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INVITED REVIEW

Integrated strategies for the diagnosis of venous thromboembolism

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Summary. Diagnosis of deep vein thrombosis (DVT) and pulmonary embolism (PE) is an important medical problem because of the high fatality rate from PE and the large number of cases not diagnosed before causing death. Over the last decade, there has been considerable research into the diagnostic process. It is widely accepted that venous ultrasound imaging is an accurate test for the diagnosis of DVT and is the imaging test of choice. For PE, computer tomographic pulmonary angiography (CTPA) is replacing ventilation perfusion lung scanning. Technology for CTPA is rapidly evolving and multi-row detector scans have quite reasonable sensitivity and specificity. Despite the accuracy of imaging tests, the post-test probability of disease is highly dependent on pretest probability. Clinical evaluation tools have developed that enable us to accurately categorize patients' risk prior to diagnostic imaging. One advantage of this characterization is an ability to exclude the diagnosis of DVT or PE if clinical probability is sufficiently low and when the D-dimer is negative. There are now a number of D-dimer assays that have well-defined specificities and sensitivities, which enable use in conjunction with clinical probability. A careful combination of clinical assessment, D-dimer and imaging enables safe PE rule out protocols without imaging, an ability to suspect false positive imaging results, and more accurate determination of true positive imaging. These integration strategies result in safer, more convenient and cost-effective care for patients.

Keywords: clinical probability, computerized tomographic pulmonary angiography, D-dimer, deep vein thrombosis, diagnosis, pulmonary embolism, venous ultrasound imaging.

Introduction

Venous thromboembolism (VTE), manifesting as deep vein thrombosis (DVT) or pulmonary embolism (PE), is one of the most common cardiovascular disorders in industrialized countries, affecting about 5% of people in their lifetime [1]. PE is highly fatal and in 22% of cases is not diagnosed before causing death [2,3]. The signs and symptoms of both DVT and PE are largely non-specific and as a consequence many patients presenting with leg pain or swelling, or chest pain or dyspnea, are investigated but do not have DVT or PE. Mismanagement of PE has been a frequent problem [4], at least in part because of limitations of diagnostic tests. Imaging tests still have limitations but these can be better managed as the diagnostic workup for suspected PE has now evolved to an integrated approach that includes clinical pretest probability assessment and D-dimer testing in combination with imaging. In fact, we are currently observing an encouraging decrease in mortality from PE, which may reflect both more accurate diagnosis and the use of diagnostic algorithms [5–7]. In this review, I summarize the literature on clinical probability assessment, D-dimer, and the imaging tests used for VTE, with a focus on integration of these diagnostic modalities. Integrated strategies enable application of Bayes Theorem, that is, pretest odds times the likelihood ratio (especially pertinent is the negative likelihood ratio of 1 minus sensitivity divided by specificity) = post-test odds [8,9].

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Diagnosis of DVT

Imaging tests for DVT

The test of choice for clinically suspected DVT is the highly specific venous ultrasound; a positive result is sufficiently predictive in most patients that treatment can be initiated. [10–13]. The exceptions are patients with a previous history of DVT and low pretest probability in which the positive predictive value is less [14].

In many centres ultrasound testing is limited to the proximal veins (distally to the region of the calf veins where they join the popliteal vein) as the sensitivity for proximal DVT has been reported as 97% but for calf DVT it appears to be considerably less (73%) [15]. In these centers, it has been suggested that a negative ultrasound should be repeated 1 week later (serial testing) to detect extending calf DVT [11]. However, in symptomatic patients, only 10% to 20% of thrombi detected are isolated to the calf, and only 20–30% of these extend, so routine serial testing is inefficient and inconvenient. Indeed,

studies suggest very few patients (1–2% in two recent studies) who have a negative initial ultrasound test will be confirmed to have proximal DVT upon serial testing [15,16]. As a result, serial testing is not cost-effective [17,18]. Three recent studies have suggested that imaging of the entire deep vein system, excluding DVT with a single negative result, is a safe strategy [19–21]. However, no prospective randomized trials have compared the safety of this with strategies that only evaluate the proximal venous system. It is unknown if the single whole-leg vein assessment can be widely applied with the accuracy described in these studies, it is more laborious, and it would still result in many needless tests. As I will discuss, a strategy that employs a combination of D-dimer, clinical probability and ultrasound imaging is ideal.

