The Economic Value of Hybrid Single-photon Emission Computed Tomography With Computed Tomography Imaging in Pulmonary Embolism Diagnosis

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ABSTRACT

Objective: The objective was to quantify the potential economic value of single-photon emission computed tomography (SPECT) with computed tomography (CT; SPECT/CT) versus CT pulmonary angiography (CTPA), ventilation–perfusion (V/Q) planar scintigraphy, and V/Q SPECT imaging modalities for diagnosing suspected pulmonary embolism (PE) patients in an emergency setting.

Methods: An Excel-based simulation model was developed to compare SPECT/CT versus the alternate scanning technologies from a payer's perspective. Clinical endpoints (diagnosis, treatment, complications, and mortality) and their corresponding cost data (2016 USD) were obtained by performing a best evidence review of the published literature. Studies were pooled and parameters were weighted by sample size. Outcomes measured included differences in 1) excess costs, 2) total costs, and 3) lives lost per annum between SPECT/CT and the other imaging modalities. One-way (±25%) sensitivity and three scenario analyses were performed to gauge the robustness of the results.

Results: For every 1,000 suspected PE patients undergoing imaging, expected annual economic burden by modality was found to be 3.2 million (SPECT/CT), 3.8 million (CTPA), 5.8 million (planar), and 3.6 million (SPECT) USD, with a switch to SPECT/CT technology yielding per-patient-per-month cost savings of $51.80 (vs. CTPA), $213.80 (vs. planar), and $36.30 (vs. SPECT), respectively. The model calculated that the incremental number of lives saved with SPECT/CT was six (vs. CTPA) and three (vs. planar). Utilizing SPECT/CT as the initial imaging modality for workup of acute PE was also expected to save $994,777 (vs. CTPA), $2,852,014 (vs. planar), and $435,038 (vs. SPECT) in "potentially avoidable"' excess costs per annum for a payer or health plan.

Conclusion: Compared to the currently available scanning technologies for diagnosing suspected PE, SPECT/CT appears to confer superior economic value, primarily via improved sensitivity and specificity and low nondiagnostic rates. In turn, the improved diagnostic accuracy accords this modality the lowest ratio of expenses attributable to potentially avoidable complications, misdiagnosis, and underdiagnosis.

Every year in the United States, an estimated 600,000 to 900,000 individuals suffer from acute pulmonary embolism (PE) and account for an estimated 200,000 to 300,000 hospital admissions.[1–3] Acute PE is a potentially fatal disease with mortality between 10 and 30% if untreated.[4,5] Although various symptoms, signs,

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laboratory tests, and/or predisposing patient factors can be used to formulate a clinical likelihood of PE, these parameters are often nonspecific[6,7] making PE diagnosis very challenging even in a highly suspected case.

For suspected acute PE patients, clinical evaluation followed by laboratory testing is a crucial part of the initial care pathway. Historically, diagnostic evaluation for acute PE was performed with ventilation–perfusion (V/Q) planar lung scintigraphy, which can depict the perfusion defects caused by emboli. However, planar scan was surpassed in the 1990s by computed tomographic pulmonary angiography (CTPA) as the imaging modality of choice for diagnosing acute PE, due to several factors, including the inherent limitation of two-dimensional imaging, higher-than-acceptable nondiagnostic rate, and limited speed and access particularly on nights and weekends.[8,9] Multidetector CTPA has since become the primary radiologic tool to establish PE diagnosis in daily clinical practice due to its speed, reliability, accessibility, and relatively acceptable sensitivity and specificity.[1] V/Q single-photon emission computed tomography (V/Q SPECT), which utilizes three-dimensional nuclear medicine imaging of ventilation and perfusion, is an underutilized but valuable tool to evaluate and quantify the extent of acute PE, as well as establish alternate diagnoses.[10] The imaging practice guidelines of the Society of Nuclear Medicine detail the advantage of using SPECT to obtain a three-dimensional evaluation of the lungs,[11] while the European Association of Nuclear Medicine guidelines recommend V/Q SPECT as the preferred modality whenever possible.[4] Despite its high diagnostic accuracy, the use of SPECT for evaluation of acute PE remains limited.[12] This is attributed partially to the restricted access and availability of the SPECT scanners and may also be related to the limitations of the ordering physician's familiarity with this procedure.

