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Abstract

Rapid quantitative D-dimer assays (DD), lower extremity venous duplex ultrasonography (US), and multislice computed tomographic (CT) angiography have been shown to have adequate sensitivities and specificities for diagnostic purpose. The purpose of this study was to evaluate cost-effectiveness of diagnostic strategies for pulmonary embolism (PE) in patients with a high, intermediate, or low clinical probability of PE. A formal cost-effectiveness analysis for the diagnosis of PE was performed. The main outcome measure for effectiveness was 3-month expected survival. The strategy of DD followed by CT was cost-effective and had the lowest cost per life saved for all patients suspected with PE. The conventional strategy including ventilation and perfusion lung scanning followed by pulmonary angiography (PA) or CT was not cost-effective. The leg US after CT was not also cost-effective. In clinical practice, the individual patient's condition should be considered when choosing appropriate diagnostic tests.

Keywords

cost-effectiveness analysis, pulmonary embolism, diagnosis, clinical probability, D-dimer, multislice computer tomographic angiography, venous duplex ultrasonography

Introduction

Pulmonary embolism (PE) is a major health care concern affecting approximately 600 000 new patients each year in the United States.¹ Approximately 1% of hospitalized patients are diagnosed with PE. Pulmonary embolism is responsible for at least 10% of inpatient deaths.¹ The purpose of this study was to perform a cost-effectiveness analysis (CEA) for the diagnosis of PE, given the recent improvements in multislice computed tomographic (CT) angiography for detecting PE, lower extremity venous duplex ultrasonography (US), and rapid quantitative D-dimer (DD) assays.

A wide variety of diagnostic strategies for PE have previously been evaluated using CEA methods,²⁻¹¹ but as the technology changes and the accuracy of diagnostic tests improves, CEAs need to be updated. Spiral CT angiography has been documented as a cost-effective alternative to ventilation and perfusion (V/Q) scans for the diagnosis of PE.³⁻¹¹ Most of the previous analyses compared single-slice CTs with V/Q scans and reported that the use of spiral CT may increase costs if more tests were required due to insufficient sensitivity (70%-95%) for spiral CT.¹¹ However, more recent studies have used multislice CT improving the image quality for defining peripheral emboli; making CT more accurate in the diagnosis of PE.¹²⁻¹⁴ The Second Prospective Investigation of PE Diagnosis (PIOPED II) reported a sensitivity of 83% and a specificity of 96% for the multislice spiral CT in determining subsegmental PE.¹³

The combination of a pretest clinical probability of PE and a normal DD test has been suggested by some authors to be accurate enough for the exclusion of PE.^{12,14,15} The diagnostic performance of DD is strongly dependent on the reliability of the DD assay being used. New DD assays with improved accuracy and rapid test results have been introduced since the PIOPED II study and have been clinically validated.^{12,16,17}

Methods

Decision Model

A decision model (Figure 1) was constructed (TreeAge Pro Suite, TreeAge Pro Software, Inc, Williamston, Massachusetts)