The clinical diagnosis of deep vein thrombosis

Although the clinical diagnosis of DVT is non-unspecific, it has now been well established that a clinical prediction rule incorporating signs, symptoms and risk factors, can be accurately applied to categorize patients as low, moderate or high probability for DVT (Table 1). Alternatively, the same rule can be used to categorize patients as 'DVT likely' or 'DVT unlikely' [22]. A recent systematic review (all studies included used the same clinical prediction rule) demonstrated that the incidence of DVT in the low, moderate and high clinical probability groups was 5.0% (95% CI, 4.0–8.0%), 17% (95% CI, 13–23%) and 53% (95% CI, 44–61%), respectively [23]. Inter-observer reliability has not been widely evaluated, but the reported studies involved many different physicians with a wide range of clinical experience, including junior residents. One study specifically demonstrated the model's reproducibility by resident physicians [24]. Determination of pretest probability allows for several potential diagnostic strategies. Used in combination with ultrasound imaging it has been demonstrated that patients at low pretest probability can have DVT safely excluded on the basis of a single negative ultrasound test without serial testing [14]. However, it is my opinion that pretest probability determination is best used in algorithms that also incorporate D-dimer.

Table 1 Simplified clinical model for assessment of DVT*

Clinical variable	Score
Active cancer (treatment ongoing or within previous 6 months or palliative)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recently bedridden for 3 days or more, or major surgery within the previous 12 weeks requiring general or regional anesthesia	1
Localized tenderness along the distribution of the deep venous system	1
Entire leg swelling	1
Calf swelling at least 3 cm larger than that on the asymptomatic leg (measured 10 cm below the tibial tuberosity)	1
Pitting edema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
Alternative diagnosis at least as likely as DVT	−2

DVT, deep vein thrombosis. *≥2, probability of DVT is 'likely'. ≤ 1, probability for DVT is 'unlikely'. Alternatively, < 1 is low probability, moderate is 1 or 2, and high is > 2.

D-dimer for the diagnosis of DVT or PE

D-dimer, a degradation product of cross-linked fibrin, is typically elevated with acute VTE. D-dimer levels may also be increased by a variety of non-thrombotic disorders, including recent major surgery, hemorrhage, trauma, malignancy or sepsis, and D-dimer levels increase with age and through pregnancy [25–28]. D-dimer assays are sensitive but non-specific markers for VTE so positive D-dimer results are *not* useful to 'rule in' the diagnosis; rather the potential value is for a negative test result to 'rule out' the diagnosis. Although the negative predictive value of the D-dimer increases proportionately with increase in sensitivity, as with all tests the negative predictive value of the D-dimer is inversely related to the incidence of VTE in the population under study. Specificity is important because use of a very non-specific assay or the testing of very ill hospitalized patients would be of limited value because of the expected high number of positive results, many in patients with no VTE (i.e. false positives). Data suggest that most D-dimer assays lie on the same receiver operating characteristic curve [29–31], although one meta-analysis suggests three tests had significantly worse diagnostic odds ratios then the reference D-dimer used in the analysis (the VIDAS assay) [32]. I believe it is best to consider D-dimer assays as those with moderate sensitivity and moderate specificity or those with high sensitivity and poor specificity. The former consist of latex agglutination assays (qualitative or quantitative) and the whole blood assays, which are predominantly qualitative. The sensitivities and specificities for the agglutination assays have been in the range of 85–90%, and 50–80%, respectively [23,32,33]. Qualitative D-dimer assays have the advantages that they are simple, have a rapid turn round time and are inexpensive, but as they are interpreted by visual inspection, it is advisable that only trained observers perform and interpret them. Recent studies have proven that the sensitivity is highest for many of the quantitative assays but the specificity is less with these methods. Rapid, automated ELISA assays such as the Vidas DD test® (bioMerieux, Marcy l'Etoile, France), have demonstrated the highest sensitivity at an average of 95–98% but with specificity of 36–58%.

