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CLINICAL GUIDELINE

Evaluation of Patients With Suspected Acute Pulmonary Embolism: Best Practice Advice From the Clinical Guidelines Committee of the American College of Physicians

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Description: Pulmonary embolism (PE) can be a severe disease but is also difficult to diagnose, given its nonspecific signs and symptoms. Because of this, testing of patients with suspected acute PE has risen drastically. However, the overuse of some tests, particularly computed tomography (CT) and plasma D-dimer, may not improve care while potentially leading to patient harm and unnecessary expense.

Methods: The literature search encompassed studies indexed by MEDLINE (1966–2014; English-language only) and included all clinical trials and meta-analyses on diagnostic strategies, decision rules, laboratory tests, and imaging studies for the diagnosis of PE. This document is not based on a formal systematic review, but instead seeks to provide practical advice based on the best available evidence and recent guidelines. The target audience for this paper is all clinicians; the target patient population is all adults, both inpatient and outpatient, suspected of having acute PE.

Best Practice Advice 1: Clinicians should use validated clinical prediction rules to estimate pretest probability in patients in whom acute PE is being considered.

Best Practice Advice 2: Clinicians should not obtain D-dimer measurements or imaging studies in patients with a low pretest probability of PE and who meet all Pulmonary Embolism Rule-Out Criteria.

Best Practice Advice 3: Clinicians should obtain a high-sensitivity D-dimer measurement as the initial diagnostic test in patients who have an intermediate pretest probability of PE or in patients with low pretest probability of PE who do not meet all Pulmonary Embolism Rule-Out Criteria. Clinicians should not use imaging studies as the initial test in patients who have a low or intermediate pretest probability of PE.

Best Practice Advice 4: Clinicians should use age-adjusted D-dimer thresholds (age × 10 ng/mL rather than a generic 500 ng/mL) in patients older than 50 years to determine whether imaging is warranted.

Best Practice Advice 5: Clinicians should not obtain any imaging studies in patients with a D-dimer level below the age-adjusted cutoff.

Best Practice Advice 6: Clinicians should obtain imaging with CT pulmonary angiography (CTPA) in patients with high pretest probability of PE. Clinicians should reserve ventilation–perfusion scans for patients who have a contraindication to CTPA or if CTPA is not available. Clinicians should not obtain a D-dimer measurement in patients with a high pretest probability of PE.

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Although pulmonary embolism (PE) due to thrombotic occlusion of the main or branching pulmonary arteries is common (1), it remains difficult to diagnose owing to the nonspecific signs, symptoms, and risk factors with which it is associated (2, 3). Acute PE can lead to significant morbidity and mortality (4, 5), and patients presenting to their physicians or to an emergency department (ED) with cardiopulmonary symptoms are often evaluated for the disease.

Because no individual risk factor, patient symptom, or clinical sign can definitively diagnose or exclude PE (6), clinical decision tools have been developed to help guide clinicians during their evaluation of patients with suspected acute PE. These decision tools (discussed below) are meant to help physicians stratify patients into groups for whom different diagnostic strategies are appropriate: those for whom PE is so unlikely that they need no further testing, those for whom plasma D-dimer testing can provide additional risk stratification, and those who are at high enough risk that imaging is indicated.

Highly sensitive plasma D-dimer tests (those that measure the level of this fibrin degradation product by using enzyme-linked immunosorbent assays) can be used to rule out PE in patients with low or intermediate pretest probability of PE, whereas older latex or erythrocyte agglutination assays can only rule out PE in patients with low pretest probability (7, 8). For the purposes of these guidelines, we will assume that highly sensitive D-dimer assays are being used.

Computed tomography (CT) has become the predominant imaging modality used for the diagnosis of PE. Although the use of CT for the evaluation of patients with suspected PE is increasing in the inpatient,

outpatient, and ED settings (9–14), no evidence indicates that this increased use has led to improved patient outcomes. In fact, evidence suggests that many of the PEs diagnosed with increasing use of CT may be less severe (15–17). As a result, although the incidence of PE has risen significantly with the use of CT, there has been minimal or no associated change in mortality (9, 10). This questionable benefit of increased testing, in combination with the significant expense of PE evaluations and the unintended costs of follow-up imaging needed for incidental findings discovered on these potentially inappropriate CTs (5, 18), has led some to conclude that current practice patterns for the evaluation of PE are not cost-effective (5, 19–21).

Given this lack of clear benefits, the potential risks from CT make its increasing use even more concerning. Radiation from CT is thought to be a risk factor for cancer. In one recent study, a cohort of children with CT exposure was found to have a significantly higher incidence of leukemia and brain tumors later in life (22–24). Given the radiosensitive thoracic and breast tissue imaged during the evaluation of patients with suspected PE, this potential risk is concerning, especially in women. In addition, the contrast dye used in CTs for the evaluation of PE may cause nephropathy (25, 26). These risks are compounded by the fact that repeated imaging may be common: In one study performed at a large academic center, at least one third of ED patients who had CT for the evaluation of PE underwent another CT for the same reason within 5 years (27).

With the rising cost of PE evaluations, along with increasing awareness of potential harm and doubts about mortality benefits (5), a more focused strategy is needed. This report aims to present an evidence-based and high-value diagnostic strategy for the diagnosis of PE. Its goal is to help clinicians understand the potential hurdles to such an approach and outline performance improvement strategies to overcome them.

METHODS

The literature search encompassed studies indexed by MEDLINE (1966–2014; English-language only) by using the search terms ((pulmonary embol* or pulmonary thromboembol*) and (diagnosis or diagnostic)), limited to meta-analyses; clinical trials; and randomized, controlled trials. This resulted in 1752 articles, including studies of decision rules, laboratory tests, and imaging studies for the diagnosis of PE. One author reviewed all titles and selected relevant abstracts. Articles found to be germane to this Best Practice Advice publication were independently reviewed for incorporation into this manuscript by 3 authors, to ensure that all Best Practice Advice statements were based on the highest-quality evidence; disagreements were resolved via discussion. Notably, however, this document is not based on a formal systematic review. Instead, it seeks to provide practical advice based on the best available evidence.

The target audience for this publication is all clinicians; the target patient population is all adults, both inpatient and outpatient, suspected of having acute PE.

RESULTS

What Are the Evidence-Based Recommendations for Use of Laboratory and Imaging Tests in Patients With Suspected Acute PE?

Clinical guidelines advocating for the focused evaluation of patients with suspected PE have been published by professional societies, including the American College of Physicians/American Academy of Family Physicians (28), the American College of Emergency Physicians (29), and the European Society of Cardiology (30). These guidelines are all based on the use of Bayesian analysis, in which pretest probability is combined with elements from the history, physical examination, and laboratory results to identify patients at such low risk for PE that further testing is both unnecessary and may lead to false-positive results. These analyses involve the use of clinical decision tools or clinician gestalt to determine whether individual patients require additional testing (either plasma D-dimer measurement or diagnostic imaging) on the basis of risk stratification (3).

Although clinician gestalt varies among clinicians and its quality is probably dependent on expertise and familiarity with pathophysiology and presentation of PEs (31, 32), the overall accuracy of experienced clinicians' gestalt seems to be similar to that of structured decision tools (33). However, a benefit of decision tools is that they help standardize the evaluation for clinicians who find themselves only infrequently evaluating for PE.

The majority of these decision tools—including the original Wells criteria, the dichotomized Wells criteria, and the simplified Wells criteria (**Appendix Table 1**, available at www.annals.org) (34, 35), as well as the revised Geneva score and the simplified Geneva score (**Appendix Table 2**, available at www.annals.org) (36, 37)—use D-dimer testing for patients at lower risk for PE, with the aim of avoiding unnecessary CT if D-dimer levels are normal. Of note, the specificity of an elevated D-dimer level may be lower in inpatients than in outpatients or ED patients, probably owing to comorbidities in the inpatient population (38, 39). However, use of D-dimer testing as an initial step for inpatients suspected of having PE is still appropriate, because the test remains highly sensitive for the disease and a normal level, in combination with appropriate pretest risk stratification, can prevent unnecessary imaging (40, 41). Both the Wells and Geneva tools have been externally validated, but neither has been found to be superior to the other or to risk stratification by using clinician gestalt (6, 32, 42).