SPECT/CT (SPECT combined with computed tomography), which enables the acquisition of V/Q SPECT and CT scans of the lung in a single imaging session, provides further advantage over SPECT. Fusing coregistered functional and anatomic data results in more accurate localization and definition of scintigraphic findings, thus giving SPECT/CT added clinical value over SPECT or stand-alone CT imaging.[5,13] Gutte et al.,[14] performing a head-to-head comparison of V/Q SPECT/CT, V/Q SPECT, and CTPA, demonstrated that V/Q SPECT/CT and SPECT had the highest sensitivity (97%), whereas V/Q SPECT/CT and CTPA had the highest specificity (100%), and that V/Q SPECT/CT alone had the highest accuracy rate (99%) among the three modalities. Specifically, the addition of low-dose noncontrast CT to V/Q SPECT increased specificity from 88% to 100%, without affecting sensitivity. This was attributed to the additional information available on CT, which may provide alternative explanations for subtle perfusion defects (e.g., small interlobar fissures, emphysema) that may otherwise be falsely interpreted as PE (e.g., by SPECT). SPECT/CT was also associated with zero inconclusive assessments, in comparison to 5% for V/Q SPECT, along with improvements in interpretation confidence. The relatively small sample sizes in this prospective trial warrant confirmation with larger studies.

Given the current challenges in healthcare to contain costs while improving patient outcomes, we attempted to quantify the potential economic value of SPECT/CT versus other imaging modalities (CTPA, planar, and SPECT), to establish the diagnosis of suspected PE patients in an emergency department (ED) setting from a health plan payer's perspective. The primary study objective was to evaluate the 1) total cost burden and 2) magnitude of "potentially wasteful" excess costs associated with each imaging modality under consideration. A secondary objective of this simulation model focused on estimating the total lives lost following each imaging strategy.

METHODS

To compare the cost impact of V/Q SPECT/CT versus CTPA, V/Q planar scintigraphy, and V/Q SPECT, a simulation model was built using MS Excel 2013. A best evidence review of articles via PubMed published between January 1, 2005, and February 29, 2016, was performed. A total of 81 comparative studies assessing the sensitivity, specificity, and/or nondiagnostic rates of PE diagnosis were identified in this preliminary search. Inclusion criteria included 1) English language studies, 2) adult human subjects (≥18 years of age), 3) relevant (e.g., in vivo) clinical and imaging application(s), 4) ED evaluation, and 5) use of any type of V/Q imaging (i.e., planar, SPECT, and SPECT/CT). The following types of studies were excluded: 1) ventilation or perfusion only; 2) pediatrics or adolescents only; 3) in vitro, animal, or cadaver research; and 4) case reports, commentaries, and editorials. Estimates obtained from all the studies meeting the inclusion criteria (n = 49) were then pooled and weighted by their respective sample sizes (see Table 1).[15,16]