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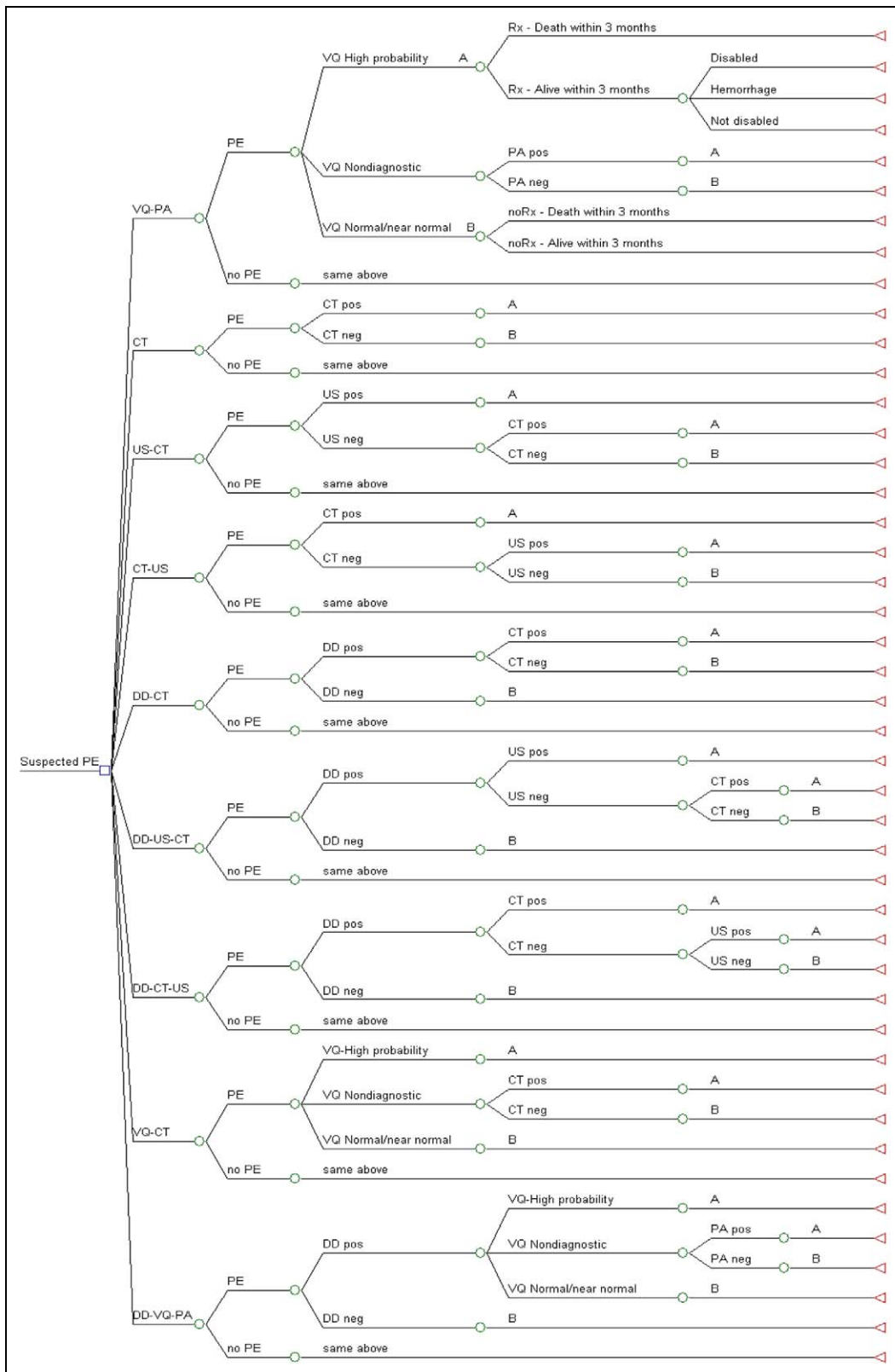


Figure 1. Decision model for PE diagnostic strategies. A, A subtree for PE diagnosis with anticoagulation therapy. B, A subtree for no-PE diagnosis with no therapy. CT indicates multislice computer tomographic; DD, d-dimer (a rapid qualitative ELISA); US, lower extremity venous duplex ultrasonography; V/Q, ventilation and perfusion scan; PA, pulmonary angiography; Rx, anticoagulation therapy; noRx, no treatment; pos, positive; neg, negative; PE, pulmonary embolism; ELISA, enzyme-linked immunosorbent assay.

Table 1. Prevalence of PE and Diagnostic Tests: Baseline Values and Ranges for Parameters

