

## **CLINICAL PRACTICE GUIDELINE: PULMONARY EMBOLISM (6A)**

### **SYSTEMATIC REVIEW FOR IMAGING OF PULMONARY EMBOLISM**

#### **CPG 6A Abstract (Updated July 2018)**

Acute pulmonary embolism (PE) is a common and sometimes fatal disease. The approach to the evaluation should be efficient while simultaneously avoiding the risks of unnecessary testing so that therapy can be promptly initiated, and potential morbidity and mortality avoided (Raja et al., 2015; Jimenez et al., 2016; Lucassen et al., 2011). Since no specific sign, symptom, or risk factor can diagnose or exclude PE, clinical decision tools have been developed to risk stratify patients into specific diagnostic categories (see below) (Stein et al., 2006). These diagnostic tools predict the pre-test probability of PE that, in turn, either exclude imaging ('low' probability of PE) or indicate that imaging is appropriate ('high' probability of PE). When clinicians have persistent concern for PE, however, even patients with low risk may (or may not) undergo imaging based upon the laboratory results of an age-adjusted d-dimer test (Gupta et al., 2009).

Clinical guidelines advocating for the focused evaluation of patients with suspected PE have been published by professional societies, including the American Thoracic Society (ATS, 2017), American College of Physicians/American Academy of Family Physicians (Segal et al., 2007), the American College of Emergency Physicians (Fesmire et al., 2011), and the European Society of Cardiology (Konstantinides, 2014). 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 (plasma D-dimer measurement and diagnostic imaging) based on risk stratification (Lucassen et al., 2011).

The pre-test probability of PE can be calculated by using a validated pre-test probability score e.g., Wells (Wells et al., 2000), Simplified Wells (van Es et al., 2017) or Modified Geneva score (Le Gal et al., 2006). Most of the clinicians prefer the Wells criteria that includes the following:

Items	Original Wells Score (points)	Simplified Wells Score (points)
Clinical symptoms of DVT	3	1
Other diagnoses are less likely than PE	3	1
Heart Rate > 100	1.5	1
Immobilization 3 or more days or surgery in previous 4 weeks	1.5	1
Prior DVT/PE	1.5	1
Hemoptysis	1	1
Malignancy	1	1
<b>Score calculation:</b>	Low (score<2): Low probability of PE Intermediate (score 2-6): Intermediate probability of PE High (score>6): High probability of PE	PE unlikely $\leq 1$ PE likely $\geq 1$

For patients with a low probability of PE, an additional decision tool called the **Pulmonary Embolism Rule-Out Criteria (PERC)** (Singh et al., 2012) is used to determine whether diagnostic testing with D-Dimer is indicated. The PERC has eight criteria:

- Age < 50 years
- Heart Rate < 100 beats/minute
- Oxyhemoglobin saturation > 95%
- No hemoptysis
- No estrogen use
- No prior DVT or PE
- No unilateral leg swelling
- No surgery/trauma requiring hospitalization within prior 4 weeks

In patients with a low probability of PE who fulfill all eight criteria, the likelihood of PE is sufficiently low that further testing is not indicated. PERC is only valid in clinical settings with a low prevalence of PE (typically Emergency Departments).

In patients with an intermediate probability of PE, a sensitive D-Dimer level is measured. A normal D-Dimer level (<500 ng/ml) effectively excludes PE in these patients.

For patients with high pretest probability of PE, imaging studies are indicated. Current guidelines recommend computed tomography pulmonary angiography (CTPA) (Konstantinides et al., 2016; Raja et al.,2015). Ventilation/perfusion (V/Q) lung scanning is an appropriate alternative when CTPA is contraindicated/unavailable (Konstantinides et al., 2016; Raja et al.,2015). Of note, recent data indicates that V/Q imaging with single photon emission CT (V/Q SPECT) technology provides 3-D imaging that is comparable to CTPA in terms of diagnostic accuracy and has the advantage of low radiation and no iodinated contrast exposure (Reinartz et al., 2004). However, both CTPA and V/Q SPECT at varying times have been questioned in terms of each modality identifying clinically insignificant clots in the pulmonary vasculature that may or may not warrant anticoagulation. Stated another way, although the use of CTPA for the evaluation of suspected PE has increased, thus leading to an increased incidence of PE being reported, there is no indication of patient benefit since there has been little if any associated change in mortality (Minges et al., 2015).

#### **PE and Pregnancy:**

Clinical diagnosis of pulmonary thromboembolism in pregnancy remains difficult because symptoms such as shortness of breath or leg swelling are common and can mimic those of thromboembolic events. Also, D-dimer levels increase during pregnancy, reducing the likelihood of a negative result. In pregnant women with suspected PE, when imaging is necessary, ultrasound of the lower extremities is performed first as this is not associated with radiation exposure and confirmation of deep venous thrombosis (DVT) precludes further imaging.

However, in cases where PE is still suspected, and further diagnostic imaging is warranted, the choice of modality remains debatable. Some studies suggest there is decreased radiation risk to the fetus with CTPA (Cahill et al., 2009; Nijkeuter et al., 2006) compared with V/Q scintigraphy; others support V/Q (“scanning”) scintigraphy as the imaging modality of choice (Simcox et al., 2015). Further, the risk of a missed diagnosis of PE outweighs the risk of radiation exposure, and CTPA and V/Q scintigraphy and/or SPECT demonstrate comparable rates of radiation risk and diagnostic performance (Revel et al., 2011). The choice of imaging approach should be based on other considerations, such as patient-specific characteristics, differential diagnoses, and availability of expertise/equipment.

**Multiple factors affect the decision-making process when evaluating the appropriateness of ordering imaging studies. These include current community standards, availability, patient preference and expectations, radiation exposure, adverse reactions to contrast agents and prior imaging results. Further, such factors are not always quantifiable and frequently vary across therapeutic settings. Panelists review available literature to recommend appropriate imaging studies in specific clinical scenarios but realize that these other variables impact the decision-making process and are not necessarily addressed by published literature.**

**Search Strategy:** A systematic search was conducted to review of the current medical literature published through June 2018. Mentioned databases were systematically searched for literature pertaining to pulmonary embolism and the associated imaging. Articles associated with children were excluded. The search was focused on diagnostic imaging techniques, not upon treatment choices. Final inclusion was based on the specific PICO question being addressed.

**Keywords:** Pulmonary embolism, PE, V/Q scan, V/Q SPECT, CT angiogram, CTPA, DVT, ECHO, Ultrasound, CTPA, Wells score/criteria, PE and pregnancy

**Methods:** Below mentioned databases were searched for literature pertaining to Pulmonary embolism. Abstracts and unpublished studies were not included. An initial search for pulmonary embolism and imaging found 52,217 citations This was refined by limiting studies to adult and imaging. This resulted in 14015 articles. This group was further screened by the imaging modalities being investigated in the PICO question of interest. After further review, 158 relevant studies were obtained in full text form. These studies were then reviewed by SEMPI clinical analysts for inclusion. Panelists can also submit relevant articles for inclusion. Articles selected for final analysis were chosen based on study design, quality of research, publication date, sample size and relevance.