Earlier data had suggested that D-dimer testing was appropriate only for risk stratification of the lowest-risk patients, and that patients at intermediate risk of PE need imaging (34). However, 3 more recent studies have demonstrated that a normal high-sensitivity

Table 1. Pulmonary Embolism Rule-Out Criteria for Predicting Probability of Pulmonary Embolism in Patients With Low Pretest Probability*

Clinical Characteristic	Meets Criterion	Does Not Meet Criterion
Age < 50 y	0	1
Initial heart rate < 100 beats/min	0	1
Initial oxygen saturation > 94% on room air	0	1
No unilateral leg swelling	0	1
No hemoptysis	0	1
No surgery or trauma within 4 wk	0	1
No history of venous thromboembolism	0	1
No estrogen use	0	1
	Pretest probability with score of 0 is < 1%	

* Information from reference 46.

D-dimer level can be used to further risk-stratify patients at both low and intermediate risk for PE. The first study, by Perrier and colleagues (43), enrolled 674 non–high-risk patients (at either low or intermediate risk for PE). Those with normal D-dimer levels were followed for 3 months, and no thromboembolic events were noted.

The latter 2 studies both looked specifically at intermediate-risk groups: Warren and Matthews (44) used the Wells criteria, and Gupta and colleagues (45) used the revised Geneva score. They evaluated 1679 and 330 patients, respectively, who were determined to be at intermediate risk for PE and found that a normal D-dimer level was 99.5% and 100% sensitive for excluding PE on CT.

The most recent decision tool was developed in response to growing use of D-dimer testing (a test with known low specificity) among patients with the wide range of signs and symptoms potentially suggestive of PE. The Pulmonary Embolism Rule-Out Criteria (PERC) (Table 1) were specifically developed to help guide clinicians in identifying low-risk patients in whom the risks of any testing, including a plasma D-dimer level, outweigh the risk for PE (~1%) (46–49). The PERC are not a screening tool for all patients, but rather is meant to be applied to patients in whom a clinician has a genuine concern about PE and whose initial risk stratification identifies them as being at very low risk. When used in this manner, the PERC should decrease the use of D-dimer testing only in patients who would have otherwise been tested, rather than increase D-dimer testing in patients in whom PE is not reasonably suspected. A recent large meta-analysis of 12 studies determined that the overall proportion of missed PEs by using PERC was only 0.3% (44 of 14 844 total cases) (49). The pooled sensitivity of PERC for all 12 studies was 97% (95% CI, 96% to 98%), and the pooled specificity was 22% (CI, 22% to 23%), indicating that 22% of D-dimer tests could have been safely avoided had the PERC been universally applied.

The low specificity of D-dimer testing has also resulted in changes to the acceptable normal ranges of the plasma test. To date, most recommendations have considered any value above 499 ng/mL as elevated. However, some studies have used age-adjusted D-dimer cutoffs, and a recent meta-analysis of 13 studies and 12 497 patients without high pretest probability found that the use of age-adjusted D-dimer cutoffs for patients older than 50 years (age × 10 ng/mL) maintained a sensitivity for PE above 97% while significantly increasing specificity (50).

Taking into account all of this evidence, the approaches below represent the current evidence-based, high-value approaches to the diagnosis of PE (Figure 1).

Diagnostic Approach for Patients With Low Pretest Probability of PE

In patients believed to be at low risk for PE, the PERC criteria should be applied. In those who meet all 8 PERC criteria (Table 1), the risk for PE is lower than the risks of testing; do not order a plasma D-dimer test (49). Those who do not meet all of the criteria should be further stratified by using a plasma D-dimer test. A normal plasma D-dimer level (ideally, age-adjusted [age × 10 ng/mL] but otherwise <500 ng/mL) provides sufficient negative predictive value for PE; do not order imaging studies (28). An elevated plasma D-dimer level should lead to imaging studies.

Diagnostic Approach for Patients With Intermediate Pretest Probability of PE

For patients at intermediate risk for PE, D-dimer testing is warranted. As for patients at low pretest probability, a normal plasma D-dimer level (ideally, age-adjusted [age × 10 ng/mL] but otherwise <500 ng/mL) provides sufficient negative predictive value for PE; no imaging studies are indicated (43–45). An elevated plasma D-dimer level should prompt imaging studies (43–45).

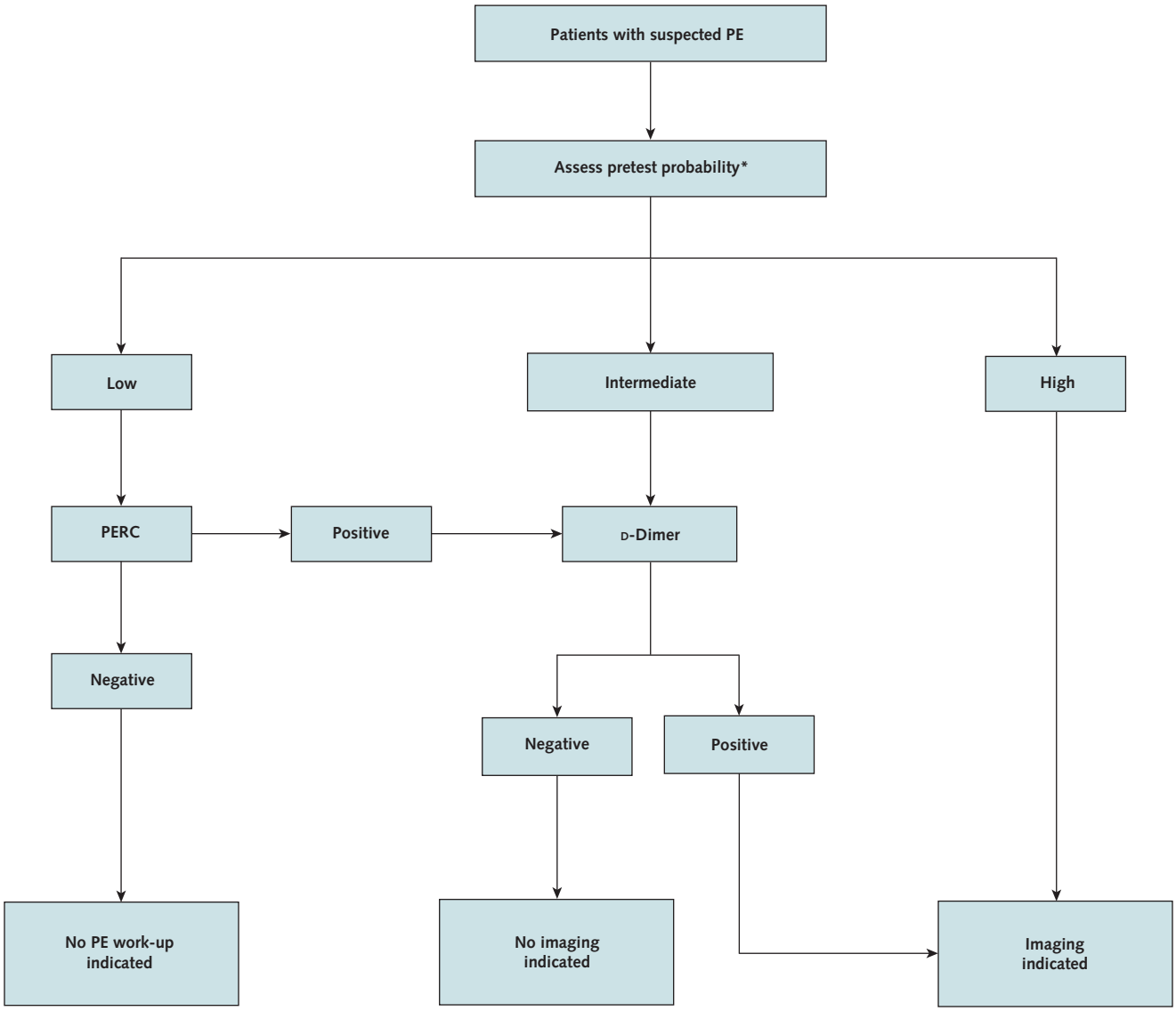
Diagnostic Approach for Patients With High Pretest Probability of PE