Parameter	Baseline	Range	References
Prevalence of PE according to clinical probability			PIOPED study ¹⁸
Overall PE prevalence	0.284	0.15–0.50	Perrier et al ⁸
High	0.69	0.65–0.80	
Intermediate	0.37	0.25–0.40	
Low	0.10	0.05–0.15	
Outcome of V/Q scan in patients with PE			PIOPED study ^{18,a}
High probability of PE	0.57	0.41 ^a –0.70 ^b	Wells et al ^{19,b}
Nondiagnostic	0.41	0.28 ^b –0.57 ^a	Perrier et al ⁸
Normal/near normal	0.20	–	
Outcome of V/Q scan in patients without PE			
High probability of PE	0.02	–	
Nondiagnostic	0.67	0.66 ^b –0.78 ^a	
Normal/near normal	0.31	0.20 ^a –0.32 ^b	
D-dimer (rapid ELISA method) for PE			Stein et al ²⁰
Sensitivity	0.97	0.83–1.00	Di Nisio et al ²¹
Specificity	0.41	0.28–0.51	Le Gal et al ²²
Lower extremity venous duplex ultrasonography for DVT			
Sensitivity	0.39	0.32–0.46	
Specificity	0.99	0.97–1.0	
Multislice CT angiography			PIOPED II study ^{13,c}
Sensitivity	0.83 ^c	0.62–0.95	Perrier et al ⁸
Specificity	0.96 ^c	0.86–0.97	Paterson et al ⁶
Pulmonary angiography			Perrier et al ⁸
Sensitivity	0.97	0.9–1.0	
Specificity	0.98	0.9–1.0	

Note: PE = pulmonary embolism; V/Q = ventilation and perfusion; DVT = deep vein thrombosis; CT = computed tomography; ELISA = enzyme-linked immunosorbent assay.

for the following 9 diagnostic strategies for patients with suspected PE:

V/Q ± PA: Patients undergo a V/Q lung scan. Patients with a high probability of PE receive treatment. Patients with a nondiagnostic V/Q results undergo pulmonary angiography (PA).

V/Q ± CT: This strategy is similar to V/Q ± PA.

CT: Patients with suspected PE undergo a spiral CT scan as a single test for PE diagnosis.

CT ± US: Patients with an initial normal CT undergo a lower extremity US and are treated according to the results.

US ± CT: Patients undergo lower extremity US. Patients with a normal US undergo a spiral CT scan and are treated accordingly.

DD ± CT: Testing starts with DD. An abnormal DD is followed by a spiral CT scan.

DD ± US ± CT: DD test is performed as an initial test followed by a lower extremity US in patients with an abnormal DD result. Those with a negative US undergo CT scan. Patients with positive CT scan receive anticoagulation treatment.

DD ± CT ± US: This strategy is similar to DD ± US ± CT except for the order of the CT and US.

DD ± V/Q ± PA: DD test is performed first. Patients with an abnormal DD test undergo a V/Q lung scan followed by a PA if the V/Q scan is nondiagnostic.

Parameters Used in the Analysis

Table 1 presents the parameters for the prevalence of PE and characteristics of individual tests.

Prevalence of PE according to clinical probability. Each diagnostic strategy for PE was evaluated for 3 levels of clinical probability of PE (low, intermediate, and high) since most PE diagnostic algorithms recommend patients be assessed according to their clinical probability or likelihood of having a PE.^{12,14,15,23} The clinical probability of PE can be assessed empirically by experienced clinicians using patient history and physical examination, including chest X-ray or/and arterial blood gas analysis¹⁸ or by standardized clinical assessment tools (eg, Wells score^{19,24,25} or Geneva score²⁶).

D-dimer. DD is a degradation product of cross-linked fibrin and is used as a screening blood test used to access patients with suspected PE. Various types of DD assays are available. In this analysis, a rapid quantitative enzyme-linked immunosorbent assays (ELISA) of DD was used for conducting the CEA, for

Table 2. Clinical Outcomes for Base Case Analysis and Sensitivity Analyses^a

Probability	Baseline	Range	References
Death from PE within 3 months			
Untreated mortality	0.25	0.15–0.35	Perrier et al ⁸
Treated mortality	0.08	0.02–0.015	Perrier et al ⁸
No PE	0.30	0–0.60	Paterson et al ⁶
Anticoagulation therapy			Perrier et al ⁸
Mortality	0.002	0.001–0.004	
Major Bleeding	0.008	0.006–0.012	
Risk of permanent disability	0.08	0.04–0.01	
Adjusted quality of life factor for permanent disability	0.005	0.002–0.008	
Spiral CT			Perrier et al ⁸
Mortality	0.0001	0.00005–0.0002	
Pulmonary angiography (PA)			Perrier et al ⁸
Mortality	0.002	0–0.003	
Among patients with PA receiving contrast material need for short-term hemodialysis	0.0029	0–0.0095	Paterson et al ⁶

Note: PE = pulmonary embolism; CT = computed tomography.