**Database Source:** Research Gate, PubMed, Cochrane Library, Google Scholar

## Clinical Focus Questions

**PICO #1:** In adults with suspected pulmonary embolism (PE), can clinical assessment alone be used for identifying risk compared to initial imaging?

**PICO #2:** In adults with suspected pulmonary embolism (PE) and at moderate to high risk for PE, should planar (traditional) V/Q imaging be performed compared to V/Q SPECT (Single Photon Emission CT or VQ SPECT/CT) imaging for optimal diagnostic accuracy?

**PICO #3:** In adults with suspected pulmonary embolism (PE) and at moderate to high risk for PE, should CTPA (CT Pulmonary Angiography) be performed compared to VQ SPECT (Single Photon Emission CT) for optimal patient outcome(s)?

**PICO #4:** In adults at high risk for pulmonary embolism (PE) and for whom definitive imaging is unsafe (e.g. hemodynamically unstable) should echocardiography (ECHO) be performed compared to other initial imaging for optimal diagnostic accuracy?

**PICO #5:** In adults with clinically suspected DVT (Deep Venous Thrombosis), should lower extremity US (Ultrasound) imaging be performed for optimal patient management?

**PICO #1:** In adults with suspected pulmonary embolism (PE), can clinical assessment alone be used for identifying risk compared to initial imaging?

SEMPI Grading QOE – Table 6A.1a—Summary of Findings						
PICO #1: In adults with suspected pulmonary embolism (PE), can clinical assessment alone be used for identifying risk compared to initial imaging?						
Author/Year/Title	Design	Population	Intervention Vs Comparator	Results	Conclusion Summary	SEMPI QOE Rating
van Es et al., 2017 <a href="#">The original and simplified Wells rules and age-adjusted D-dimer testing to rule out pulmonary embolism: an individual patient data meta-analysis</a>	Meta-analysis	N=6 studies 7268 patients with suspected PE	Wells score (simplified vs original)	<b>Performance (c-statistic):</b> Original: 0.73(95% CI 0.72-0.75) Simplified: 0.72(95% CI 0.70-0.73). <b>Combined with age-adjusted D-dimer:</b> Original: 3% (95% CI 25-42%) Simplified: 30% (95% CI 21-40%) <b>Failure rates:</b> Original:0.9% (95% CI 0.6-1.5%) Simplified: 0.8% (95% CI 0.5-1.3%)	Original and simplified Wells rules combined with age-adjusted D-dimer testing have similar performances in ruling out PE	<b>Moderate</b>
Raja et al., 2015 <a href="#">Evaluation of Patients with Suspected Acute Pulmonary Embolism: Best Practice Advice From the Clinical Guidelines Committee of the American College of Physicians</a>	Systemic literature review for guideline development (studies limited to meta-analysis, clinical trials, and RCTs)	Adults being evaluated for PE or VTE (1752 articles screened)	Clinical precision rules versus imaging versus follow-up	Not applicable	Clinicians should use validated clinical prediction rules to estimate pretest probability in patients in whom acute PE is being considered and should not obtain imaging studies in patients with a low pretest probability of PE and PERC - patients 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 obtain a D-dimer measurement as the initial diagnostic test and should not	<b>Moderate</b>

					use imaging studies as the initial test	
Kline et al., 2008 <a href="#">Prospective multicenter evaluation of the pulmonary embolism rule-out criteria</a>	Prospective consecutive enrollment (13 institutions)	8138 adult patients with suspected PE (dyspnea or chest pain)	PE rule out criteria (PERC) versus PE diagnosis via imaging and follow-up  PERC criteria: -age < 50 years -pulse < 100 -SaO2 > 95% -no hemoptysis -no estrogen -no surgery within 4 weeks -no prior VTE -no unilateral leg swelling	The main outcome was VTE (+) or death within 45 days  Among the low suspicion and PERC (-) patients (1666), 15 were VTE (+) and one patient died, yielding a false-negative rate of (1.0%, 0.6–1.6%)  As a diagnostic test, low suspicion and PERC (-) had a sensitivity of 97.4% (95.8–98.5%) and a specificity of 21.9% (21.0–22.9%)	The combination of gestalt estimate of low suspicion for PE and PERC - reduces the probability of VTE to below 2% in patients with suspected PE	<b>Moderate</b>
Stein et al., 2006 <a href="#">Diagnostic Pathways in Acute Pulmonary Embolism: Recommendations of The PIOPED II Investigators</a>	PIOPED II and Randomized Outcome studies PIOPED II (Prospective Investigation of Pulmonary Embolism Diagnosis II)	Adults being evaluated for PE	Clinical Assessment versus imaging versus follow-up	Clinical assessment (via an objective method) should be made before imaging	The PIOPED II investigators recommend stratification of all patients with suspected PE according to an objective clinical probability assessment. D-dimer should be measured and the combination of a negative D-dimer with a low or moderate clinical probability can safely exclude pulmonary embolism in many patients	<b>Moderate</b>
Wells et al., 2001 <a href="#">Excluding Pulmonary Embolism at the Bedside without Diagnostic Imaging: Management of Patients with Suspected Pulmonary Embolism Presenting to the Emergency</a>	Prospective cohort study (4 tertiary hospitals in Canada)	930 consecutive adult patients with suspected PE	Clinical prediction rules versus laboratory studies versus imaging versus follow-up	Of the 437 patients with a negative D-dimer result and low clinical probability, only 1 developed pulmonary embolism during follow-up  Therefore, the negative predictive value for the combined strategy of using the clinical model with D-	Managing patients for suspected pulmonary embolism on the basis of pretest probability and D-dimer result is safe and decreases the need for diagnostic imaging	<b>Moderate</b>

<a href="#">Department by Using a Simple Clinical Model and D-Dimer</a>				dimer testing in these patients was 99.5% (CI, 99.1% to 100%)		
Initial QOE Score across studies for PICO #1: <b>Moderate (2)</b>						

SEMPI Grading QOE – Table 6A.1b—Risk of Bias		
<b>PICO #1:</b> In adults with suspected pulmonary embolism (PE), can clinical assessment alone be used for identifying risk compared to initial imaging?		
Evaluate Outcome for Risk of Bias Across Studies		
Initial QOE Score Across Studies for PICO: <b>MODERATE</b>		
Criteria	Assessment	Reason for Assessment
<b>Negative Bias</b>		
Risk of bias	Not Serious	
Inconsistency	Not Serious	
Indirectness	Serious	Clinical assessment used as surrogate for no imaging
Imprecision	Not Serious	
<b>Positive Bias</b>		
Strength of association	Moderate	Clinical assessment rules show high predictive value
Other Considerations	No	
<b>Overall Effect of Bias on Initial QOE Grade: No Change</b>		
<b>Final QOE Grade for Outcome Across Studies: MODERATE</b>		
<p><b>High</b> – Very confident the true effect lies close to that of the estimate of the effect</p> <p><b>Moderate</b> – Moderately confident in the effect estimate (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different)</p> <p><b>Low</b> – Confidence in the effect estimate is limited (the true effect may be substantially different from the estimate of effect)</p> <p><b>Very Low</b> – Very little confidence in the effect estimate (the true effect is likely to be substantially different from the estimate of effect)</p>		

## SEMPI Grading QOE – Table 6A.1c—Evidence to Recommendations

**PICO #1:** In adults with suspected pulmonary embolism (PE), can clinical assessment alone be used for identifying risk compared to initial imaging?