For patients with high pretest probability of PE according to either clinician gestalt or a clinical prediction tool, imaging studies should be performed. Computed tomographic pulmonary angiography (CTPA) is the preferred method of diagnosis when it is available and there is no contraindication to radiographic contrast dye. Ventilation–perfusion (V/Q) lung scanning should be used when CTPA is unavailable or contraindicated. Of note, a D-dimer assay should not be obtained in patients with a high pretest probability of PE because a negative value will not obviate the need for imaging (Figure 1).

Does Practice Follow the Evidence?

Although professional society guidelines and well-validated decision tools exist to determine which patients should undergo work-up for suspected PE, current practice does not follow guidelines (51). Retrospective chart reviews of ED, inpatient, and outpatient data have demonstrated that a substantial proportion of patients with suspected acute PE who are

Figure 1. Pathway for the evaluation of patients with suspected PE.



PE = pulmonary embolism; PERC = Pulmonary Embolism Rule-Out Criteria.
* Pretest probability may be assessed by using either a clinical decision tool or gestalt.

risk-stratified as low or intermediate risk either have no plasma D-dimer value obtained or go on to have CT despite normal D-dimer levels, both of which are contrary to guidelines for these patients (51–55). Conversely, many patients who have elevated D-dimer levels (which, if obtained, should be used to determine the need for additional imaging) do not have follow-up CT, again contrary to evidence-based guidelines (52–55).

What Factors Promote the Overuse of Imaging in Patients With Suspected Acute PE?

Overuse of imaging is driven by physician-, patient-, and systems-level factors. Several issues may underlie physicians' tendencies to overuse imaging tests in the evaluation for PE. Some physicians, especially those who do not evaluate for PE regularly, may assume that each epidemiologic risk factor for PE contributes to an individual patient's predicted risk for PE when using a validated prediction tool (for example, the Wells criteria). Many population-level risk factors do not add meaningfully to those that have been included in a validated risk prediction tool. For example, the analyses leading to the Wells criteria found that adding family history, the postpartum period, or lower-extremity fracture to the risk factors that were included in the final tool did not add to its performance (34). Similarly, pregnancy, the postpartum period, and a history of congestive heart failure or stroke are not included in the Geneva score because they did not add to this tool's predictive performance. Notably, a recent

large meta-analysis confirmed that pregnancy itself does not confer a greater risk for acute PE (56, 57). Thus, physicians may note the presence of an epidemiologic risk factor without realizing that it is not part of validated decision algorithms.

In addition, because PEs may be life-threatening events, physicians may feel they need to rule out the condition even if its likelihood is extremely low. This is compounded by the fact that some physicians may be less than comfortable with the Bayesian analyses described above, either owing to a lack of training or because they simply feel more comfortable with tests that they perceive as giving a dichotomous true/false answer, such as CT (58). Furthermore, even when physicians are aware of the low likelihood of PE, the fear of litigation from missing a potentially fatal diagnosis may lead them to order imaging tests anyway (59, 60). The use of the well-validated decision tools outlined above can help avoid these issues by providing clinicians who infrequently evaluate for PE with pretest probability estimates that are as accurate as the gestalt of experts, and also by providing risk-averse clinicians with evidence-based guidance.

Patients themselves may prefer to have their history and physical examinations supplemented by laboratory tests and imaging for certain symptom presentations (61). This may be a result of insufficient patient–physician communication about their individual risk factors and how they fit into validated decision algorithms; although this patient-centered communication does take more time, it has also been found to be associated with less use of diagnostic testing (62).

Finally, several trends in the healthcare system have resulted in physicians being more likely to use imaging, especially CT, for patient evaluation. First is the growth in availability and use of CT scanners in EDs in general, where many patients with suspected PEs are evaluated (12, 63). In addition, CTPA for suspected PE can be ordered and carried out quickly, and the tests interpreted rapidly, especially with the growth of after-hours remote radiology services.

Second is the phenomenon of supply-sensitive care: There is a documented connection between the availability of health care technologies, including imaging technology, and their use (64). Thus, the growth in availability of imaging modalities not only makes their use easier, but may also promote overuse. Reasons for this connection may include cultural tendencies, as more providers are trained in environments with rapid access to newer imaging tests, as well as the financial incentives given to providers and hospitals from the use of imaging.

Finally, the desire to determine the cause of symptoms may prompt unwarranted imaging. Although the advice given here is specifically related to the evaluation of patients with suspected acute PE, evidence-based reasoning should be applied when considering chest imaging for the evaluation of any cardiopulmonary symptoms.

How Can Physicians Reduce Overuse of Imaging for Patients With Suspected Acute PE?

Physicians can reduce the use of imaging for PE by focusing on several critical decisions in the work-up of PE. First, identify which patients require any diagnostic testing at all. The mere presence of 1 or more of multiple symptoms that could be consistent with PE does not always indicate that testing for PE is needed. Clinical judgment is needed to determine whether a patient requires evaluation for PE, and if the decision is made to do so, the clinician should determine the patient's pretest probability of PE by using a validated decision rule or their gestalt.

In patients with low pretest probability, application of PERC can safely identify patients for whom diagnostic testing is not necessary (48, 65, 66). If a patient with low pretest probability of PE meets all 8 PERC criteria, their likelihood of PE is 0.3% and no further testing is required (49). In a meta-analysis of 12 studies, which included 14 844 patients, the PERC were found to have a sensitivity of 97% (49). By avoiding D-dimer testing in these low-risk patients, physicians can avoid false-positive D-dimer results and subsequent CT, which is unnecessary. Of note, the PERC should not be applied to patients at intermediate or high risk for PE.

Second, the diagnostic testing strategy for patients with low pretest probability who do not meet all of the PERC (as well as all patients with intermediate pretest probability) should begin with D-dimer testing. Studies have shown that approximately one third of ED patients who receive CT for PE either did not have a D-dimer test performed or had a negative D-dimer result (51). On the other hand, implementation of pathways to standardize the appropriate use of D-dimer in the evaluation of patients with suspected PE decreased use of CT in one Australian tertiary care hospital by 27% (67).

Third, age-adjusted D-dimer thresholds should be used to determine whether imaging is warranted. Although it is highly sensitive, plasma D-dimer testing is nonspecific, and false-positive results can lead to unnecessary ima1.83ging. In the meta-analysis mentioned above, the use of an age-adjusted threshold of age × 10 ng/mL (rather than a generic value of 500 ng/mL) resulted in maintenance of sensitivities greater than 97% in all age groups (50). In addition, specificities increased significantly in all age groups, from 57.6% to 62.3% in patients aged 51 to 60 years, 39.4% to 49.5% in patients aged 61 to 70 years, 24.5% to 44.2% in patients aged 71 to 80 years, and 14.7% to 35.2% in patients older than 80 years. These findings were confirmed in a recent large multicenter, multinational prospective trial in which the use of age-adjusted D-dimer testing resulted in maintenance of sensitivity and a significant increase in specificity for the diagnosis of acute PE (68). Given these results, we recommend using age-adjusted D-dimer thresholds to determine D-dimer elevation in patients older than 50 years.