^a Patients without PE who are not treated have a 3-month expected survival of 100%. Patients with PE who are treated have an expected survival of 91.8% (100% minus a mortality of 8% associated with treating PE and minus a mortality of 0.2% from 3 months of anticoagulation therapy). The 0.064% risk of permanent disability is derived from the 0.8% risk of major hemorrhage associated with anticoagulation therapy multiplied by the 8% risk of permanent disability due primarily to hemorrhagic stroke. Therefore, the final expected survival for the patients with permanent disability due to anticoagulation treatment is estimated to be 91.768% (91.8% – [0.064% × 0.5]).

which results can be obtained within 30 to 60 minutes, with 97% sensitivity and 41% specificity.^{20,21}

Lower extremity venous duplex US. Venous thromboembolism (VTE) manifests as a PE or deep vein thrombosis (DVT), which shares the same pathophysiologic process and thus, the treatment for stable PE and DVT are the same. Approximately 50% to 70% of patients with proven PE have concomitant DVT.^{27–29} Therefore, a lower extremity examination by US has been suggested as an initial diagnostic test to reduce unnecessary V/Q scans or as a secondary diagnostic test if the V/Q scan is indeterminate.^{12,30} The diagnostic accuracy of US is higher in patients with clinical symptoms of DVT (sensitivity 72%, 95% confidential interval [CI] = 58–83, specificity 100%, 95% CI = 83–100) than those without clinical symptoms (sensitivity 38%, 95% CI = 21–36, specificity 99%, 95% CI = 97–100).²² We used 39% of US sensitivity (95% CI = 32–46) and 99% of US specificity (95% CI = 97–100) in patients with suspected PE with/without leg symptoms reported by Le Gal et al.²²

Computed tomographic pulmonary angiography. Spiral CT has become the preferred initial diagnostic modality for PE because it is convenient, less invasive than PA, and because of its additional advantage over V/Q lung scans by revealing alternative diagnoses such as pneumonia, pneumothorax, aortic dissection, or tumor.³¹ A major concern of the single-slice CT scanner is the wide range of reported sensitivities^{32,33} and specificities^{32,34} and its inability to identify subsegmental PE.¹³ However, the new generation multislice CT scanners were used in

this analysis because they can detect peripherally located thrombi in fifth-order branches with 1 breath-hold,³⁵ with improved sensitivities and specificities.^{12,13,17,36}

Ventilation and perfusion lung scan. The British Thoracic Society Guidelines³⁷ suggest the V/Q scan as a first imaging test for PE diagnosis. However, more than 60% of patients who undergo V/Q scanning have a nondiagnostic scan (low or intermediate probability of PE),¹⁸ which necessitates further diagnostic testing, and the interobserver correlation for results of V/Q scans has also been reported to be poor.³⁸

Pulmonary angiography. Pulmonary angiography (PA) is the most specific examination for the diagnosis of PE and can detect emboli as small as 1 to 2 mm.³⁵ Thus, PA was long considered the gold standard for PE diagnosis; however, PA is rarely performed because it is too expensive, invasive, requires the use of a contrast agent, and has a high rate of interobserver disagreement for subsegmental PE.³⁹

The main outcome measure for effectiveness was a 3-month expected survival expressed as a percentage. Patients diagnosed with PE are assumed to receive at least 3 months of anticoagulation therapy. Table 2 presents the probability of mortality and morbidity associated with PE and the individual diagnostic tests.

The analysis took the perspective of the US government as a third-party payer for health services. Indirect costs such as the loss of earnings were not considered in this model. The costs of the diagnostic procedures and resulting therapies for PE are

Table 3. Costs of Diagnostic Tests and Anticoagulation Therapy

Variables	Baseline ^a	Range	References
Diagnostic tests			CMS ^b
D-dimer: quantitative	\$14	\$8–19	
Lower extremity venous duplex ultrasonography (bilateral)	\$266	\$199–346	
V/Q scan: pulmonary perfusion with ventilation	\$202	\$158–258	
Spiral CT: CT angiography chest with/without contrast	\$648	\$486–852	
Pulmonary angiography (bilateral)	\$651	\$488–855	
Anticoagulation therapy ^c (mean cost per patient) ^d	\$7 687	\$2570–10 280	Perrier et al ⁸
Contrast-induced acute renal failure, requiring hemodialysis [§]	\$10 743	\$5.371–32 228	Paterson et al ⁶

Note: CMS = The Centers for Medicare and Medicaid Services.; V/Q = ventilation and perfusion; CT = computed tomography.