Approach to patients for the diagnosis of a first episode of deep vein thrombosis

Patients with leg symptoms compatible with DVT should initially have a determination of pretest probability of DVT using an established prediction model/rule such as the one we have validated (Table 1). It is important that a history and physical examination be performed first and only if DVT

remains a diagnostic possibility should the model be applied. If it is obvious that the symptoms are due to an alternative problem DVT does not need to be a diagnostic possibility. If doubt remains or if DVT risk factors exist the physician may be wise to apply the model but individual judgment must be applied. After the pretest probability is determined a D-dimer test should be performed. If moderate sensitivity D-dimers are used then the pretest clinical probability should be < 10% to enable a negative D-dimer to exclude the diagnosis without the need for ultrasound. In our centre a score of ≤ 1 (unlikely DVT) in our model is sufficient to use with a qualitative D-dimer such as the IL-test or the SimpliRED™. However, most studies have employed our earlier scoring system and as such use a score of zero or less to enable exclusion of DVT with a negative moderate sensitivity D-dimer [23,34]. This strategy should be applicable to up to 40% of patients referred with suspected DVT. It should be kept in mind that ultrasound may provide information helpful to establish an alternative diagnosis but ultrasound imaging for DVT is not required to rule out DVT with low/unlikely probability and a negative D-dimer. Because of its better negative likelihood ratio of 0.08 (vs. 0.20 for moderate sensitivity assays) a negative Vidas DD test® (and other high sensitivity assays) may be used to exclude the diagnosis of venous thromboembolism when the pretest probability is less than 20%, which is a score ≤ 2 [35]. In my opinion, no D-dimer assay should be used to exclude DVT in patients who have high pretest probability.

Clinical assessment and D-dimer testing have the further advantage of enabling management at times when imaging is not available. Patients with moderate/high clinical probability may receive an injection of low-molecular-weight heparin (treatment dose) and imaging arranged the following day (Figs 1 and 2) [36,37]. Patients at low risk (by clinical models or negative sensitive D-dimer) may have diagnostic imaging delayed for a 12- to 24-h period without the need for anticoagulants, although typically we also anticoagulate these patients. When imaging is indicated, ultrasound is performed, limited to the proximal veins from the groin proceeding distally

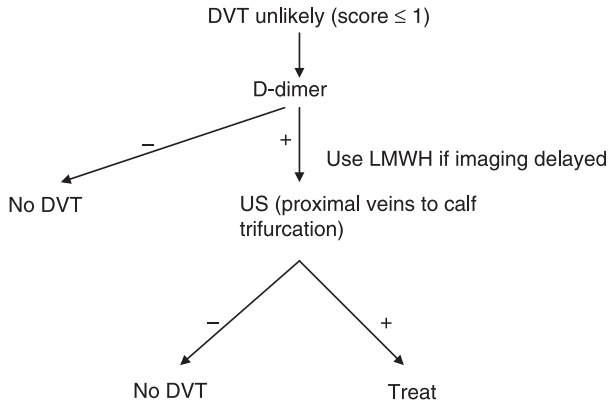

Fig. 1. Diagnostic algorithm using clinical probability, D-dimer and ultrasound in patients with suspected DVT. DVT, deep vein thrombosis; US, ultrasound; LMWH, low-molecular-weight heparin.

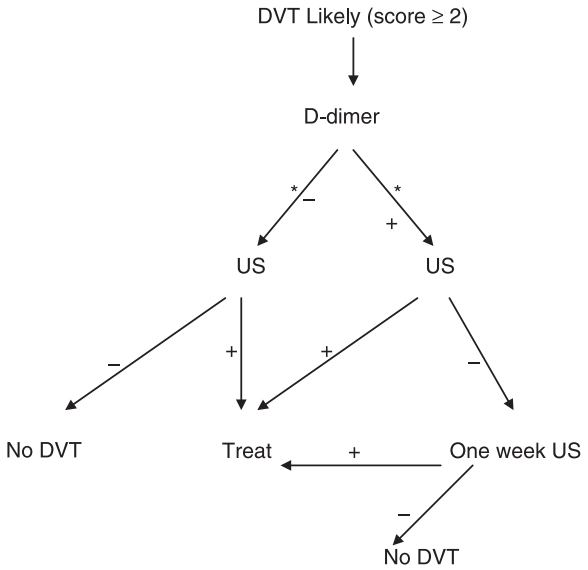

Fig. 2. Diagnostic algorithm using clinical probability of DVT likely, D-dimer and ultrasound in patients with suspected DVT. DVT, deep vein thrombosis; US, ultrasound. *Use low-molecular-weight heparin if imaging is to be delayed.