Finally, physicians, hospitals, and EDs should develop diagnostic and treatment pathways for patients with a history of multiple CTs for PE. Typically, such patients have a history of PE and have recurrent symp-

Table 2. Suggestions for Imaging in Patients With Suspected PE

Clinical Situation	Basis for Imaging Action (Reference)
Immediate CT	
Hemodynamically unstable, with suspected PE*	Risks of inaction outweigh risks of CT
High pretest probability of PE	Incidence of PE 19%–28% even with a D-dimer level <500 ng/mL (7, 74)
Defer CT Until After d-Dimer Result	
Intermediate pretest probability	Low incidence of PE (<1.1%) if D-dimer level <500 ng/mL (41–43)
Low pretest probability and PERC > 0	
No CT or D-Dimer Test	
Low pretest probability and PERC = 0	Incidence of PE <1% (47)
Begin With Lower-Extremity Venous Ultrasonography	
Patients with symptoms of DVT and PE	Similar treatment will be pursued without exposing the patient to the risks of radiation or intravenous contrast

CT = computed tomography; DVT = deep venous thrombosis; PE = pulmonary embolism; PERC = Pulmonary Embolism Rule-Out Criteria.
* Hemodynamic instability may make transport for imaging problematic. Supportive measures or empirical anticoagulation until imaging can be obtained may be required.

toms that are suspicious for PE, such as chest pain. Each time they present to their physician or the ED, CT might be performed because their pretest probability may be high. At least 1 study has demonstrated that patients evaluated for PE by using CT had a significant probability of having another CT performed for PE within 5 years. In fact, 5% of the patients in this study had 5 or more CTs for PE (27).

Preventing this frequent use of repeated CT requires thoughtful planning. Clinicians should educate these patients about the risk of radiation from multiple CTs. When such patients develop symptoms, providers should review them in the context of their prior symptoms and discuss testing strategies with the patients and their primary care providers. An individualized approach to testing is reasonable, including lower-extremity venous ultrasonography or V/Q scanning when appropriate (although V/Q scanning may not be useful in patients with chronic obstructive pulmonary disease, pneumonia, or pulmonary edema). For patients in whom V/Q scanning cannot be done, lower-extremity venous ultrasonography can be used; magnetic resonance imaging should not be done, because it has not been found to have the sensitivity necessary to detect segmental or subsegmental PEs (69, 70).

Several alternative approaches to the work-up of PE may also be beneficial. One approach is to perform lower-extremity venous ultrasonography before CT (71, 72). In hemodynamically stable patients with lower-extremity symptoms, identifying deep venous thrombosis can eliminate the need to perform CT, because the need for anticoagulation will have already been established. For the patients in this group who have cardiothoracic symptoms, the need for long-term anticoagulation (for example, in cases of unprovoked or recurrent PE) can be determined after the initial treatment period. This approach has particular utility in pregnant patients in the first trimester with suspected PE, in whom the risks and benefits of CT should be weighed even more carefully. Although CT exposes these patients to less radiation than V/Q imaging does (73), it may have teratogenic effects, making the use of lower-extremity ultrasonography in patients with lower-extremity symptoms a valid strategy. A summary of imaging suggestions for patients with various clinical scenarios in whom PE is suspected is provided in Table 2.

Another approach is to actively engage patients in the diagnostic process and use informed decision making to help reduce testing. Studies have shown that the use of decision tools and quantitative estimates to educate patients with chest pain about their risk for acute coronary syndrome result in both lower health care resource utilization and higher patient satisfaction scores (75, 76). Similarly, at least 1 study has shown that the use of evidence-based decision aids (to demonstrate to patients the comparative risks for PE and of any diagnostic tests) may reduce imaging in patients with suspected acute PE (77). Ideally, this kind of shared decision-making model would allow patients to weigh their options and decide, with their physicians, whether to pursue laboratory testing or CT. Nevertheless, some patients may prefer to have CT performed even if it is inappropriate (61), necessitating that physicians continue to act as the final decision makers regarding diagnostic testing.

Physician practices and EDs can also reduce the use of CT for PE by implementing systems-based processes to monitor utilization and appropriateness of CT for PE. A promising intervention to improve appropriateness is integrated computerized clinical decision support. One version of this is decision support that prompts the ordering clinician to document the pretest probability using one of the validated clinical decision rules and D-dimer results (when appropriate). If the patient does not fall into the appropriate testing group, clinical decision support can offer alternatives, such as ordering a D-dimer test, and can offer resistance to test ordering. This resistance can range from requiring the clinician to attest to the indication to requiring formal authorization from a utilization review clinician on call.

Although computerized point-of-care clinical decision support has been shown to reduce ordering of CTs for PE in EDs using electronic health records (63, 78–80), it is also possible to add basic decision support

Figure 2. Summary of the American College of Physicians best practice advice for the evaluation of patients with suspected acute pulmonary embolism.

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SUMMARY OF THE AMERICAN COLLEGE OF PHYSICIANS BEST PRACTICE ADVICE FOR THE EVALUATION OF PATIENTS WITH SUSPECTED ACUTE PULMONARY EMBOLISM

Disease/Condition	Pulmonary embolism
Target Audience	Internists, family physicians, emergency physicians, other clinicians
Target Patient Population	Adults with suspected acute pulmonary embolism, both inpatient and outpatient
Diagnostic Tests	Sensitive D-dimer assays (ELISA, quantitative rapid ELISA, and advanced turbidimetric D-dimer determinations) Pulmonary imaging studies (CTPA, V̇/Q̇ scintigraphy, or pulmonary angiography) Lower-extremity venous ultrasonography
Evidence on Diagnostic Tests for PE	CT angiography has a sensitivity and specificity for PE of 95% to 100% in patients with low or intermediate pretest probability and a sensitivity of 85% to 95% in patients with high pretest probability The sensitivity of V̇/Q̇ scan for PE is 50% to 98%, and specificity is 20% to 60% Pulmonary angiography is an invasive test that should only be reserved in patients where the diagnosis is still uncertain after CT angiography or V̇/Q̇ scan Age-adjusted (age × 10 ng/mL) D-dimer cutoffs can be used to exclude PE in non–high clinical probability patients who are >50 years of age, with a sensitivity of > 97% and higher specificities than the conventional cutoff of 500 ng/mL
Evidence That Expanding Testing to Patients Without These Indications Does Not Improve	Well-validated decision rules have found that the risk for PE in patients who do not meet their criteria for additional testing is very low Despite a significant increase in diagnoses of PE, mortality has remained unchanged, suggesting that we are overdiagnosing PEs that are not clinically significant
Harms of Imaging	Radiation exposure Contrast-induced nephropathy and contrast allergy Cost Overdiagnosis and resultant overtreatment with anticoagulants Detection and further work-up of incidental findings
Approaches to Overcome Barriers to Evidence-Based Practice	Patient expectations or preferences for imaging: use evidence to aid education Practice pattern variation: use individual or group-wide feedback on appropriateness, use, and yield Integrated computerized decision support Incentives and benchmarking using national quality measures
Best Practice Advice	***Best Practice Advice 1: Clinicians should use validated clinical prediction rules to estimate pretest probability in patients in whom acute PE is being considered.*** ***Best Practice Advice 2: Clinicians should not obtain D-dimer measurements or imaging studies in patients with a low pretest probability of PE and who meet all PERC.*** ***Best Practice Advice 3: Clinicians should obtain a high-sensitivity D-dimer measurement as the initial diagnostic test in patients who have an intermediate pretest probability of PE or in patients with low pretest probability of PE who do not meet all PERC. Clinicians should not use imaging studies as the initial test in patients who have a low or intermediate pretest probability of PE.*** ***Best Practice Advice 4: Clinicians should use age adjusted D-dimer thresholds (age × 10 ng/mL rather than a generic 500 ng/mL) in patients older than 50 years to determine whether imaging is warranted.*** ***Best Practice Advice 5: Clinicians should not obtain any imaging studies in patients with a D-dimer level below the age-adjusted cutoff.*** ***Best Practice Advice 6: Clinicians should obtain imaging with CTPA in patients with high pretest probability of PE. Clinicians should reserve V̇/Q̇ scans for patients who have a contraindication to CTPA or if CTPA is not available. Clinicians should not obtain a D-dimer measurement in patients with a high pretest probability of PE.***
Talking Points for Clinicians When Discussing PE Evaluation With Patients	Routine imaging has risks The PERC exclude PE in patients with low pretest probability D-Dimer testing excludes PE in patients at low pretest probability who do not meet the PERC or patients at intermediate pretest probability Alternative diagnostic strategies exist for patients who cannot have CT