### SEMPI Quality of Evidence (QOE) & Recommendation Strength

Author/Year/Title	Highlights	SEMPI QOE Rating	Final QOE Category	Recommendation Strength
van Es et al., 2017 <a href="#">The original and simplified Wells rules and age-adjusted D-dimer testing to rule out pulmonary embolism: an individual patient data meta-analysis</a>	Original and simplified Wells rules combined with age-adjusted D-dimer testing have similar performances in ruling out PE	Moderate	Moderate (2)	Strong (A)
Raja et al., 2015 <a href="#">Evaluation of Patients with Suspected Acute Pulmonary Embolism: Best Practice Advice from the Clinical Guidelines Committee of the American College of Physicians</a>	Clinicians should use validated clinical prediction rules to estimate pretest probability in patients in whom acute PE is being considered and should not obtain imaging studies in patients with a low pretest probability of PE and PERC (-) patients  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 obtain a D-dimer measurement as the initial diagnostic test and should not use imaging studies as the initial test	Moderate		
Kline et al., 2008 <a href="#">Prospective multicenter evaluation of the pulmonary embolism rule-out criteria</a>	The combination of gestalt estimate of low suspicion for PE and PERC (-) reduces the probability of VTE to below 2% in patients with suspected PE	Moderate		
Stein et al., 2006 <a href="#">Diagnostic Pathways in Acute Pulmonary Embolism: Recommendations of The PIOPED II Investigators</a>	The PIOPED II investigators recommend stratification of all patients with suspected PE according to an objective clinical probability assessment. D-dimer should be measured and the combination of a negative D-dimer with a low or moderate clinical probability can safely exclude pulmonary embolism in many patients	Moderate		

<p>Wells et al., 2001  <a href="#">Excluding Pulmonary Embolism at the Bedside without Diagnostic Imaging: Management of Patients with Suspected Pulmonary Embolism Presenting to the Emergency Department by Using a Simple Clinical Model and D-Dimer</a></p>	<p>Managing patients for suspected pulmonary embolism on the basis of pretest probability and D-dimer result is safe and decreases the need for diagnostic imaging</p>	<p>Moderate</p>		
<p><b>Recommendation Rating: 2A</b>—Strong recommendation for the intervention based on moderate quality evidence  <b>Justification:</b> Although Clinical assessment criteria are surrogate markers for PE this is balanced by high predictive value of such criteria and consistency of evidence which supports a strong recommendation.</p>				
<p><b>Rating Definitions:</b>  <b>Quality of Evidence:</b> High quality = 1; Moderate quality = 2; Low quality = 3; Very low quality = 4  <b>Strength of Recommendation:</b> A = Strength of Recommendation from Consistent Evidence; B = Strength of Recommendation from Panel Consensus</p>				
<p><b>Conclusion:</b> Various clinical assessment/prediction criteria or rules exist (several in combination with laboratory studies) can identify a subgroup of patients being evaluated for dyspnea and/or chest pain where there is a low probability of pulmonary embolism and thus do not warrant initial imaging. Furthermore, follow-up of these patients has demonstrated that such an approach is both safe and cost-effective.</p>				
<p><b>Final Recommendation: 2A</b>—In adults who are at low risk for pulmonary embolism (PE) based on clinical assessment, no imaging evaluation is recommended.</p>				

**PICO #2:** In adults with suspected pulmonary embolism (PE) and at moderate to high risk for PE, should planar (traditional) V/Q imaging be performed compared to V/Q SPECT (Single Photon Emission CT or VQ SPECT/CT) imaging for optimal diagnostic accuracy?

SEMPI Grading QOE – Table 6A.2a—Summary of Findings						
PICO #2: In adults with suspected pulmonary embolism (PE) and at moderate to high risk for PE, should planar (traditional) V/Q imaging be performed compared to V/Q SPECT (Single Photon Emission CT or VQ SPECT/CT) imaging for optimal diagnostic accuracy?						
Author/Year/Title	Design	Population	Intervention Vs Comparator	Results	Conclusion Summary	SEMPI QOE Rating
Kan et al., 2015 <a href="#">The accuracy of V/Q SPECT in the diagnosis of pulmonary embolism: a meta-analysis</a>	Meta-analysis	Nine studies with 3454 total patients	V/Q SPECT	<u>V/Q SPECT</u> Sensitivity-96% Specificity-97%	V/Q SPECT is accurate with high sensitivity and specificity	<b>Moderate</b>
Quirce et al., 2014 <a href="#">Contribution of V/Q SPECT to planar scintigraphy in the diagnosis of pulmonary embolism</a>	Prospective consecutive enrollment	102 patients	V/Q SPECT vs Planar (traditional) V/Q	V/Q SPECT was diagnostic in 97 of 102 scans Planar (traditional) V/Q was diagnostic in 58 of 102 scans	V/Q SPECT has a higher diagnostic yield and is a feasible technique for the diagnosis of pulmonary embolism	<b>Moderate</b>
Gutte et al., 2010 <a href="#">Comparison of V/Q SPECT and planar V/Q lung scintigraphy in diagnosing acute pulmonary embolism</a>	Prospective, consecutive enrollment	36 patients	V/Q SPECT vs Planar (traditional) V/Q	<u>Planar (traditional) V/Q-</u> Sensitivity-64% Specificity -72% <u>V/Q SPECT-</u> Sensitivity-100% Specificity-87%	V/Q SPECT is superior to Planar (traditional) V/Q for diagnosis of pulmonary embolism	<b>Moderate</b>
Reinartz et al., 2004 <a href="#">Tomographic imaging in the diagnosis of pulmonary embolism: a comparison between V/Q lung scintigraphy in SPECT technique and multislice spiral CT</a>	Retrospective	83 patients that had both V/Q scintigraphy in SPECT technique and CT within three days	Multislice spiral CT vs planar V/Q vs V/Q SPECT	<u>CT</u> Sensitivity-86% Specificity-98% <u>V/Q SPECT</u> Sensitivity-97% Specificity-91% <u>V/Q planar</u> Sensitivity-76% Specificity-85%	V/Q SPECT imaging is superior to planar V/Q for the diagnosis of pulmonary embolism and comparable to multi-slice spiral CT	<b>Low</b>
Initial QOE Score across studies for PICO #2: <b>Moderate (2)</b>						