to the trifurcation region. If the test is positive (lack of complete vein compressibility) the diagnosis is confirmed. If the veins are completely compressible a repeat ultrasound no more then 1 week later has generally been recommended. Five studies reported sufficient data to determine that a negative D-dimer result with a clinical probability estimate of moderate/high and normal initial ultrasound enables exclusion of DVT without a serial ultrasound test [22,37–40]. This strategy without use of pretest probability was validated in at least one study [41]. Serial testing after an initially normal ultrasound result can be confined to high probability patients with positive D-dimer results (Fig. 2). Note that false negative D-dimer results may occur in patients with prolonged symptoms of DVT or after prolonged heparin therapy (more than 24 h) [42]. Finally, it is important that the D-dimer should only be employed if the physician is convinced that DVT is a diagnostic possibility and not as a screening test. Indiscriminant use of D-dimer as a screening test will result in many unnecessary ultrasound tests.

Recurrent DVT

A randomized trial demonstrated the safety of combining clinical probability, D-dimer and ultrasound for diagnosis of recurrent DVT. [22]. The biggest concern is false positive ultrasound results. It is helpful to recognize that if the ultrasound reveals thrombosis that is echogenic, non-occlusive or discontinuous then chronic DVT should be considered. Serial testing or venography can help clarify the issue. If previous ultrasound results are available, an increase in clot diameter by 4 mm is suggestive of recurrence [43]. A recent study has suggested a negative sensitive D-dimer result can exclude recurrence without ultrasound, but Bayes theorem demonstrates the danger of this strategy as high pretest

probability patients may have over 20% probability of DVT after a negative highly sensitive D-dimer test [44].

Diagnosis of pulmonary embolism

Imaging procedures for pulmonary embolism

Pulmonary angiography is regarded as the gold standard test for the diagnosis of PE, and although the procedure is usually well tolerated, it is invasive, expensive and requires a skilled radiologist and a cooperative patient [45,46]. In addition, a negative result does not entirely exclude VTE, because in the PIOPED study 1.6% of patients with normal results developed PE over the 1-year follow-up, most in the first month [47,48].

Ventilation-perfusion (V/Q) lung scanning has been the imaging procedure of choice in patients with suspected PE. A normal scan essentially excludes the diagnosis of PE (1% VTE rate in follow-up), and a high-probability lung scan has an 85–90% predictive value for PE [47–49]. Unfortunately, most lung scans fit into a non-diagnostic category, in which the incidence of PE varies from 10% to 30% and further investigation is necessary. As a consequence the first imaging test in many centers is now computerized tomographic pulmonary angiography (CTPA). However, CTPA also has limitations, many of which are not appreciated by clinicians. CTPA is an evolving technology, with early single-slice detectors unable to visualize subsegmental arteries sufficiently [50]. Indeed, the first studies comparing single-slice detector CT to pulmonary angiography determined that CTPA had a sensitivity between 53% and 100% and a specificity between 81% and 100% [51]. However, in a more recent meta-analysis the pooled sensitivity and the specificity of CTPA were 86% and 93.7%, respectively [52]. A recent study suggests higher sensitivity with multi-detector row CTPA [53]. However, the less than perfect sensitivity and specificity mandates a need for management studies with CTPA. As discussed below, management studies have now been carried out, and the initial fears that CT would miss many PE seem to be unfounded and indeed, with current multi-detector row scanners, diagnostic sensitivity is such that false detection of PE, or detection of clinically irrelevant PE is a now a pressing issue. Magnetic resonance pulmonary angiography also holds promise as an imaging modality but will also inevitably benefit from integrated approaches [54–56].