^a Costs are expressed in 2006 US dollars.

^b Costs of PE diagnostic tests were from CMS 2006 United States Medicare fee for service payment: www.cms.gov.

^c Anticoagulation therapy includes a 8-day hospital stay, 3-month warfarin therapy, and the risk and cost of major hemorrhage was also included.

^d Costs for anticoagulation therapy and contrast-induced acute renal failure were adjusted to 2006 values using Consumer Price Index (CPI) from US Department of Labor, Bureau of Labor Statistics <http://www.bls.gov/>.

presented in Table 3. All costs were expressed in 2006 US dollars.

To determine cost-effectiveness, the costs and survival rates for each strategy were plotted to determine the dominant strategies. Strategies are dominant if they have lower costs and better survival compared to other strategies, that is strategies to the upper left in a plot of survival versus cost. The incremental cost-effectiveness ratio (ICER), the ratio of the difference in cost divided by the difference in survival between the 2 strategies, is calculated to compare the dominant strategies.

Sensitivity analyses were performed to test the stability of the results over a wide range of clinically relevant values.

Results

Baseline Analysis

Plots of survival versus cost for each diagnostic strategy are presented in Figure 2. The 3 different plots represent each of the 3 different a priori clinical probabilities of PE (high, intermediate, and low). Three strategies (DD ± CT, DD ± US ± CT, and US ± CT) dominated all the other strategies in patients with a high or intermediate clinical probability of PE. The dominant strategies in patients with a low clinical probability of PE were DD ± CT, CT alone, and US ± CT. The dominated strategies cost more for equivalent or worse survival. The strategy of CT first and then leg US was dominated by the strategies of US followed by CT in all patients suspected with PE.

Table 4 presents cost, survival, and incremental cost-effectiveness (cost per additional life saved) for the dominant PE diagnostic strategies. The strategy with the lowest cost per life saved was DD ± CT in all 3 clinical probabilities of PE categories. In patients with either a high or intermediate clinical probability of PE, DD ± US ± CT saved more lives compared to DD ± CT but costs more; and US ± CT saved even more lives compared to DD ± US ± CT but costs even more. In patients with a low clinical probability of PE, the CT alone strategy saved more lives compared to DD ± CT but costs

more and the US ± CT cost was much higher than the strategies of DD ± CT and CT alone test.

The incremental cost per additional life saved in using DD ± US ± CT instead of DD ± CT was \$72 446 in the high and \$110 933 in the intermediate clinical PE probability category. The incremental cost per additional life saved in using US ± CT instead of DD ± US ± CT was \$124 815 in the high and \$300 377 in the intermediate clinical PE probability categories. In the low clinical probability category, when switching the strategy from DD ± CT to CT alone and from CT to US ± CT, the incremental costs per additional life saved were \$507 658 and \$4 064 823, respectively.

Sensitivity Analysis

One-way sensitivity analyses were conducted on all parameters in the model (Tables 1-3) for each clinical probability of PE category (high, intermediate, and low). With one exception, the ranking of strategies was robust in the high and intermediate probability categories, whereas the value of some parameters affected the dominant diagnostic strategies in patients with low clinical probability of PE. When the sensitivity of DD was 99% or above, the strategy of US ± CT was no longer dominant in high and intermediate clinical probability categories.

In the low PE clinical probability category, when the specificity of CT was lower than 95%, the strategy of DD ± VQ ± PA became an additional dominant strategy with a cost per life saved only slightly lower than DD ± CT. With a specificity of 97% for CT or when the specificity of US was less than 98%, US ± CT was no longer dominant. When the cost of CT was \$760 or higher, the strategy of DD ± VQ ± PA became an additional dominant strategy with a cost per life saved only slightly lower than DD ± CT.

When the sensitivity of US was less than 34%, US ± CT was no longer dominant in the low PE clinical probability category and the strategy of DD ± CT ± US became dominant instead of DD ± US ± CT in high and intermediate PE clinical probability categories.