SEMPI Grading QOE – Table 6A.2b—Risk of Bias		
<b>PICO #2:</b> In adults with suspected pulmonary embolism (PE) and at moderate to high risk for PE, should planar (traditional) V/Q imaging be performed compared to V/Q SPECT (Single Photon Emission CT or VQ SPECT/CT) imaging for optimal diagnostic accuracy?		
Evaluate Outcome for Risk of Bias Across Studies		
Initial QOE Score Across Studies for PICO: <b>MODERATE</b>		
Criteria	Assessment	Reason for Assessment
<b>Negative Bias</b>		
Risk of bias	Not Serious	Consecutive enrollment in multiple studies
Inconsistency	Not Serious	
Indirectness	Not Serious	No direct comparator in Kan et al. study
Imprecision	Not Serious	
<b>Positive Bias</b>		
Strength of association	Moderate	Similar results in all studies
Other Considerations	No	
<b>Overall Effect of Bias on Initial QOE Grade: No Change</b>		
<b>Final QOE Grade for Outcome Across Studies: MODERATE</b>		
<p><b>High</b> – Very confident the true effect lies close to that of the estimate of the effect</p> <p><b>Moderate</b> – Moderately confident in the effect estimate (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different)</p> <p><b>Low</b> – Confidence in the effect estimate is limited (the true effect may be substantially different from the estimate of effect)</p> <p><b>Very Low</b> – Very little confidence in the effect estimate (the true effect is likely to be substantially different from the estimate of effect)</p>		

## SEMPI Grading QOE – Table 6A.2c—Evidence to Recommendations

**PICO #2:** In adults with suspected pulmonary embolism (PE) and at moderate to high risk for PE, should planar (traditional) V/Q imaging be performed compared to V/Q SPECT (Single Photon Emission CT or VQ SPECT/CT) imaging for optimal diagnostic accuracy?

### SEMPI Quality of Evidence (QOE) & Recommendation Strength

Author/Year/Title	Highlights	SEMPI QOE Rating	Final QOE Category	Recommendation Strength
Kan et al., 2015 <a href="#">The accuracy of V/Q SPECT in the diagnosis of pulmonary embolism: a meta-analysis</a>	V/Q SPECT is accurate and high a high sensitivity and specificity	Moderate	Moderate (2)	Strong (A)
Quirce et al., 2014 <a href="#">Contribution of V/Q SPECT to planar scintigraphy in the diagnosis of pulmonary embolism</a>	V/Q SPECT has a higher diagnostic yield and is a feasible technique for the diagnosis of pulmonary embolism	Moderate		
Gutte et al., 2010 <a href="#">Comparison of V/Q SPECT and planar V/Q lung scintigraphy in diagnosing acute pulmonary embolism</a>	V/Q SPECT is superior to V/Q scintigraphy for diagnosis of pulmonary embolism	Moderate		
Reinartz et al., 2004 <a href="#">Tomographic imaging in the diagnosis of pulmonary embolism: a comparison between V/Q lung scintigraphy in SPECT technique and multislice spiral CT</a>	V/Q SPECT imaging is superior to planar V/Q for the diagnosis of pulmonary embolism and comparable to spiral CT	Low		

**Recommendation Rating: 2A**—Strong recommendation for the intervention based on moderate quality evidence

**Justification:** Consistent evidence from prospective studies demonstrate V/Q SPECT is superior to planar V/Q.

**Rating Definitions:**

**Quality of Evidence:** High quality = 1; Moderate quality = 2; Low quality = 3; Very low quality = 4

**Strength of Recommendation:** A = Strength of Recommendation from Consistent Evidence; B = Strength of Recommendation from Panel Consensus

**Conclusion:** Originally, strong evidence appeared to support the use of V/Q SPECT (Ventilation/Perfusion Single Photon Emission Computed Tomography) over planar (conventional) V/Q scanning for the detection of pulmonary embolism. SPECT’s three-dimensional nature allows for better visualization of the structures involved and can reduce the number of “inconclusive” tests. More recent data suggest that the addition of low-dose CT imaging to V/Q SPECT increases the specificity, has no effect on sensitivity, and thus increases the diagnostic accuracy of V/Q SPECT alone (Mortensen & Gutte, 2014). The presence of low-dose CT imaging in SPECT scintigraphy improves specificity by providing alternate etiologies for subtle perfusion defects (e.g., interlobar fissures, localized hyperinflation, pleural fluid, atelectasis, pneumonia) thus improving radiologist confidence and reducing the “inconclusive” assessment rates (Konstantinides et al., 2014). Nonetheless, further comparisons between V/Q SPECT and V/Q SPECT/CT are needed to determine if one modality is significantly more accurate than the other.

**Final Recommendation: 2A**— In adults with symptoms suspicious for pulmonary embolism and at moderate to high risk for PE, V/Q SPECT or V/Q SPECT/CT is recommended compared to planar (conventional) V/Q imaging for optimal diagnostic accuracy.

**PICO #3:** In adults with suspected pulmonary embolism (PE) and at moderate to high risk for PE, should CTPA (CT Pulmonary Angiography) be performed compared to VQ SPECT (Single Photon Emission CT) for optimal patient outcome(s)?

SEMPI Grading QOE – Table 6A.3a—Summary of Findings						
PICO #3: In adults with suspected pulmonary embolism (PE) and at moderate to high risk for PE, should CTPA (CT Pulmonary Angiography) be performed compared to VQ SPECT (Single Photon Emission CT) for optimal patient outcome(s)?						
Author/Year/Title	Design	Population	Intervention Vs Comparator	Results	Conclusion Summary	SEMPI QOE Rating
Phillips et al., 2015 <a href="#">Planar and SPECT ventilation/perfusion imaging and computed tomography for the diagnosis of pulmonary embolism: A systematic review and meta-analysis of the literature, and cost and dose comparison</a>	Systematic literature review (19 studies)	5923 adult patients with suspected PE (6393 exams)	Planar VQ versus VQ SPECT versus CTPA	Planar VQ was significantly inferior to both VQ SPECT and CTPA with no difference between the latter two CTPA represents best value per correct diagnosis compared to VQ SPECT and planar VQ V/Q SPECT was the most effective with the lowest radiation dose per correct diagnosis compared with planar VQ and CTPA	No performance difference between V/Q SPECT and CTPA was identified.  CTPA is clearly the most cost-effective technique  V/Q SPECT should be considered in situations where radiation dose is of concern or CTPA is inappropriate (e.g., pregnancy)	<b>Moderate</b>
Gutte et al., 2009 <a href="#">Detection of Pulmonary Embolism with Combined Ventilation–Perfusion SPECT and Low-Dose CT: Head-to-Head Comparison with Multidetector CT Angiography</a>	Prospective non-randomized cohort study	81 adult patients with intermediate or high clinical probability of PE	A V/Q SPECT and CTPA was performed on all patients	31 of 81 (38%) of patients had PE. V/Q SPECT had a sensitivity of 97% and a specificity of 88%. When low-dose CT was added, the sensitivity was still 97% and the specificity increased to 100%. MDCT angiography alone had a sensitivity of 68% and a specificity of 100%	V/Q SPECT in combination with low-dose CT has an excellent diagnostic performance and should therefore probably be considered first-line imaging in the workup of PE in most cases	<b>Moderate</b>
Miles et al., 2009 <a href="#">A Comparison of Single-Photon Emission CT Lung Scintigraphy and CT Pulmonary Angiography for the Diagnosis of Pulmonary Embolism</a>	Prospective observational study across 5 primary care hospitals	79 adult patients with suspected PE	VQ SPECT and CTPA was performed on all patients	The percentage of agreement between VQ SPECT and CTPA data for the diagnosis of PE was 95%	VQ SPECT is a viable alternative to CTPA for the diagnosis of PE and has potential advantages in that it was feasible in more patients, had fewer contraindications, a lower radiation dose; and fewer non-diagnostic findings than CTPA	<b>Moderate</b>
Initial QOE Score across studies for PICO #3: <b>Moderate (2)</b>						