Clinical diagnosis of pulmonary embolism

Pulmonary embolism is suspected in many patients with respiratory or chest complaints because of the non-specific nature of the presenting signs and symptoms. Despite the limitations of the individual clinical predictors [57–67], the PIOPED investigators and others have demonstrated that the clinicians' overall diagnostic impression could be useful in management [48,68–70]. Physician gestalt (empiric assessment) has worked but most of this data came from centres that also use predefined clinical decision tools, so, it is not clear if empiric assessment can be generalized. In addition, with empiric assessment, the exact methods used by each clinician to estimate pretest probably are difficult to measure or reproduce [71], clinicians often disagree (even for broad categories) on the pretest probability of pulmonary embolism [72], the clinician's experience level appears to influence assessment [73], and probability estimates tend to follow a middle road, categorizing fewer into the more useful low- or high-probability groups. Thus, the empirical method has drawbacks, but it is the easiest method to use.

Several explicit clinical models have been described to determine pretest probability for PE using clinical findings, ECG and chest X-ray [62,74–77]. The most widely applied model has been published by our Canadian group (Table 2) [74,78]. At least 12 studies and over 10 000 patients have been evaluated, including five studies and over 5800 patients using the dichotomous scoring system of PE unlikely (score ≤ 4) or PE likely (score of > 4) [26,74,79–87]. The main limitation of this model is the need for the physician to consider an alternative diagnosis, which may be dependent on the physician's experience. However, the Kappa for inter-observer variability was reasonable, despite performing the repeat assessment up to 18 h after the first assessment [88]. At least three studies have demonstrated moderate to substantial interrater agreement and reproducibility of the Wells *et al.* model [83,88,89] but one study noted only moderate agreement [70]. The latter study reported a higher interobserver agreement for the Charlotte rule but that rule only has safe and unsafe categories. To my knowledge no other prediction rule has evaluated interrater agreement and reproducibility.

Other clinical assessment/prediction rules have also been reported. Miniati reported that a combination of clinical predictors (symptoms, ECG findings and chest X-ray findings) had a negative predictive value of 94%, and PE could be excluded in 42% of patients in their validation set [90]. Wicki *et al.* [69,75,91] devised a model in emergency room patients that in comparison to our model seems to be equally effective.

Table 2 Variables used to determine patient pretest probability for pulmonary embolism*

Clinical variable	Score
Clinical signs and symptoms of DVT (minimum of leg swelling and pain with palpation of the deep veins)	3
PE as or more likely than an alternative diagnosis	3
Heart rate greater than 100	1.5
Immobilization or surgery in the previous 4 weeks	1.5
Previous DVT/PE	1.5
Hemoptysis	1
Malignancy (on treatment, treated in the last 6 months or palliative)	1

DVT, deep vein thrombosis; PE, pulmonary embolism. *> 4, probability of PE is 'likely'. ≤ 4, probability for PE is 'unlikely'. Alternatively, < 2 is low probability, moderate is 2–6, and high is > 6.

This model has subsequently been revised (called the Geneva Rule) and no longer requires a blood gas [76].

Kline *et al*., in a series of studies, have evaluated PE diagnosis in the emergency department, where the need to rule out PE generally results in screening many patients with a low incidence of PE [92–94]. Their strategy doubled the rate of screening for PE, had a false negative rate of less than 1%, and did not increase imaging [95]. Their decision rule was: 'a patient aged 50 years or older or any (patient with) a pulse rate greater than the systolic blood pressure, *and* either (i) unexplained hypoxemia (SaO_2 on pulse oximetry < 95% while breathing room air) or (ii) unilateral leg swelling or recent surgery or hemoptysis, was unsafe' and required a V/Q scan or CTPA. If the physician felt that his/her unstructured estimate of PE was high regardless of the above, patients underwent imaging. In a further study, they suggested that if all the above factors are negative *and* the patient has no prior VTE *and* is not on hormone therapy, the patient is at low risk for PE [77]. Finally, a rule published by Hyers *et al*. [96] has demonstrated utility in two management studies [97,98].

