with lung scanning. See Figure 3 for diagnostic algorithms for patients with suspected PE.

For patients undergoing lung scanning, a normal scan excludes the diagnosis of PE. If the lung scan result is high probability, then the diagnosis of PE can be made with over 90% certainty as long as the clinical suspicion for PE is moderate or high. If the clinical likelihood of PE is low, patients with high probability lung scans should undergo testing with either pulmonary angiography or spiral CT to confirm the diagnosis.

If the lung scan is a non-high probability study, additional diagnostic testing is required to confirm or exclude the diagnosis of PE. Historically, it has been recommended that patients with non-high probability lung scans undergo pulmonary angiography. In recent years, much attention has focused on the use of noninvasive tests for DVT in patients with suspected PE who have non-high probability lung scans.62-63 The rationale for this approach is that the current management of DVT and PE are similar. If non-invasive testing confirms the presence of DVT, then appropriate antithrombotic therapy can be initiated without the need to conclusively demonstrate by angiography whether PE is present or not. On the other hand if noninvasive testing for proximal DVT is negative, then it may be reasonable to withhold antithrombotic therapy because such patients would potentially be at relatively low risk for additional pulmonary emboli.

Hull and colleagues first demonstrated the potential feasibil-
ity of this approach in a study of patients with suspected PE who had non-high probability lung scans and then underwent serial IPG testing over a 2-week period. Less than 2% of patients with non-high probability lung scans and initial negative ultrasounds could be safely followed with serial ultrasonography, without the need to institute anticoagulant therapy or perform pulmonary angiography. Those 665 patients who had two or three negative ultrasounds performed over a 2-week period following their initial evaluation had no greater risk (0.5%: 95% CI 0, 1%-1.3%) of developing venous thromboembolic complications over a 3-month period than patients whose initial lung scan was normal (0.6%; 95% CI 0.1%-1.8%).

Although the serial ultrasonography approach described above appears safe, it is inconvenient for patients and healthcare providers. Also, algorithms avoiding the need for follow-up testing would be beneficial. An alternative approach for the management of patients with non-high probability lung scans is to incorporate clinical probability and D-dimer assays into the management algorithm. Perrier and colleagues performed two studies evaluating over 700 patients presenting to the emergency department with suspected PE, who underwent clinical evaluation, bilateral ultrasonography, and ELISA D-dimer testing. Pulmonary embolism was excluded by a normal D-dimer in the latter study. The remaining patients underwent lung scanning, and VTE was diagnosed by a high probability scan or by the presence of DVT. For patients with nondiagnostic lung scans and normal venous ultrasound imaging, PE was considered excluded by a normal D-dimer or a low pre-test probability clinical assessment. Patients with non-diagnostic lung scans, who had a positive D-dimer, normal bilateral ultrasonography, and who were judged to be at intermediate or high pre-test probability for PE, were referred for pulmonary angiography. This approach limited the need for pulmonary angiography to only about one-third of patients with non-high probability lung scans and to less than 10% of the entire cohort. In the 6 months follow-up period, only about 1% of patients in whom the diagnosis of PE was initially considered excluded developed non-fatal venous thromboembolic events.

Ferretti and colleagues examined the impact of managing patients with intermediate probability lung scans and normal bilateral venous ultrasound using spiral CT. In 164 patients, spiral CT detected pulmonary emboli in 29 (23.8%; 95% CI, 18%-30%). Fifteen patients with negative spiral CT underwent pulmonary angiography at the request of their attending physicians, and only 1 patient (6%) had a subsegmental PE detected. The remaining 129 patients were not treated with anticoagulant therapy, and in the 3-month follow-up period, 5% developed symptomatic venous thromboembolic complications, three with pulmonary emboli, including one fatality, and three with DVT. Further research is required to determine whether D-dimer or clinical probability may be used as adjunctive tests in patients with normal spiral CT investigations who have normal venous ultrasound imaging studies to increase the safety of this approach.

Summary and Conclusions

Recent advances in the management of patients with suspected VTE have resulted in improvements in the diagnostic testing accuracy and the development of management algorithms that are safer and more accessible. Ongoing clinical trials are evaluating whether these diagnostic management strategies can be made even simpler and less expensive. Diagnostic procedures for VTE continue to be refined, and modalities, such as magnetic resonance imaging and spiral CT, have the potential to further increase the accuracy of the investigation approach. There is still need to improve management strategies for the diagnosis of recurrent venous thrombosis and to determine whether diagnostic testing results may be correlated with long-term patient treatment needs.

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