## SEMPI Grading QOE – Table 6A.3b—Risk of Bias

**PICO #3:** In adults with suspected pulmonary embolism (PE) and at moderate to high risk for PE, should CTPA (CT Pulmonary Angiography) be performed compared to VQ SPECT (Single Photon Emission CT) for optimal patient outcome(s)?

### Evaluate Outcome for Risk of Bias Across Studies

Initial QOE Score Across Studies for PICO: **MODERATE**

Criteria	Assessment	Reason for Assessment
<b>Negative Bias</b>		
Risk of bias	Not Serious	
Inconsistency	Serious	Conclusions differ among studies, but different clinical scenarios apply
Indirectness	Not Serious	
Imprecision	Not Serious	
<b>Positive Bias</b>		
Strength of association	Moderate	Prospective studies and systematic review support similar modality
Other Considerations	No	
<b>Overall Effect of Bias on Initial QOE Grade: No change</b>		
<b>Final QOE Grade for Outcome Across Studies: MODERATE</b>		
<p><b>High</b> – Very confident the true effect lies close to that of the estimate of the effect</p> <p><b>Moderate</b> – Moderately confident in the effect estimate (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different)</p> <p><b>Low</b> – Confidence in the effect estimate is limited (the true effect may be substantially different from the estimate of effect)</p> <p><b>Very Low</b> – Very little confidence in the effect estimate (the true effect is likely to be substantially different from the estimate of effect)</p>		

## SEMPI Grading QOE – Table 6A.3c—Evidence to Recommendations

**PICO #3:** In adults with suspected pulmonary embolism (PE) and at moderate to high risk for PE, should CTPA (CT Pulmonary Angiography) be performed compared to VQ SPECT (Single Photon Emission CT) for optimal patient outcome(s)?

### SEMPI Quality of Evidence (QOE) & Recommendation Strength

Author/Year/Title	Highlights	SEMPI QOE Rating	Final QOE Category	Recommendation Strength
Phillips et al., 2015 <a href="#">Planar and SPECT ventilation/perfusion imaging and computed tomography for the diagnosis of pulmonary embolism: A systematic review and meta-analysis of the literature, and cost and dose comparison</a>	No performance difference between V/Q SPECT and CTPA was identified CTPA is clearly the most cost-effective technique V/Q SPECT should be considered in situations where radiation dose is of concern or CTPA is inappropriate (e.g. pregnancy)	Moderate	Moderate (2)	Strong (A)
Gutte et al., 2009 <a href="#">Detection of Pulmonary Embolism with Combined Ventilation–Perfusion SPECT and Low-Dose CT: Head-to-Head Comparison with Multidetector CT Angiography</a>	V/Q SPECT in combination with low-dose CT has an excellent diagnostic performance and should therefore probably be considered first-line imaging in the workup of PE in most cases	Moderate		
Miles et al., 2009 <a href="#">A Comparison of Single-Photon Emission CT Lung Scintigraphy and CT Pulmonary Angiography for the Diagnosis of Pulmonary Embolism</a>	VQ SPECT scintigraphy is a viable alternative to CTPA for the diagnosis of PE and has potential advantages in that it was feasible in more patients, had fewer contraindications, a lower radiation dose; and fewer non-diagnostic findings than CTPA	Moderate		

**Recommendation Rating: 2A**—Strong recommendation for the intervention based on moderate quality evidence

**Justification:** Although quality studies exist to address the PICO question, conclusions differ and thus guidelines must in part rely upon patient characteristics, facility resources, and expert opinion.

**Rating Definitions:**

**Quality of Evidence:** High quality = 1; Moderate quality = 2; Low quality = 3; Very low quality = 4

**Strength of Recommendation:** A = Strength of Recommendation from Consistent Evidence; B = Strength of Recommendation from Panel Consensus

**Conclusion:** CTPA (CT Pulmonary Angiography—using Spiral/Helical CT) is considered the gold standard for diagnosis of PE with superior diagnostic accuracy. The advent of VQ SPECT, however, has dramatically increased the power and utility of VQ scanning. Several studies have compared VQ SPECT to the accuracy of CTPA and found them to have comparable diagnostic accuracy. CTPA is less expensive and more readily available, yet issues of radiation exposure and lack of sensitivity have been raised. VQ SPECT is highly sensitive and specific, involves less radiation, and is applicable to a larger subset of patients. Drawbacks with VQ SPECT include availability, cost, and the identification of sub-segmental defects, which may be of little clinical importance. As such, it appears that any recommendation must take into account the specific patient population and setting.

**Final Recommendation: 2A**—In adults with symptoms suspicious for pulmonary embolism and at moderate to high risk for PE, CTPA (CT Pulmonary Angiography—using Spiral/Helical CT) is recommended unless contraindications exist, in which case VQ SPECT is an equivalent alternative.

**PICO #4:** In adults at high risk for pulmonary embolism (PE) and for whom definitive imaging is unsafe (e.g. hemodynamically unstable) should echocardiography (ECHO) be performed compared to other initial imaging for optimal diagnostic accuracy?

SEMPI Grading QOE — Table 6A.4a—Summary of Findings						
PICO #4: In adults at high risk for pulmonary embolism (PE) and for whom definitive imaging is unsafe (e.g. hemodynamically unstable) should echocardiography (ECHO) be performed compared to other initial imaging for optimal diagnostic accuracy?						
Author/Year/Title	Design	Population	Intervention Vs Comparator	Results	Conclusion Summary	SEMPI QOE Rating
Fields et al., 2017 <a href="#">Transthoracic Echocardiography for Diagnosing Pulmonary Embolism: A Systematic Review and Meta-Analysis</a>	Systematic review and meta-analysis	N=22 studies	ECHO (Diagnostic accuracy)	"Right heart strain" test: Sensitivity - 53% (95% CI, 45%-61%) Specificity - 83% (95% CI, 74%-90%). Eleven other distinct signs were identified: ventricle size ratio, abnormal septal motion, tricuspid regurgitation, 60/60 sign, McConnell's sign, right heart thrombus, right ventricle-hypokinesis, pulmonary hypertension, right ventricular end-diastolic diameter, tricuspid annular plane systolic excursion, and right ventricular systolic pressure	Echocardiography has high specificity and low sensitivity in the diagnosis of PE and is an adequate rule-in test at the bedside in critical care settings, especially in those who are unable to get other confirmatory studies	<b>Moderate</b>