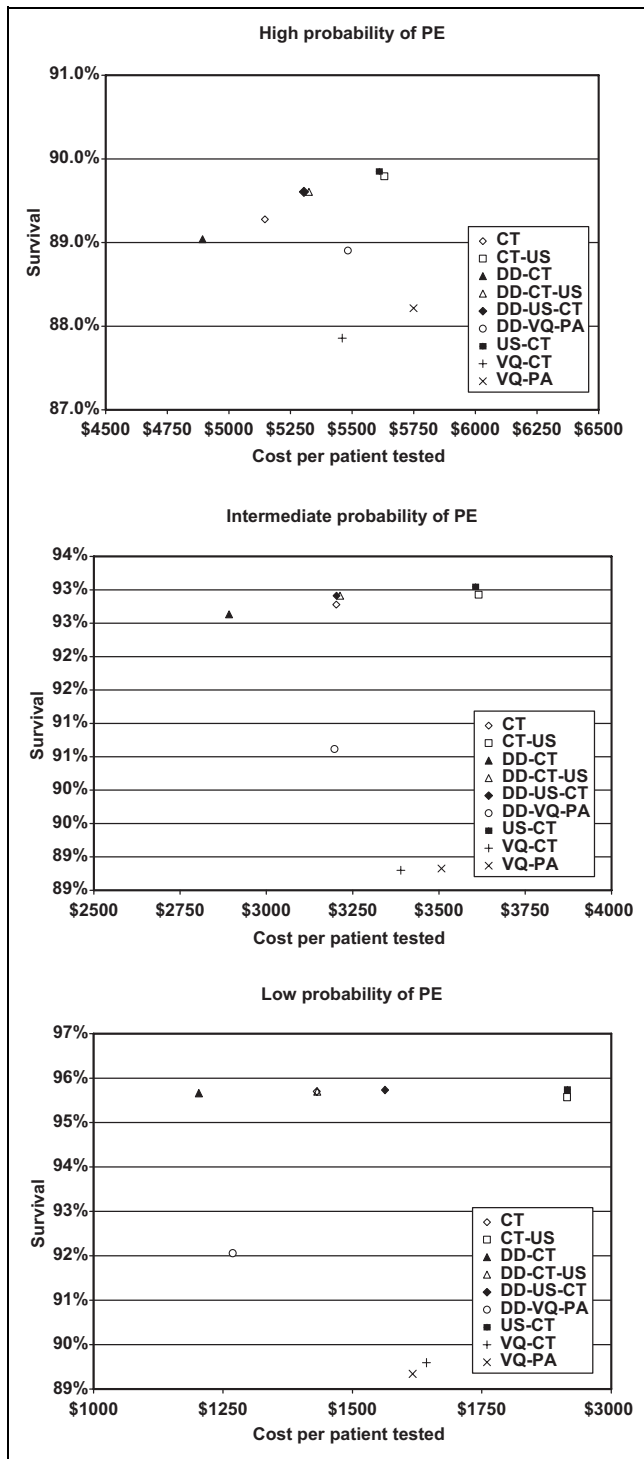


Figure 2. Cost per patient tested and percentage surviving for each strategy by clinical probability of PE. Dominated strategies are in boldface.

Discussion

The results from this analysis using updated sensitivities and specificities for multislice CT angiography, lower extremity venous US, and rapid quantitative DD assays for the diagnosis of PE indicates that the strategy of DD ± CT had the lowest

cost per life saved in patients with a low, intermediate, or high clinical probability of PE. DD ± US ± CT and to a greater extent US ± CT saved more lives but at a higher cost compared to DD ± CT in patients with a high or intermediate clinical probability of PE. For patients with a low clinical probability of PE, the strategies of CT as a single test and US ± CT saved more lives than DD ± CT. However, its rather modest incremental cost per additional life saved indicates that US ± CT could be the strategy of choice in patients with intermediate (\$300 377 per additional life saved) or high (\$124 815 per additional life saved) clinical probability of PE. For patients with a low clinical probability of PE, the \$4 064 823 incremental cost per additional life saved for US ± CT may be viewed as too high and CT as a single test would more likely be selected because of its more reasonable cost of \$507 658 per additional life saved.