In summary, there are several prediction rules to choose from, and not much evidence exists to prefer one above the other, but the use of these rules appears to help categorize patient pretest probability and should improve the diagnostic process as I outline below. All these rules have limitations, predominantly the fact that they have several variables and complex scoring systems. Efforts to simplify the rule are ongoing. We have published one potential simplification and it appears to work in our patient data bases but it has not yet been validated [99]. The Wells *et al*. [100] model used in the Christopher Study was re-evaluated with the intent of developing an easier model. The simplified model assigns one point to all the variables in the model and if any point is present imaging is indicated. This new model appears to work well in this data set but further validation will be necessary.

Approach to patients with suspected pulmonary embolism

As with the diagnosis of DVT the safety of a protocol for the diagnosis of PE is primarily defined by the rate of PE eventually detected in patients in whom the protocol excluded the diagnosis (i.e. the false-negative rate). As protocols are very unlikely to result in a zero post-test probability, a low threshold of about 1–2% is targeted. This threshold is comparable with the rate of PE or DVT at follow-up after a normal pulmonary angiogram, a negative CTPA [101] or a normal result on a V/Q scan [102–104]. Trying to achieve an even lower PE rate with a negative result seems unrealistic, as the rate of PE discovered in a composite population of hospitalized patients and outpatients without recognized signs or symptoms of PE, but who underwent contrast-enhanced CT of the chest, ranged from 1.5% to 3.4% [105,106]. Finally, a cut-off lower than 1% would lead to an unacceptable trade-off in increased imaging, and increased false-positive diagnosis of PE. Many studies have now been published using integrated strategies and the low follow-up VTE event rates validate these approaches [26,74,79–89].

My recommended approach is to first perform clinical probability assessment. Subsequently, if patients are less then 80 years old, and are not ICU patients[107], then a D-dimer is performed using a D-dimer test that has been evaluated in VTE patients to have a negative likelihood ratio of ≤ 0.20. Patients who are PE unlikely or low probability can have PE excluded with a negative D-dimer. The likelihood ratio of 0.06–0.09 with high sensitivity D-dimer test enables PE to be excluded with moderate pretest probability (≤ 22%) when the D-dimer is negative (Figs 3 and 4). However, the high sensitivity D-dimers are limited by very low specificity in the elderly and hospitalized patients and are of little use in these groups. Seven studies using our model reported follow-up data on patients in whom PE was ruled out on the basis of clinical probability (low probability or PE unlikely) and negative D-dimer testing [26,74,79,81,82,85,86]. The VTE event rates in follow-up were less than 0.5%. Studies employing similar strategies but using other clinical assessment tools also reported very low rates of follow-up events [53,98]. Thus, the D-dimer assay can be the first objective test used after clinical assessment with the goal of determining which patients require diagnostic imaging.

If patients are high pretest probability or PE likely or they have a positive D-dimer then imaging (VQ scan or CTPA) is required. If the imaging test is a V/Q scan then lower extremity venous ultrasound is also recommended when the VQ is non-diagnostic (i.e. neither normal nor high probability, Figs 3 and 5) [26,74,85,86,108]. If low pretest probability patients have a high probability VQ scan it is important to verify the diagnosis

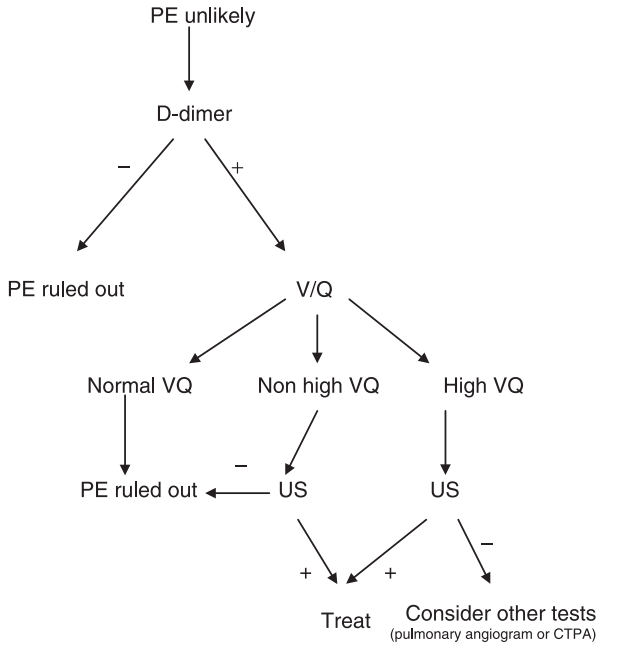

Fig. 3. Strategy for diagnosis of PE using V/Q in patients who are PE unlikely. US, ultrasound; V/Q, ventilation perfusion lung scan; PE, pulmonary embolism; CTPA, computerized tomographic pulmonary angiography.