<p>Dresden et al., 2014  <a href="#">Right Ventricular Dilatation on Bedside Echocardiography Performed by Emergency Physicians Aids in the Diagnosis of Pulmonary Embolism</a></p>	<p>Prospective Observational</p>	<p>Enrolled=166 ED patients &gt;21 years Bedside echo performed in 146 (Patients with suspected moderate to high pretest probability or confirmed pulmonary embolism) and with an intent to obtain definitive imaging for PE 20/146 were classified as having high probability on basis of Well's criteria</p>	<p>Bedside echocardiography (other imaging studies performed CT pulmonary angiogram or Ventilation-Perfusion scan) Physicians performing bedside ECHO were blinded to these results)</p>	<p>17 had RV:LV&gt;1:1  PE positive =15  PE negative =2</p> <p>N=129 had RV:LV&lt;1:1  PE positive =15  PE negative =114</p> <p>RV dilatation on bedside ECHO for diagnosing PE;</p> <p><b>For finding PE:</b>  Sensitivity: 50 %  Specificity:98%  PPV:88%  NPP:88%  PLR :29  NLR: 0.51</p>	<p>Right ventricular dilatation on ECHO helps emergency physicians rule in PE before definitive testing</p> <p>Patients with moderate to high pretest probability for PE and ECHO positive RV dilatation should be considered for anticoagulation before definitive testing</p>	<p><b>Moderate</b></p>
<p>Kucher et al., 2005  <a href="#">Prognostic Role of Echocardiography Among Patients With Acute Pulmonary Embolism and a Systolic Arterial Pressure of 90 mm Hg or Higher</a></p>	<p>Prospective (ICOPER registry)</p>	<p>N= 1035 patients presented with systolic systemic arterial pressure of 90 mm Hg or higher and who underwent echocardiography within 24 hours of a diagnosis of pulmonary embolism, showing presence (n = 405) or absence (n = 630) of RV hypokinesis</p>	<p>Echocardiograph</p>	<p>In patients with RV hypokinesis, the initial systolic systemic pressure was lower (125 ± 22 mm Hg vs 131 ± 22 mm Hg ;P ,(001.&gt;and the initial heart rate was higher (104 ± 21 beats per minute vs 99 ± 22 beats per minute ;P (001.&gt;than in patients without RV hypokinesis</p>	<p>Echocardiography identified RV hypokinesis independently predicts decreased 30-day survival This finding is clinically important because it facilitates rapid identification of high risk patients who present with a preserved systemic arterial pressure and who might deceptively seem to be stable and at low risk</p>	<p><b>Moderate</b></p>
<p>Kasper et al., 1997  <a href="#">Management Strategies and Determinants of Outcome in Acute</a></p>	<p>Retrospective data collection  Prospective grouping</p>	<p>N=1001 patients (204 participating centers)  The inclusion criteria were</p>	<p>ECG, ECHO, Pulmonary Angiogram and cardiac catheterization</p>	<p><b>Gp1- N=407</b>  ECG: 405 (99.5%)  ECHO: 325 (80%)  Lung Scan: 278 (68%)  Right Heart Cath: 119 (29%)</p>	<p>In the presence of severe hemodynamic compromise, findings of bedside echocardiography are relied upon to proceed thrombolytic</p>	<p><b>Moderate</b></p>

<a href="#">Major Pulmonary Embolism: Results of a Multicenter Registry</a>		<p>based on the clinical findings at presentation and the results of electrocardiographic, echocardiographic, nuclear imaging and cardiac catheterization studies</p> <p>prospectively defined 4 patient groups of increasing clinical and hemodynamic instability:</p> <p><b>Group 1=</b> Patients with acute pulmonary embolism on ECHO</p> <p><b>Group 2=</b> Patients presenting with arterial hypotension</p> <p><b>Group 3=</b> Patients with arterial hypotension accompanied by cardiogenic shock</p> <p><b>Group 4=</b> Patients with circulatory collapse who underwent cardiopulmonary resuscitation</p>		<p>Pulm angio: 92 (23%) US-Doppler: 357 (88%)</p> <p><b>Gp2- N=316</b> ECG: 312 (99%) ECHO: 230 (73%) Lung Scan: 189 (60%) Right Heart Cath: 73 (23%) Pulm angio: 46 (15%) US-Doppler: 248 (79%)</p> <p><b>Gp3-N=102</b> ECG: 102 (100%) ECHO: 69 (68%) Lung Scan: 58 (57%) Right Heart Cath: 26 (26%) Pulm angio: 14 (14%) US-Doppler: 76 (75%)</p> <p><b>Gp4-N=176</b> ECG: 162 (92%) ECHO: 117 (66%) Lung Scan: 42 (24%) Right Heart Cath: 43 (24%) Pulm angio: 14 (15%) US-Doppler: 40 (79%)</p> <p>Echocardiography was the most frequently performed diagnostic procedure (74%) Lung scan or pulmonary angiography were performed in 79% of clinically stable patients but much less frequently in those with circulatory collapse at presentation (32%, p &lt; 0.001)</p>	<p>treatment without seeking further diagnostic certainty in nuclear imaging or angiographic studies</p>	
<p>Kasper et al., 1997 <a href="#">Prognostic significance of right ventricular</a></p>	<p>Prospective</p>	<p>N=317 patients with clinically</p>	<p>ECHO Lung scan or Pulmonary</p>	<p>RV afterload stress diagnosed in 87 patients (27%)</p>	<p>Echocardiograph Identified RV stress afterload is a major determinant</p>	<p><b>Low</b></p>

<a href="#">afterload stress detected by echocardiography in patients with clinically suspected pulmonary embolism</a>		suspected pulmonary embolism prospectively evaluated by echocardiography for the presence of right ventricular afterload stress and right heart or pulmonary artery thrombi	Angiography was obtained in 164 (52%) Deep venous thrombosis was established in 90 of 158 patients (57%) using phlebographic or Doppler sonographic studies	Objective confirmation of pulmonary embolism and diagnosis of deep venous thrombosis was more common in patients with right ventricular afterload stress than in those without (83% v 40% and 46% v 22%, respectively; P < 0.001) One year mortality from pulmonary embolism was 13% in patients with right ventricular afterload stress at presentation compared with 1-3% in those without (P < 0.001)	of prognosis in patients with clinically suspected acute pulmonary embolism	
<a href="#">Pruszczyk et al., 1995 Transoesophageal echocardiography for definitive diagnosis of haemodynamically significant pulmonary embolism</a>	Prospective (Consecutive enrollment)	N=32 (32 to 80 years) patients with clinically suspected acute or chronic pulmonary embolism presenting signs of right ventricular overload at transthoracic echocardiographic examination	TEE (Trans-esophageal echocardiography) Patients had Transthoracic echocardiographic (TTE) evaluation done prior to TEE	Intraluminal thrombi identified in 88.5% of 26 patients unstable acute or chronic PE  Sensitivity : 80% for acute PE 73% for chronic  Specificity:100%	Direct visualization of pulmonary arterial thrombi by Trans-esophageal echocardiograph (TEE) is useful for prompt and definitive diagnosis of hemodynamically significant PE	<b>Low</b>
Initial QOE Score across studies for PICO #4: <b>Moderate (2)</b>						