The combination of assessment of clinical probability for PE and DD testing has been recommended as an initial workup in outpatients with suspected PE before a decision on further diagnostic testing is made.²⁵ However, the results of DD testing are affected by comorbidities such as postsurgery, malignancy, acute infection, pregnancy, or postpartum, which are common conditions of hospitalized patients.⁴⁰ Our finding that US ± CT without DD has an acceptable cost per additional life saved for patients with intermediate or high clinical probability of PE suggests that DD may not be necessary for those patients. We used a sensitivity of 97% for DD in our baseline analysis. Our sensitivity analysis indicated that only when the sensitivity of DD is 99% or above is US ± CT dominated by DD ± US ± CT. Only if there is good evidence that the sensitivity of DD is 99% or greater would DD ± US ± CT be the strategy of choice for patients with intermediate or high clinical probability of PE.

The sensitivity analysis indicated that the dominant strategies changed somewhat in the low clinical probability group depending on the specificity of CT and specificity of US and the cost of CT. However, none of these changes would affect our conclusion that DD ± CT is the strategy of choice for patients with a low clinical probability of PE.

In this analysis, the cost-effectiveness of DD ± CT ± US and CT ± US strategies were compared to DD ± US ± CT and US ± CT. The strategies where CT came before US were dominated by and therefore were less cost-effective than the strategies where US came before CT. This is because the cost of venous duplex ultrasound is less than the cost of multislice CT scanning. The treatment for DVT and stable PE are the same since their pathophysiology is similar.⁴¹ This means that if a lower extremity US is positive for an acute DVT, the patient can be treated with anticoagulants. If lower extremity US fails to find a thrombus in the legs, then a CT scan is used to rule out PE. The use of lower extremity US before spiral CT can also reduce the risks of radiation associated with CT scanning.

A recent CEA of PE diagnostic strategies was performed by Righini and colleagues⁴² using data from 2 prospective multicenter outcome studies.^{12,23} Righini et al focused on the influence of age on the diagnostic strategies including clinical probability assessment, DD measurement, lower limb venous ultrasound, and spiral CT. Similar to our study results, the

Table 4. Cost, Survival, and Incremental Cost-effectiveness of Dominant Strategies for PE Diagnosis

Strategy in Each Clinical Probability Category	Cost per Patient	Survival per Patient	Cost per Life Saved ^a	Incremental Cost per Additional Life Saved ^b
High clinical probability				
DD ± CT	\$4893	89.04%	\$5496	
DD ± US ± CT	\$5304	89.61%	\$5919	\$72 446
US ± CT	\$5610	89.85%	\$6243	\$124 815
Intermediate clinical probability				
DD ± CT	\$ 2892	92.63%	\$3122	
DD ± US ± CT	\$ 3203	92.91%	\$3448	\$110 933
US ± CT	\$ 3606	93.05%	\$3875	\$300 377
Low clinical probability				
DD ± CT	\$ 1204	95.66%	\$1258	
CT	\$ 1563	95.73%	\$1633	\$507,658
US ± CT	\$ 1915	95.74%	\$2000	\$4,064,823

^a Cost per life save (cost-effectiveness ratio) = cost per patient/improved survival per patient.

^b Incremental cost per additional life saved (incremental cost-effectiveness ratio) = difference in cost/difference in survival.

strategies in Righini's study using DD were cost-effective in all age groups, except the 80 years and older group. Righini et al addressed the issue of compression ultrasound being costly and only marginally improving the effectiveness of diagnostic strategies for PE. However, they did not look at the ICER for the testing strategies. As shown in Table 4, the ICERs were compared among dominating strategies for PE diagnosis in our analysis. The strategies including leg US saved more lives with an acceptable cost increase than the strategies without US in patients with a high or intermediate clinical probability of PE.

Recently, Righini et al evaluated the safety of the strategy of DD followed by CT compared with the strategy of DD ± CT ± US in the diagnosis of PE in a multicenter randomized controlled trial.⁴³ They concluded that the strategy of DD ± CT is as safe as DD ± CT ± US and leg US should be applicable for those with a contraindication to CT. The result from our theoretical cost-effective analysis supported their finding through clinical studies.