CT = computed tomography; CTPA = computed tomographic pulmonary angiography; ELISA = enzyme-linked immunosorbent assay; PE = pulmonary embolism; PERC = Pulmonary Embolism Rule-Out Criteria; V/Q = ventilation-perfusion.

without an electronic health record by using a simple radiology order form that requires the clinician to document the pretest probability and D-dimer result (for an example, see reference 67) (67, 74). The radiologist can then review this form before beginning the study and discuss any inappropriate imaging orders with the ordering clinician. These interventions may result in true patient-oriented outcomes; a recent prospective, randomized, controlled trial of clinical decision-support effectiveness determined that both radiation dose and the cost of medical care decreased for patients with chest pain and dyspnea for whom decision support regarding PE and acute coronary syndrome were provided (81).

Of course, decision support does not have to focus on risk stratification alone; it can also present the risks and costs of alternative tests. In fact, a recent survey of U.S. physicians found that the majority would agree with the statement that "Decision support tools that show costs would be helpful in my practice" (82).

Given physician variation in use of imaging (83–85), quality improvement approaches to utilization and appropriateness of CT for PE can be used to identify and address physician practice variation and track trends in use of CT (84). If a practice has computerized decision support, it is also possible to track and give feedback on appropriateness; however, administrative data alone can be used to track utilization and diagnostic yield (80). Although there is no "ideal" or "correct" level of utilization or diagnostic yield, comparisons within a group of providers in a similar practice or ED allow the measurement of meaningful variation. Physicians with higher utilization and lower diagnostic yield can then receive focused interventions, such as education, feedback, and chart review. It is possible that such measures may be adopted by payers or health systems into public reporting or pay-for-performance programs in the near future, especially because the use of CT for PE has been identified as a test whose potentially inappropriate use can be improved upon (21).

CONCLUSION

The first step when evaluating a patient with suspected acute PE is to establish his or her pretest probability of PE. The Wells and Geneva rules have been validated and are considered equally accurate in predicting the probability of PE, as is clinician gestalt when used for risk stratification. The PERC were specifically developed to help guide clinicians in identifying patients with low pretest probabilities of PE in whom the risks of any testing outweigh the risk for PE.

ACP BEST PRACTICE ADVICE

Best Practice Advice 1: Clinicians should use validated clinical prediction rules to estimate pretest probability in patients in whom acute PE is being considered.

Best Practice Advice 2: Clinicians should not obtain D-dimer measurements or imaging studies in patients with a low pretest probability of PE and who meet all PERC.

Best Practice Advice 3: Clinicians should obtain a high-sensitivity D-dimer measurement as the initial diagnostic test in patients who have an intermediate pretest probability of PE or in patients with low pretest probability of PE who do not meet all PERC. Clinicians should not use imaging studies as the initial test in patients who have a low or intermediate pretest probability of PE.

Best Practice Advice 4: Clinicians should use age-adjusted D-dimer thresholds (age × 10 ng/mL rather than a generic 500 ng/mL) in patients older than 50 years to determine whether imaging is warranted.

Best Practice Advice 5: Clinicians should not obtain any imaging studies in patients with a D-dimer level below the age-adjusted cutoff.

Best Practice Advice 6: Clinicians should obtain imaging with CTPA in patients with high pretest probability of PE. Clinicians should reserve V/Q scans for patients who have a contraindication to CTPA or if CTPA is not available. Clinicians should not obtain a D-dimer measurement in patients with high pretest probability of PE.

Figure 2 summarizes the recommendations and clinical considerations.