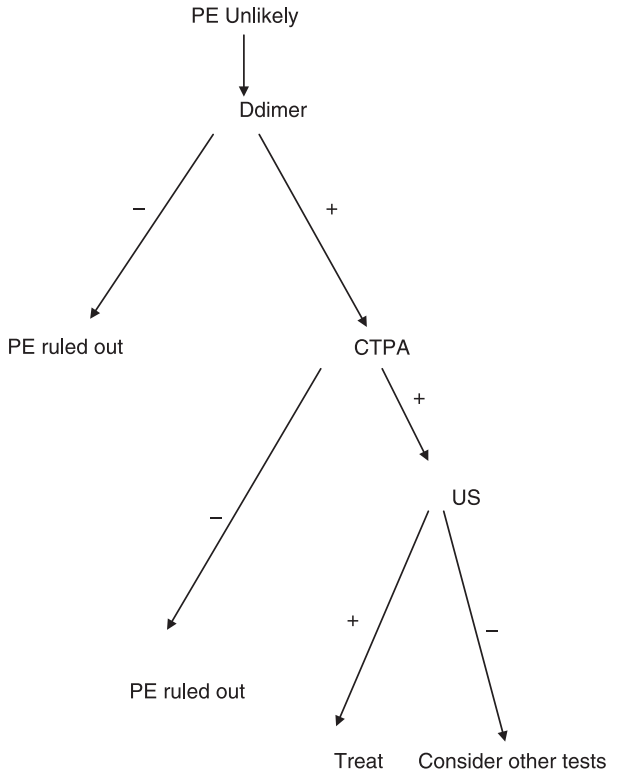

Fig. 4. Strategy for diagnosis of PE using CTPA in patients who are PE unlikely. US, ultrasound; V/Q, ventilation perfusion lung scan; PE, pulmonary embolism; CTPA, computerized tomographic pulmonary angiography.

with an ultrasound study, pulmonary angiogram or CTPA [62,109].

If the imaging test is CTPA we have conflicting data on the need for ultrasound when the CTPA is negative for PE. Two large prospective CTPA studies combined clinical probability and ultrasound with single row detector CTPA [84,97]. Patients with a negative CTPA, negative ultrasound, and low or moderate pretest probability had PE excluded (follow-up event rates 0.4–1.8%). Importantly, 15–18% of patients had negative CTPA but positive ultrasound studies. However, two more recent large studies in which many patients underwent multidetector row CTPA suggested very little additional yield from ultrasound, with only 0.9–1.4% of patients with a negative CTPA having a positive ultrasound result [53,79]. As further evidence, three large studies totaling over 4600 patients have now demonstrated that the combination of clinical probability, D-dimer testing and CTPA results in a strategy that safely excludes PE without ultrasound imaging [81,82,98]. With the lack of direct comparison of the two strategies it seems reasonable to perform ultrasound if clinical suspicion remains high despite a normal CTPA, if the patient has leg symptoms (indeed US could be performed first because of its high positive predictive value and thereby spare radiation exposure) [110] or if single detector row CTPA is employed (Fig. 6).

Bayes theorem predicts that using a (generous) sensitivity of 92% and a specificity of 94% for CTPA, patients who have low (5%) pretest probability for PE will have a false positive rate in the order of 55% and 21% false positive rate for moderate (20%) pretest probability [111]. Furthermore, in a large accuracy study of CTPA (PIOPED II) it was reported that the positive predictive values for PE detected by CTPA in the lobar, segmental and subsegmental vessels were 97%, 68% and 25%, respectively [112]. To complicate the issue, the Kappa value for interobserver agreement when evaluating segmental vessels using CTPA with 3 mm collimation was only 0.47 [113] and a recent accuracy study comparing multidetector row CTPA with pulmonary angiography demonstrated a false positive CTPA rate of 30% with most false CT results incorrectly detecting PE in isolated segmental vessels or subsegmental vessels [114]. Clinical probability assessment enables a strategy to deal with potentially false positive results.