SEMPI Grading QOE – Table 6A.4b—Risk of Bias		
<b>PICO #4:</b> In adults at high risk for pulmonary embolism (PE) and for whom definitive imaging is unsafe (e.g. hemodynamically unstable) should echocardiography (ECHO) be performed compared to other initial imaging for optimal diagnostic accuracy?		
Evaluate Outcome for Risk of Bias Across Studies		
Initial QOE Score Across Studies for PICO: <b>MODERATE</b>		
Criteria	Assessment	Reason for Assessment
<b>Negative Bias</b>		
Risk of bias	Serious	No randomization, selection bias, no direct comparators
Inconsistency	Not Serious	
Indirectness	Not Serious	
Imprecision	Serious	Detailed and exact sensitivities and specificities not explained for outcome measures
<b>Positive Bias</b>		
Strength of association	Moderate	
Other Considerations	Yes	Mainly registry data studied Large sample size
<b>Overall Effect of Bias on Initial QOE Grade: No Change</b>		
Final QOE Grade for Outcome Across Studies: <b>MODERATE</b>		
<p><b>High</b> – Very confident the true effect lies close to that of the estimate of the effect</p> <p><b>Moderate</b> – Moderately confident in the effect estimate (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different)</p> <p><b>Low</b> – Confidence in the effect estimate is limited (the true effect may be substantially different from the estimate of effect)</p> <p><b>Very Low</b> – Very little confidence in the effect estimate (the true effect is likely to be substantially different from the estimate of effect)</p>		

## SEMPI Grading QOE – Table 6A.4c—Evidence to Recommendations

**PICO #4:** In adults at high risk for pulmonary embolism (PE) and for whom definitive imaging is unsafe (e.g. hemodynamically unstable) should echocardiography (ECHO) be performed compared to other initial imaging for optimal diagnostic accuracy?

### SEMPI Quality of Evidence (QOE) & Recommendation Strength

Author/Year/Title	Highlights	SEMPI QOE Rating	Final QOE Category	Recommendation Strength
Fields et al., 2017 <a href="#">Transthoracic Echocardiography for Diagnosing Pulmonary Embolism: A Systematic Review and Meta-Analysis</a>	Echocardiography has high specificity and low sensitivity in the diagnosis of PE and is an adequate rule-in test at the bedside in critical care settings, especially in those who are unable to get other confirmatory studies	Moderate	Moderate (2)	Strong (A)
Dresden et al., 2014 <a href="#">Right Ventricular Dilatation on Bedside Echocardiography Performed by Emergency Physicians Aids in the Diagnosis of Pulmonary Embolism</a>	Right ventricular dilatation on ECHO helps emergency physicians rule in PE before definitive testing Patients with moderate to high pretest probability for PE and ECHO positive RV dilatation should be considered for anticoagulation before definitive testing	Moderate		
Kucher et al., 2005 <a href="#">Prognostic Role of Echocardiography Among Patients With Acute Pulmonary Embolism and a Systolic Arterial Pressure of 90 mm Hg or Higher</a>	Echocardiography identified RV hypokinesis independently predicts decreased 30-day survival This finding is clinically important because it facilitates rapid identification of high risk patients who present with a preserved systemic arterial pressure and who might deceptively seem to be stable and at low risk	Moderate		
Kasper et al., 1997 <a href="#">Management Strategies and Determinants of Outcome in Acute Major Pulmonary Embolism: Results of a Multicenter Registry</a>	In the presence of severe hemodynamic compromise, findings of bedside echocardiography are relied upon to proceed thrombolytic treatment without seeking further diagnostic certainty in nuclear imaging or angiographic studies	Moderate		

<p>Kasper et al., 1997  <a href="#">Prognostic significance of right ventricular afterload stress detected by echocardiography in patients with clinically suspected pulmonary embolism</a></p>	<p>Echocardiography identified RV stress afterload is a major determinant of prognosis in patients with clinically suspected acute pulmonary embolism</p>	<p>Low</p>		
<p>Pruszczyk et al., 1995  <a href="#">Transoesophageal echocardiography for definitive diagnosis of haemodynamically significant pulmonary embolism</a></p>	<p>Direct visualization of pulmonary arterial thrombi by Trans-esophageal echocardiography (TEE) is useful for prompt and definitive diagnosis of hemodynamically significant PE</p>	<p>Low</p>		
<p><b>Recommendation Rating: 2A</b>—Strong recommendation for the intervention based on moderate quality evidence  <b>Justification:</b> Large sample size, registry data, prospective design and consistency of findings support that ECHO can be a useful surrogate for other imaging modalities.</p>				
<p><b>Rating Definitions:</b>  <b>Quality of Evidence:</b> High quality = 1; Moderate quality = 2; Low quality = 3; Very low quality = 4  <b>Strength of Recommendation:</b> A = Strength of Recommendation from Consistent Evidence; B = Strength of Recommendation from Panel Consensus</p>				
<p><b>Conclusion:</b> Echocardiography is acceptable based upon evidence for assessment of hemodynamically unstable patients and can direct therapeutic intervention in patients at high risk for pulmonary embolism. Additional imaging may be warranted, once the patient is stable.</p>				
<p><b>Final Recommendation:2A</b>—In adults at high risk for pulmonary embolism and for whom definitive imaging is unsafe (e.g. hemodynamically unstable), echocardiography (ECHO) is recommended for optimal patient outcome(s).</p>				

**PICO #5:** In adults with clinically suspected DVT (Deep Venous Thrombosis), should lower extremity US (Ultrasound) imaging be performed for optimal patient management?

SEMPI Grading QOE – Table 6A.5a—Summary of Findings						
PICO #5: In adults with clinically suspected DVT (Deep Venous Thrombosis), should lower extremity US (Ultrasound) imaging be performed for optimal patient management?						
Author/Year/Title	Design	Population	Intervention Vs Comparator	Results	Conclusion Summary	SEMPI QOE Rating
Johnson et al., 2010 <a href="#">Risk of deep vein thrombosis following a single negative whole-leg compression ultrasound: a systematic review and meta-analysis</a>	Systematic review and meta-analysis	N=7 studies 4731 patients (Negative CUS and follow up- 3months) (13.7%) had active cancer and up to 725 patients (15.3%) recently underwent a major surgery	Compression-ultrasound (CUS)	Venous thromboembolism or suspected venous thromboembolism-related death occurred in 34 patients (0.7%): 11 patients with distal DVT (32.4%) 7 patients with proximal DVT (20.6%); 7 patients with nonfatal pulmonary emboli (20.6%); an 9 patients (26.5%), possibly related to venous thromboembolism. Combined venous thromboembolism event rate at 3 months: 0.57% (95% CI, 0.25%-0.89%).	A negative extremity US for deep vein thrombosis is associated with low risk for embolism	<b>Moderate</b>
Goodacre et al., 2005 <a href="#">Systematic review and meta-analysis of the diagnostic accuracy of ultrasonography for deep vein thrombosis</a>	Systematic review, meta-analysis and meta-regression of diagnostic cohort studies	Adult patients with clinically suspected DVT (100 studies)	Contrast venography (gold standard) versus US (compression & duplex US)	Duplex US had pooled sensitivity of 96.5% (95.1 to 97.6) for proximal DVT, 71.2% (64.6 to 77.2) for distal DVT and specificity of 94.0% (92.8 to 95.1)  Triplex US had pooled sensitivity of 96.4% (94.4 to 97.1%) for proximal DVT, 75.2% (67.7 to 81.6) for distal DVT and specificity of 94.3% (92.5 to 95.8)	Combined color-Doppler US techniques have optimal sensitivity, while compression US has optimal specificity for DVT detection in symptomatic patients	<b>Moderate</b>