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References

1. **Silverstein MD, Heit JA, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ 3rd.** Trends in the incidence of deep vein thrombosis and pulmonary embolism: a 25-year population-based study. Arch Intern Med. 1998;158:585-93. [PMID: 9521222]
2. **Moser KM, Fedullo PF, LitteJohn JK, Crawford R.** Frequent asymptomatic pulmonary embolism in patients with deep venous thrombosis. JAMA. 1994;271:223-5. [PMID: 8277550]
3. **Lucassen W, Geersing GJ, Erkens PM, Reitsma JB, Moons KG, Büller H, et al.** Clinical decision rules for excluding pulmonary embolism: a meta-analysis. Ann Intern Med. 2011;155:448-60. [PMID: 21969343] doi:10.7326/0003-4819-155-7-201110040-00007
4. **Horlander KT, Mannino DM, Leeper KV.** Pulmonary embolism mortality in the United States, 1979–1998: an analysis using multiple-cause mortality data. Arch Intern Med. 2003;163:1711-7. [PMID: 12885687]
5. **Fanikos J, Rao A, Seger AC, Carter D, Piazza G, Goldhaber SZ.** Hospital costs of acute pulmonary embolism. Am J Med. 2013;126:127-32. [PMID: 23331440] doi:10.1016/j.amjmed.2012.07.025
6. **Chunilal SD, Eikelboom JW, Attia J, Miniati M, Panju AA, Simel DL, et al.** Does this patient have pulmonary embolism? JAMA. 2003;290:2849-58. [PMID: 14657070]
7. **Stein PD, Hull RD, Patel KC, Olson RE, Ghali WA, Brant R, et al.** D-dimer for the exclusion of acute venous thrombosis and pulmonary embolism: a systematic review. Ann Intern Med. 2004;140:589-602. [PMID: 15096330] doi:10.7326/0003-4819-140-8-200404200-00005
8. **De Monyé W, Sanson BJ, Mac Gillavry MR, Pattynama PM, Büller HR, van den Berg-Huysmans AA, et al; ANTELOPE-Study Group.** Embolus location affects the sensitivity of a rapid quantitative D-dimer assay in the diagnosis of pulmonary embolism. Am J Respir Crit Care Med. 2002;165:345-8. [PMID: 11818319]
9. **Boone JM, Brunberg JA.** Computed tomography use in a tertiary care university hospital. J Am Coll Radiol. 2008;5:132-8. [PMID: 18242530] doi:10.1016/j.jacr.2007.07.008
10. **Broder J, Warshauer DM.** Increasing utilization of computed tomography in the adult emergency department, 2000–2005. Emerg Radiol. 2006;13:25-30. [PMID: 16900352]
11. **Lee J, Kirschner J, Pawa S, Wiener DE, Newman DH, Shah K.** Computed tomography use in the adult emergency department of an academic urban hospital from 2001 to 2007. Ann Emerg Med. 2010;56:591-6. [PMID: 20619935] doi:10.1016/j.annemergmed.2010.05.027
12. **Larson DB, Johnson LW, Schnell BM, Salisbury SR, Forman HP.** National trends in CT use in the emergency department: 1995–2007. Radiology. 2011;258:164-73. [PMID: 21115875] doi:10.1148/radiol.10100640
13. **Minges KE, Bikdeli B, Wang Y, Kim N, Curtis JP, Desai M, et al.** National trends in pulmonary embolism hospitalization rates and outcomes for Medicare beneficiaries, 1999–2010. J Am Coll Cardiol. 2013;61:E2070. doi:10.1016/S0735-1097(13)62070-7
14. **Feng LB, Pines JM, Yusuf HR, Grosse SD.** U.S. trends in computed tomography use and diagnoses in emergency department visits by patients with symptoms suggestive of pulmonary embolism, 2001–2009. Acad Emerg Med. 2013;20:1033-40. [PMID: 24127707] doi:10.1111/acem.12221
15. **Wiener RS, Schwartz LM, Woloshin S.** When a test is too good: how CT pulmonary angiograms find pulmonary emboli that do not need to be found. BMJ. 2013;347:f3368. [PMID: 23820021] doi:10.1136/bmj.f3368
16. **Schissler AJ, Rozenshtein A, Kulon ME, Pearson GD, Green RA, Stetson PD, et al.** CT pulmonary angiography: increasingly diagnosing less severe pulmonary emboli. PLoS One. 2013;8:e65669. [PMID: 23776522] doi:10.1371/journal.pone.0065669
17. **Carrier M, Righini M, Wells PS, Perrier A, Anderson DR, Rodger MA, et al.** Subsegmental pulmonary embolism diagnosed by computed tomography: incidence and clinical implications. A systematic review and meta-analysis of the management outcome studies. J Thromb Haemost. 2010;8:1716-22. [PMID: 20546118] doi:10.1111/j.1538-7836.2010.03938.x
18. **Hall WB, Truitt SG, Scheunemann LP, Shah SA, Rivera MP, Parker LA, et al.** The prevalence of clinically relevant incidental findings on chest computed tomographic angiograms ordered to diagnose pulmonary embolism. Arch Intern Med. 2009;169:1961-5. [PMID: 19933956] doi:10.1001/archinternmed.2009.360
19. **Duriseti RS, Brandeau ML.** Cost-effectiveness of strategies for diagnosing pulmonary embolism among emergency department patients presenting with undifferentiated symptoms. Ann Emerg Med. 2010;56:321-332.e10. [PMID: 20605261] doi:10.1016/j.annemergmed.2010.03.029
20. **Ward MJ, Sodickson A, Diercks DB, Raja AS.** Cost-effectiveness of lower extremity compression ultrasound in emergency department patients with a high risk of hemodynamically stable pulmonary embolism. Acad Emerg Med. 2011;18:22-31. [PMID: 21414059] doi:10.1111/j.1553-2712.2010.00957.x
21. **Schuur JD, Carney DP, Lyn ET, Raja AS, Michael JA, Ross NG, et al.** A top-five list for emergency medicine: a pilot project to improve the value of emergency care. JAMA Intern Med. 2014;174:509-15. [PMID: 24534899] doi:10.1001/jamainternmed.2013.12688
22. **Amis ES Jr, Butler PF, Applegate KE, Birnbaum SB, Brateman LF, Hevezi JM, et al; American College of Radiology.** American College of Radiology white paper on radiation dose in medicine. J Am Coll Radiol. 2007;4:272-84. [PMID: 17467608]
23. **Brenner DJ, Hall EJ.** Computed tomography—an increasing source of radiation exposure. N Engl J Med. 2007;357:2277-84. [PMID: 18046031]
24. **Pearce MS, Salotti JA, Little MP, McHugh K, Lee C, Kim KP, et al.** Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. Lancet. 2012;380:499-505. [PMID: 22681860] doi:10.1016/S0140-6736(12)60815-0
25. **Mitchell AM, Jones AE, Tumlin JA, Kline JA.** Incidence of contrast-induced nephropathy after contrast-enhanced computed tomography in the outpatient setting. Clin J Am Soc Nephrol. 2010;5:4-9. [PMID: 19965528] doi:10.2215/CJN.05200709
26. **Mitchell AM, Jones AE, Tumlin JA, Kline JA.** Prospective study of the incidence of contrast-induced nephropathy among patients evaluated for pulmonary embolism by contrast-enhanced computed tomography. Acad Emerg Med. 2012;19:618-25. [PMID: 22687176] doi:10.1111/j.1553-2712.2012.01374.x
27. **Kline JA, Courtney DM, Beam DM, King MC, Steuerwald M.** Incidence and predictors of repeated computed tomographic pulmonary angiography in emergency department patients. Ann Emerg Med. 2009;54:41-8. [PMID: 18838194] doi:10.1016/j.annemergmed.2008.08.015
28. **Segal JB, Eng J, Tamariz LJ, Bass EB.** Review of the evidence on diagnosis of deep venous thrombosis and pulmonary embolism. Ann Fam Med. 2007;5:63-73. [PMID: 17261866]
29. **Fesmire FM, Brown MD, Espinosa JA, Shih RD, Silvers SM, Wolf SJ, et al; American College of Emergency Physicians.** Critical issues in the evaluation and management of adult patients presenting to the emergency department with suspected pulmonary embolism. Ann Emerg Med. 2011;57:628-652.e75. [PMID: 21621092] doi:10.1016/j.annemergmed.2011.01.020
30. **Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galiè N, et al; Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC).** 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. Eur Heart J. 2014;35:3033-69, 3069a-3069k. [PMID: 25173341] doi:10.1093/eurheartj/ehu283