High-probability V/Q scans or positive results on CTPA should be considered diagnostic of PE if pretest probability is high or PE likely (Figs 5 and 6) but not when the pretest clinical probability is low (Figs 3 and 4). In this latter case, the results should be reviewed with the radiologist with consideration of a false-positive result. Confirmatory ultrasound or conventional pulmonary angiography should be considered.

It is possible that the use of diagnostic algorithms will increase the number of patients in whom a diagnosis of PE is considered as physicians may 'screen' for PE. Goldstein *et al.* [115] implemented a D-dimer-based screening system and found a 40% increase in the rate of V/Q scanning. However, the percentage of V/Q scans that were read as positive for PE increased and a PE diagnosis almost doubled using a D-dimer algorithm. Kline's group did not find an increase in imaging when D-dimer testing and algorithms were employed [95]. In addition, in hospitals where imaging is not available at night, algorithms may offer a rational method to decide which patients should receive temporary anticoagulation until

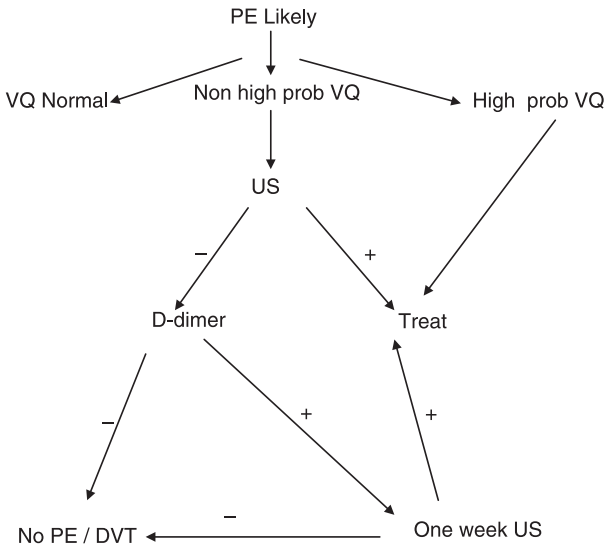

Fig. 5. Strategy for diagnosis of PE using V/Q in patients who are PE likely. US, ultrasound; V/Q, ventilation perfusion lung scan; DVT, deep vein thrombosis; PE, pulmonary embolism.

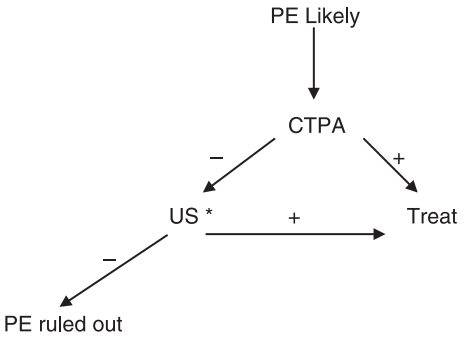

Fig. 6. Strategy for diagnosis of PE using single row detector CTPA in patients who are PE likely. US, ultrasound; PE, pulmonary embolism; CTPA, computerized tomographic pulmonary angiography. *If multidetector CTPA used, in most cases PE ruled out without need for ultrasound, but consider ultrasound if patient has leg symptoms or clinical suspicion is high.

imaging is available. Finally, it is clear that following algorithms improves patient care, as more diagnostic failures occurred if algorithms were not followed [5,7,74].

Conclusions

Recent advances in the management of patients with suspected PE and DVT have both improved diagnostic accuracy and made management algorithms safer and more accessible. Ongoing clinical trials are evaluating whether these diagnostic processes can be made even easier and less expensive. Patients at low risk with a negative D-dimer can avoid imaging tests and those at moderate risk with a negative high sensitivity D-dimer can have VTE excluded without the need for imaging. Diagnostic strategies should include pretest clinical probability, D-dimer assays and non-invasive imaging tests.

Disclosure of Conflict of Interests

PSW has received speaker honoraria from Biomerieux, Dade Behring and Sanofi-Aventis.

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