				Compression US alone had pooled sensitivity of 93.8 % (92.0 to 95.3%) for proximal DVT, 56.8% (49.0 to 66.4) for distal DVT and specificity of 97.8% (97.0 to 98.4)		
Atri et al., 1996 <a href="#">Accuracy of sonography in the evaluation of calf deep vein thrombosis in both postoperative surveillance and symptomatic patients</a>	Prospective double-blinded study, consecutive patients	287 adult patients (179 post-op & 108 symptomatic)	Contrast venography (gold standard) versus US (compression US)	The accuracy of US in detecting calf DVT with or without extension to above-the-calf veins were: Sensitivity: 92% Specificity: 100%, NPV: 98% PPV: 100% Of all calf muscular branch DVTs, 52% were detected by CS alone as compared with 21% seen on CV alone	US is a highly accurate test with acceptable reproducibility for the detection of DVT in calf veins in both postoperative and symptomatic patients	<b>Moderate</b>
Heijboer et al, 1993 <a href="#">A comparison of real-time compression ultrasonography with impedance plethysmography for the diagnosis of deep-vein thrombosis in symptomatic outpatients</a>	Randomized controlled trial of consecutive patients	985 adult patients with clinically suspected DVT	Impedance plethysmography (IP) versus US (serial compression)	The positive predictive value of an abnormal US was 94 percent (95 percent confidence interval, 87 to 98 percent), whereas the predictive value of impedance plethysmography (IP) was 83 percent (95 percent confidence interval, 75 to 90 percent) (P = 0.02).	In making the diagnosis of deep-vein thrombosis in symptomatic outpatients, serial compression ultrasonography is preferable to impedance plethysmography, in view of its superior performance in detecting venous thrombosis	<b>Moderate</b>
Initial QOE Score across studies for PICO #5: <b>Moderate (2)</b>						

SEMPI Grading QOE – Table 6A.5b—Risk of Bias		
<b>PICO #5:</b> In adults with clinically suspected DVT (Deep Venous Thrombosis), should lower extremity US (Ultrasound) imaging be performed for optimal patient management?		
Evaluate Outcome for Risk of Bias Across Studies		
Initial QOE Score Across Studies for PICO: <b>MODERATE</b>		
Criteria	Assessment	Reason for Assessment
<b>Negative Bias</b>		
Risk of bias	Not Serious	
Inconsistency	Not Serious	
Indirectness	Serious	Vintage literature uses obsolete comparator (venography, IP)
Imprecision	Not Serious	
<b>Positive Bias</b>		
Strength of association	Moderate	Strong diagnostic accuracy
Other Considerations	No	
<b>Overall Effect of Bias on Initial QOE Grade: No Change</b>		
<b>Final QOE Grade for Outcome Across Studies: MODERATE</b>		
<p><b>High</b> – Very confident the true effect lies close to that of the estimate of the effect</p> <p><b>Moderate</b> – Moderately confident in the effect estimate (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different)</p> <p><b>Low</b> – Confidence in the effect estimate is limited (the true effect may be substantially different from the estimate of effect)</p> <p><b>Very Low</b> – Very little confidence in the effect estimate (the true effect is likely to be substantially different from the estimate of effect)</p>		

## SEMPI Grading QOE – Table 6A.5c—Evidence to Recommendations

**PICO #5:** In adults with clinically suspected DVT (Deep Venous Thrombosis), should lower extremity US (Ultrasound) imaging be performed for optimal patient management?

### SEMPI Quality of Evidence (QOE) & Recommendation Strength

Author/Year/Title	Highlights	SEMPI QOE Rating	Final QOE Category	Recommendation Strength
Johnson et al., 2010 <a href="#">Risk of deep vein thrombosis following a single negative whole-leg compression ultrasound: a systematic review and meta-analysis</a>	A negative extremity US for deep vein thrombosis is associated with low risk for embolism	Moderate	Moderate (2)	Strong (A)
Goodacre et al., 2005 <a href="#">Systematic review and meta-analysis of the diagnostic accuracy of ultrasonography for deep vein thrombosis</a>	Combined color-Doppler US techniques have optimal sensitivity, while compression US has optimal specificity for DVT detection in symptomatic patients	Moderate		
Atri et al., 1996 <a href="#">Accuracy of sonography in the evaluation of calf deep vein thrombosis in both postoperative surveillance and symptomatic patients</a>	US is a highly accurate test with acceptable reproducibility for the detection of DVT in calf veins in both postoperative and symptomatic patients	Moderate		
Heijboer et al., 1993 <a href="#">A comparison of real-time compression ultrasonography with impedance plethysmography for the diagnosis of deep-vein thrombosis in symptomatic outpatients</a>	In making the diagnosis of deep-vein thrombosis in symptomatic outpatients, serial compression ultrasonography is preferable to impedance plethysmography, in view of its superior performance in detecting venous thrombosis	Moderate		

**Recommendation Rating: 2A**—Strong recommendation for the intervention based on moderate quality evidence

**Justification:** Moderate quality studies with consistent results support lower extremity US as a first-line imaging modality to detect DVT.

**Rating Definitions:**

**Quality of Evidence:** High quality = 1; Moderate quality = 2; Low quality = 3; Very low quality = 4

**Strength of Recommendation:** A = Strength of Recommendation from Consistent Evidence; B = Strength of Recommendation from Panel Consensus

**Conclusion:** Ample literature exists to recommend duplex US of the lower extremity over traditional diagnostic studies (e.g., impedance plethysmography, contrast venography) as the initial screening and diagnostic tool in the evaluation for suspected DVT. Because duplex US has a high diagnostic accuracy for DVT, it represents a reliable imaging tool upon which to base anticoagulation therapy. Furthermore, US is non-invasive, portable, readily available and relatively inexpensive. Inconclusive studies or negative studies in high risk clinical scenarios may warrant further investigation.

**Final Recommendation:** 2A—In adults with clinically suspected DVT (Deep Venous Thrombosis), lower extremity duplex US (Ultrasound) is recommended as the initial study for optimal patient management.

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