31. **Rodger MA, Maser E, Stiell I, Howley HE, Wells PS.** The interobserver reliability of pretest probability assessment in patients with suspected pulmonary embolism. Thromb Res. 2005;116:101-7. [PMID: 15907523]
32. **Kabrhel C, Camargo CA Jr, Goldhaber SZ.** Clinical gestalt and the diagnosis of pulmonary embolism: does experience matter? Chest. 2005;127:1627-30. [PMID: 15888838]
33. **Kline JA, Stubblefield WB.** Clinician gestalt estimate of pretest probability for acute coronary syndrome and pulmonary embolism in patients with chest pain and dyspnea. Ann Emerg Med. 2014;63:275-80. [PMID: 24070658] doi:10.1016/j.annemergmed.2013.08.023
34. **Wells PS, Anderson DR, Rodger M, Ginsberg JS, Kearon C, Gent M, et al.** Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. Thromb Haemost. 2000;83:416-20. [PMID: 10744147]
35. **Gibson NS, Sohne M, Kruip MJ, Tick LW, Gerdes VE, Bossuyt PM, et al; Christopher study investigators.** Further validation and simplification of the Wells clinical decision rule in pulmonary embolism. Thromb Haemost. 2008;99:229-34. [PMID: 18217159] doi:10.1160/TH07-05-0321
36. **Kline JA.** ACP Journal Club. Simplification of the revised Geneva score did not decrease accuracy for diagnosis of pulmonary embolism. Ann Intern Med. 2009;150:JC3-15. [PMID: 19306497] doi:10.7326/0003-4819-150-6-200903170-02015
37. **Le Gal G, Righini M, Roy PM, Sanchez O, Aujesky D, Bounameaux H, et al.** Prediction of pulmonary embolism in the emergency department: the revised Geneva score. Ann Intern Med. 2006;144:165-71. [PMID: 16461960] doi:10.7326/0003-4819-144-3-200602070-00004
38. **Schrecengost JE, LeGallo RD, Boyd JC, Moons KG, Gonias SL, Rose CE Jr, et al.** Comparison of diagnostic accuracies in outpatients and hospitalized patients of D-dimer testing for the evaluation of suspected pulmonary embolism. Clin Chem. 2003;49:1483-90. [PMID: 12928229]
39. **Brotman DJ, Segal JB, Jani JT, Petty BG, Kickler TS.** Limitations of D-dimer testing in unselected inpatients with suspected venous thromboembolism. Am J Med. 2003;114:276-82. [PMID: 12681454]
40. **Kearon C, Ginsberg JS, Douketis J, Turpie AG, Bates SM, Lee AY, et al; Canadian Pulmonary Embolism Diagnosis Study (CANPEDS) Group.** An evaluation of D-dimer in the diagnosis of pulmonary embolism: a randomized trial. Ann Intern Med. 2006;144:812-21. [PMID: 16754923] doi:10.7326/0003-4819-144-11-200606060-00007
41. **Kline JA, Hogg MM, Courtney DM, Miller CD, Jones AE, Smithline HA.** D-dimer threshold increase with pretest probability unlikely for pulmonary embolism to decrease unnecessary computerized tomographic pulmonary angiography. J Thromb Haemost. 2012;10:572-81. [PMID: 22284935] doi:10.1111/j.1538-7836.2012.04647.x
42. **Douma RA, Mos IC, Erkens PM, Nizet TA, Durian MF, Hovens MM, et al; Prometheus Study Group.** Performance of 4 clinical decision rules in the diagnostic management of acute pulmonary embolism: a prospective cohort study. Ann Intern Med. 2011;154:709-18. [PMID: 21646554] doi:10.7326/0003-4819-154-11-201106070-00002
43. **Perrier A, Roy PM, Sanchez O, Le Gal G, Meyer G, Gourdier AL, et al.** Multidetector-row computed tomography in suspected pulmonary embolism. N Engl J Med. 2005;352:1760-8. [PMID: 15858185]
44. **Warren DJ, Matthews S.** Pulmonary embolism: investigation of the clinically assessed intermediate risk subgroup. Br J Radiol. 2012;85:37-43. [PMID: 21937613] doi:10.1259/bjr/17451818
45. **Gupta RT, Kakarla RK, Kirshenbaum KJ, Tapson VF.** D-dimers and efficacy of clinical risk estimation algorithms: sensitivity in evaluation of acute pulmonary embolism. AJR Am J Roentgenol. 2009;193:425-30. [PMID: 19620439] doi:10.2214/AJR.08.2186
46. **Kline JA, Webb WB, Jones AE, Hernandez-Nino J.** Impact of a rapid rule-out protocol for pulmonary embolism on the rate of screening, missed cases, and pulmonary vascular imaging in an urban US emergency department. Ann Emerg Med. 2004;44:490-502. [PMID: 15520709]
47. **Kline JA, Peterson CE, Steuerwald MT.** Prospective evaluation of real-time use of the pulmonary embolism rule-out criteria in an academic emergency department. Acad Emerg Med. 2010;17:1016-9. [PMID: 20836787] doi:10.1111/j.1553-2712.2010.00826.x
48. **Kline JA, Courtney DM, Kabrhel C, Moore CL, Smithline HA, Plewa MC, et al.** Prospective multicenter evaluation of the pulmonary embolism rule-out criteria. J Thromb Haemost. 2008;6:772-80. [PMID: 18318689] doi:10.1111/j.1538-7836.2008.02944.x
49. **Singh B, Mommer SK, Erwin PJ, Mascarenhas SS, Parsaik AK.** Pulmonary embolism rule-out criteria (PERC) in pulmonary embolism–revisited: a systematic review and meta-analysis. Emerg Med J. 2013;30:701-6. [PMID: 23038695] doi:10.1136/emermed-2012-201730
50. **Schouten HJ, Geersing GJ, Koek HL, Zuithoff NP, Janssen KJ, Douma RA, et al.** Diagnostic accuracy of conventional or age adjusted D-dimer cut-off values in older patients with suspected venous thromboembolism: systematic review and meta-analysis. BMJ. 2013;346:f2492. [PMID: 23645857] doi:10.1136/bmj.f2492
51. **Venkatesh AK, Kline JA, Courtney DM, Camargo CA, Plewa MC, Nordenholz KE, et al.** Evaluation of pulmonary embolism in the emergency department and consistency with a national quality measure: quantifying the opportunity for improvement. Arch Intern Med. 2012;172:1028-32. [PMID: 22664742] doi:10.1001/archinternmed.2012.1804
52. **Corwin MT, Donohoo JH, Partridge R, Egglin TK, Mayo-Smith WW.** Do emergency physicians use serum D-dimer effectively to determine the need for CT when evaluating patients for pulmonary embolism? Review of 5,344 consecutive patients. AJR Am J Roentgenol. 2009;192:1319-23. [PMID: 19380556] doi:10.2214/AJR.08.1346
53. **Costantino MM, Randall G, Gosselin M, Brandt M, Spinning K, Vegas CD.** CT angiography in the evaluation of acute pulmonary embolus. AJR Am J Roentgenol. 2008;191:471-4. [PMID: 18647919] doi:10.2214/AJR.07.2552
54. **Teismann NA, Cheung PT, Frazee B.** Is the ordering of imaging for suspected venous thromboembolism consistent with D-dimer result? Ann Emerg Med. 2009;54:442-6. [PMID: 19394112] doi:10.1016/j.annemergmed.2009.03.017
55. **Yin F, Wilson T, Della Fave A, Larsen M, Yoon J, Nugusie B, et al.** Inappropriate use of D-dimer assay and pulmonary CT angiography in the evaluation of suspected acute pulmonary embolism. Am J Med Qual. 2012;27:74-9. [PMID: 21666066] doi:10.1177/1062860611407907
56. **Wicki J, Perneger TV, Junod AF, Bounameaux H, Perrier A.** Assessing clinical probability of pulmonary embolism in the emergency ward: a simple score. Arch Intern Med. 2001;161:92-7. [PMID: 11146703]
57. **Kline JA, Richardson DM, Than MP, Penaloza A, Roy PM.** Systematic review and meta-analysis of pregnant patients investigated for suspected pulmonary embolism in the emergency department. Acad Emerg Med. 2014;21:949-59. [PMID: 25269575] doi:10.1111/acem.12471
58. **Winkler RL.** Why Bayesian analysis hasn't caught on in healthcare decision making. Int J Technol Assess Health Care. 2001;17:56-66. [PMID: 11329845]
59. **Jena AB, Seabury S, Lakdawalla D, Chandra A.** Malpractice risk according to physician specialty. N Engl J Med. 2011;365:629-36. [PMID: 21848463] doi:10.1056/NEJMsa1012370
60. **Rohacek M, Buatsi J, Szucs-Farkas Z, Kleim B, Zimmermann H, Exadaktylos A, et al.** Ordering CT pulmonary angiography to exclude pulmonary embolism: defense versus evidence in the emergency room. Intensive Care Med. 2012;38:1345-51. [PMID: 22584801] doi:10.1007/s00134-012-2595-z
61. **Baumann BM, Chen EH, Mills AM, Glaspey L, Thompson NM, Jones MK, et al.** Patient perceptions of computed tomographic imaging and their understanding of radiation risk and exposure. Ann Emerg Med. 2011;58:1-7.e2. [PMID: 21146900] doi:10.1016/j.annemergmed.2010.10.018