In this analysis, we included US for both legs from the inferior vena cava to the calf veins, which is the diagnostic procedure used to exclude the presence of DVT recommended by the Intersocietal Commission for the Accreditation of Vascular Laboratories, the accrediting body for diagnostic vascular laboratories.⁴⁴ We did not test which US procedure, either limited to proximal legs only or extended to distal legs was more cost-effective. Elias et al addressed in their cost-effective analysis that the strategy of US extending to lower extremities ± CT improves survival at an acceptable extra cost per life saved compared with DD ± US limited to proximal legs ± CT.⁴ However, most recently, Righini et al assessed in a randomized clinical trial whether the use of additional distal vein US increased the diagnostic yield of the test in patients with suspected PE and reported that distal US has limited diagnostic performance and only modestly increased the yield of US.⁴⁵

With advances in CT technology in the past decade, multislice CT has replaced V/Q scanning for a PE diagnostic workup in modern clinical practice.⁴² The strategies including V/Q scans were not cost-effective in this analysis. However, V/Q

scanning has merits including lower radiation exposure, lower costs, and better availability in some clinical settings compared to multislice CT scans.⁴⁶ V/Q scans combined with clinical probability assessments and lower extremity US are recommended for pregnant and nursing women and for patients with contrast allergies.⁴⁶

The choice of strategy depends on the willingness to pay threshold.⁴⁷ There has not been a consensus on the willingness to pay threshold for saving a life in medicine in the United States. However, approximately \$50 000 to 60 000 per quality-adjusted life year (QALY) threshold has been accepted for medical interventions.⁴⁸⁻⁵⁰ Therefore, a rough estimate for the threshold per life saved could be derived from the cost per QALY threshold, life expectancy of a person with PE, and the QALYs in each of his or her remaining years. The incidence of PE increases sharply after age 60 in both females and males.⁵¹ The life expectancy is 20.4 years for a 60-year-old man and 23.5 years for a 60-year-old woman.⁵² Although the QALYs for each remaining year would be somewhat less than 1 (1 equals perfect health) for a 60-year-old person with his or her possible comorbidities, assuming a QALY of 1 to each remaining year would produce a "generous" estimate of a threshold for the willingness to pay to avoid a death from PE. In this case, the cost per life saved would be \$1 100 000 (\$50 000 [cost per QALY threshold] × 22 years [life expectancy] × 1 [QALY]).

With the threshold of \$1 100 000 per life saved, the strategy of US ± CT for patients with a high or intermediate clinical probability of PE would be cost-effective and have a reasonable incremental cost per life saved. The incremental cost per additional life saved with the diagnostic strategy of US ± CT changing from DD ± US ± CT was \$124 815 for patients with high clinical probability and \$300 377 for intermediate clinical probability of PE (see Table 4). The strategy of CT alone for patients with a low clinical probability of PE had a moderate incremental cost per life saved (\$300 377) relative to the strategy of DD ± CT and would therefore be considered cost-effective. Because of the relatively large incremental cost

per life saved of US \pm CT (\$4 064 823) relative to CT alone, the strategy of US \pm CT would not be viewed as being cost-effective for patients with a low clinical probability of PE.

In summary, this CEA showed that the strategy combining clinical probability assessment, DD (rapid quantitative ELISA), and multislice CT scan had the lowest cost per life saved in patients with suspected PE. However, the analyses demonstrated that a maximum number of lives could be saved at reasonable cost (*a*) for patients with an intermediate and high clinical probability of PE with the use of US \pm CT (lower extremity US followed by a multislice CT scan); and (*b*) for patients with a low clinical probability of PE with the use of multislice CT alone. The results of this study are based on an assumption that all patients were assessed for their clinical probability of having a PE using a standard scoring tool (Wells score, Geneva score, etc). This study does not suggest that all patients with PE symptoms have venous duplex scanning as the initial diagnostic test. Patients need to be assessed for their clinical probability of having a PE prior to undergoing further diagnostic studies. In clinical settings, health care providers should also consider individual patient conditions (eg, pregnancy, renal insufficiency) in the choice of diagnostic tests so as to decrease cost and exposure to radiation.

Declaration of Conflicting Interests

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