62. **Epstein RM, Franks P, Shields CG, Meldrum SC, Miller KN, Campbell TL, et al.** Patient-centered communication and diagnostic testing. Ann Fam Med. 2005;3:415-21. [PMID: 16189057]
63. **Raja AS, Ip IK, Prevedello LM, Sodickson AD, Farkas C, Zane RD, et al.** Effect of computerized clinical decision support on the use and yield of CT pulmonary angiography in the emergency department. Radiology. 2012;262:468-74. [PMID: 22187633] doi:10.1148/radiol.11110951
64. **Fisher ES, Wennberg DE, Stukel TA, Gottlieb DJ.** Variations in the longitudinal efficiency of academic medical centers. Health Aff (Millwood). 2004;Suppl Variation:VAR19-32. [PMID: 15471777]
65. **Penaloza A, Verschuren F, Dambrine S, Zech F, Thys F, Roy PM.** Performance of the Pulmonary Embolism Rule-out Criteria (the PERC rule) combined with low clinical probability in high prevalence population. Thromb Res. 2012;129:e189-93. [PMID: 22424852] doi:10.1016/j.thromres.2012.02.016
66. **Bokobza J, Aubry A, Nakle N, Vincent-Cassy C, Pateron D, Devilliers C, et al.** Pulmonary embolism rule-out criteria vs D-dimer testing in low-risk patients for pulmonary embolism: a retrospective study. Am J Emerg Med. 2014;32:609-13. [PMID: 24736129] doi:10.1016/j.ajem.2014.03.008
67. **Ong CW, Malipatil V, Lavercombe M, Teo KG, Coughlin PB, Leach D, et al.** Implementation of a clinical prediction tool for pulmonary embolism diagnosis in a tertiary teaching hospital reduces the number of computed tomography pulmonary angiograms performed. Intern Med J. 2013;43:169-74. [PMID: 22909177] doi:10.1111/j.1445-5994.2012.02926.x
68. **Righini M, Van Es J, Den Exter PL, Roy PM, Verschuren F, Ghuysen A, et al.** Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study. JAMA. 2014;311:1117-24. [PMID: 24643601] doi:10.1001/jama.2014.2135
69. **Revel MP, Sanchez O, Couchon S, Planquette B, Hernigou A, Niarra R, et al.** Diagnostic accuracy of magnetic resonance imaging for an acute pulmonary embolism: results of the 'IRM-EP' study. J Thromb Haemost. 2012;10:743-50. [PMID: 22321816] doi:10.1111/j.1538-7836.2012.04652.x
70. **Revel MP, Sanchez O, Lefort C, Meyer G, Couchon S, Hernigou A, et al.** Diagnostic accuracy of unenhanced, contrast-enhanced perfusion and angiographic MRI sequences for pulmonary embolism diagnosis: results of independent sequence readings. Eur Radiol. 2013;23:2374-82. [PMID: 23652845] doi:10.1007/s00330-013-2852-8
71. **Salaun PY, Couturaud F, Le Duc-Pennec A, Lacut K, Le Roux PY, Guillo P, et al.** Noninvasive diagnosis of pulmonary embolism. Chest. 2011;139:1294-8. [PMID: 20724733] doi:10.1378/chest.10-1209
72. **Righini M, Le Gal G, Aujesky D, Roy PM, Sanchez O, Verschuren F, et al.** Diagnosis of pulmonary embolism by multidetector CT alone or combined with venous ultrasonography of the leg: a randomised non-inferiority trial. Lancet. 2008;371:1343-52. [PMID: 18424324] doi:10.1016/S0140-6736(08)60594-2
73. **Winer-Muram HT, Boone JM, Brown HL, Jennings SG, Mabie WC, Lombardo GT.** Pulmonary embolism in pregnant patients: fetal radiation dose with helical CT. Radiology. 2002;224:487-92. [PMID: 12147847]
74. **Schuur J, Raja AS.** Emergency Medicine Quality Improvement Pathways. Boston: Brigham and Women's Hospital; 2014. Accessed at www.brighamandwomens.org/Departments_and_Services/emergencymedicine/Quality_Improvement.aspx?sub=0 on 13 February 2014.
75. **Hess EP, Knoedler MA, Shah ND, Kline JA, Breslin M, Branda ME, et al.** The chest pain choice decision aid: a randomized trial. Circ Cardiovasc Qual Outcomes. 2012;5:251-9. [PMID: 22496116] doi:10.1161/CIRCOUTCOMES.111.964791
76. **Kline JA, Zeitouni RA, Hernandez-Nino J, Jones AE.** Randomized trial of computerized quantitative pretest probability in low-risk chest pain patients: effect on safety and resource use. Ann Emerg Med. 2009;53:727-35.e1. [PMID: 19135281] doi:10.1016/j.annemergmed.2008.09.034
77. **Geyer BC, Xu M, Kabrhel C.** Patient preferences for testing for pulmonary embolism in the ED using a shared decision-making model. Am J Emerg Med. 2014;32:233-6. [PMID: 24370071] doi:10.1016/j.ajem.2013.11.019
78. **Roy PM, Durieux P, Gillaizeau F, Legall C, Armand-Perroux A, Martino L, et al.** A computerized handheld decision-support system to improve pulmonary embolism diagnosis: a randomized trial. Ann Intern Med. 2009;151:677-86. [PMID: 19920268] doi:10.7326/0003-4819-151-10-200911170-00003
79. **Sistrom CL, Dang PA, Weilburg JB, Dreyer KJ, Rosenthal DI, Thrall JH.** Effect of computerized order entry with integrated decision support on the growth of outpatient procedure volumes: seven-year time series analysis. Radiology. 2009;251:147-55. [PMID: 19221058] doi:10.1148/radiol.2511081174
80. **Raja AS, Gupta A, Ip IK, Mills AM, Khorasani R.** The use of decision support to measure documented adherence to a national imaging quality measure. Acad Radiol. 2014;21:378-83. [PMID: 24507424] doi:10.1016/j.acra.2013.10.017
81. **Kline JA, Jones AE, Shapiro NI, Hernandez J, Hogg MM, Troyer J, et al.** Multicenter, randomized trial of quantitative pretest probability to reduce unnecessary medical radiation exposure in emergency department patients with chest pain and dyspnea. Circ Cardiovasc Imaging. 2014;7:66-73. [PMID: 24275953] doi:10.1161/CIRCIMAGING.113.001080
82. **Tilburt JC, Wynia MK, Sheeler RD, Thorsteinsdottir B, James KM, Egginton JS, et al.** Views of US physicians about controlling health care costs. JAMA. 2013;310:380-8. [PMID: 23917288] doi:10.1001/jama.2013.8278
83. **Levine MB, Moore AB, Franck C, Li J, Kuehl DR.** Variation in use of all types of computed tomography by emergency physicians. Am J Emerg Med. 2013;31:1437-42. [PMID: 23998807] doi:10.1016/j.ajem.2013.07.003
84. **Prevedello LM, Raja AS, Zane RD, Sodickson A, Lipsitz S, Schneider L, et al.** Variation in use of head computed tomography by emergency physicians. Am J Med. 2012;125:356-64. [PMID: 22325235] doi:10.1016/j.amjmed.2011.06.023
85. **Prevedello LM, Raja AS, Ip IK, Sodickson A, Khorasani R.** Does clinical decision support reduce unwarranted variation in yield of CT pulmonary angiogram? Am J Med. 2013;126:975-81. [PMID: 24157288] doi:10.1016/j.amjmed.2013.04.018

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Appendix Table 1. Wells Prediction Rule for Pretest Probability of PE*

Clinical Characteristic	Score	Simplified Score
Previous PE or DVT	1.5	1
Heart rate > 100 beats/min	1.5	1
Recent surgery or immobilization	1.5	1
Clinical signs of DVT	3	1
Alternative diagnosis less likely than PE	3	1
Hemoptysis	1	1
Cancer	1	1
	Pretest probability: 0–1: Low 2–6: Intermediate ≥7: High Dichotomized score: ≤4: PE unlikely (low) >4: PE likely (high)	Pretest probability: ≤1: PE unlikely (low) >1: PE likely (high)

DVT = deep venous thrombosis; PE = pulmonary embolism.
* Information from references 34 and 35.

Appendix Table 2. Revised Geneva Score for Predicting Pretest Probability of PE*

Clinical Characteristic	Score	Simplified Score
Age > 65 y	1	1
Previous PE or DVT	3	1
Surgery (under general anesthesia) or fracture of the lower limbs in the past month	2	1
Cancer (solid or hematologic; currently active or considered cured for < 1 y)	2	1
Unilateral lower-limb pain	3	1
Hemoptysis	2	1
Heart rate		
75–94 beats/min	3	1
≥95 beats/min	5	2
Pain on deep venous palpation of lower limb and unilateral edema	4	1
	Pretest probability: <4: Low 4–10: Intermediate >10: High	Pretest probability: ≤2: Unlikely (low) >2: Likely (high)

DVT = deep venous thrombosis; PE = pulmonary embolism.
* Information from references 36 and 37.