Table 1
Best Evidence Literature Review Summary

Model Parameters	Weighted Average	Range	References
PE prevalence	22.7%	7.5%–66.7%	6,8,9,14,20,27,33–55
Scan Information			
Imaging and radiology commercial reimbursement cost			
SPECT/CT	$525		Medicare national payment for CPT code 78582
Unlisted respiratory procedure (used only in scenario analysis 2)	$498		Medicare national payment for CPT code 78599
CTPA	$347		Medicare national payment for CPT code 71260
Planar	$525		Medicare national payment for CPT code 78582
SPECT	$525		
Medicare-to-commercial adjusting factor	1.5	1.45–1.55	Aggregated hospital payment-to-cost ratio for private payers[21]
Sensitivity			
SPECT/CT	95.9%	92.86%–99.01%	14,27,49,56
CTPA	88.2%	67.7%–94.4%	8,14,34,36,42,54,57
Planar	78.8%	57.1%–77.4%	24,33,47,58
SPECT	95.8%	90.63%–100%	9,14,27,33,35,37,38,40,56,58
Specificity			
SPECT/CT	98.5%	90.63%–100%	14,27,49,56
CTPA	97.3%	85.7%–100%	8,14,24,34,36,42,47,54,57,58
Planar	81.1%	42.9%–98.7%	24,33,47,58
SPECT	97.0%	82.67%–100%	9,14,27,33,35,37,38,40,56,58
Nondiagnostic rate			
SPECT/CT	0.4%	0%–0.66%	14,27
CTPA	5.1%	0%–40%	8,9,14,27,34,36,40,42,45,59,60,12,47,53,55,61–63
Planar	31.2%	0%–48.98%	9,24,33,40,47,58
SPECT	5.8%	0%–17.6%	9,12,14,27,33,35,40,53,58,63,64
CTPA AEs			
Major contrast allergy rate	1.0%	0.2%–2.28%	8,9,14,34,42,45
Pretreatment cost (oral corticosteroid and diphenhydramine)	$2.5	≥0	65
CIN rate	10.3%	1.03%–16.67%	9,66–69
Treatment cost	$5,025	$4,899–$29,392	19,70–72
RF rate	0.7%	0%–2%	67,68,73
Treatment cost	$7,966	$5,974–$9,957	19,70–72,74
Mortality rate	59.4%	57.14%–66.67%	67,68
PE treatment costs			
Hospitalization costs	$9,622	$9,366–$10,928	18,19
In-hospital + 30-day mortality	12.18%	9.14%–15.23%	18,19
6-month anticoagulation therapy + follow-up visit costs	$1,457	$1,010–$1,684	25,75
Overdiagnosis			
Major bleeding episode rate	2.0%	1.5%–2.5%	76
Average bleeding event cost	$18,469	$17,764–$19,174	77
Fatal bleeding episode	10%	7.5%–12.5%	20
Underdiagnosis			
Untreated PE/DVT recurrence rate	2.7%	0.1%–11.1%	8,29,40,42,43,45–48,60,78
Untreated PE/DVT recurrence event cost	$11,014	$8,260–$13,768	75
Untreated PE mortality rate	20.0%	10%–30%	5
End-of-life care cost	$17,104	$6,027–$24,541	79,80

AE = adverse event; CTPA = CT pulmonary angiography; DVT = deep venous thrombosis; PE = pulmonary embolism; RF = renal failure; SPECT = single-photon emission CT; SPECT/CT = single-photon emission CT with CT.

Model Scaffold

Multiple guidelines, including the American College of Physicians/American Academy of Family Physicians, the American College of Emergency Physicians, and the European Society of Cardiology, recommend that PE can be ruled out if the clinical suspicion is low and the D-dimer test is negative.[17] However, in cases where the clinical suspicion is moderate or high and/or the D-dimer test is positive, a conclusive imaging test such as a V/Q study or CTPA is needed to confirm or exclude the diagnosis of PE. Therefore, the model addressed a hypothetical cohort of 1,000 patients with suspected acute PE presenting to an ED during the course of a year, who required imaging as per guideline recommendations (i.e., a Wells score of >2 *or* positive Pulmonary Embolism Rule Out Criteria score [intermediate/high] *or* D-dimer assay value > 0.2 μg/L). Figure 1 presents the hypothetical care pathway evaluated in the current study, the model scaffold, and the key assumptions behind the model.

If the initial imaging exam yielded a nondiagnostic result, the model patient followed a pathway dependent on the initial scan type. Specifically, a nondiagnostic CTPA prompted either further evaluation with V/Q planar scan (50%) or with empiric clinical management (50%). Practical considerations led us to assume that these secondary scan results would always be diagnostic. In the empirically managed patients, a repeat scan was not performed, and management was modeled as if treatment decisions were made using clinical parameters. Specifically, 75% of these patients were treated empirically with anticoagulation. For modeling purposes, it was assumed that all of the empirically treated patients who had PE were included in the subgroup that received empiric treatment. The remaining 25% would be discharged with no anticoagulation treatment. This empiric treatment scheme was informed by the clinical experience of the authors. For those patients receiving an indeterminate initial V/Q scan (of any type), a clinical

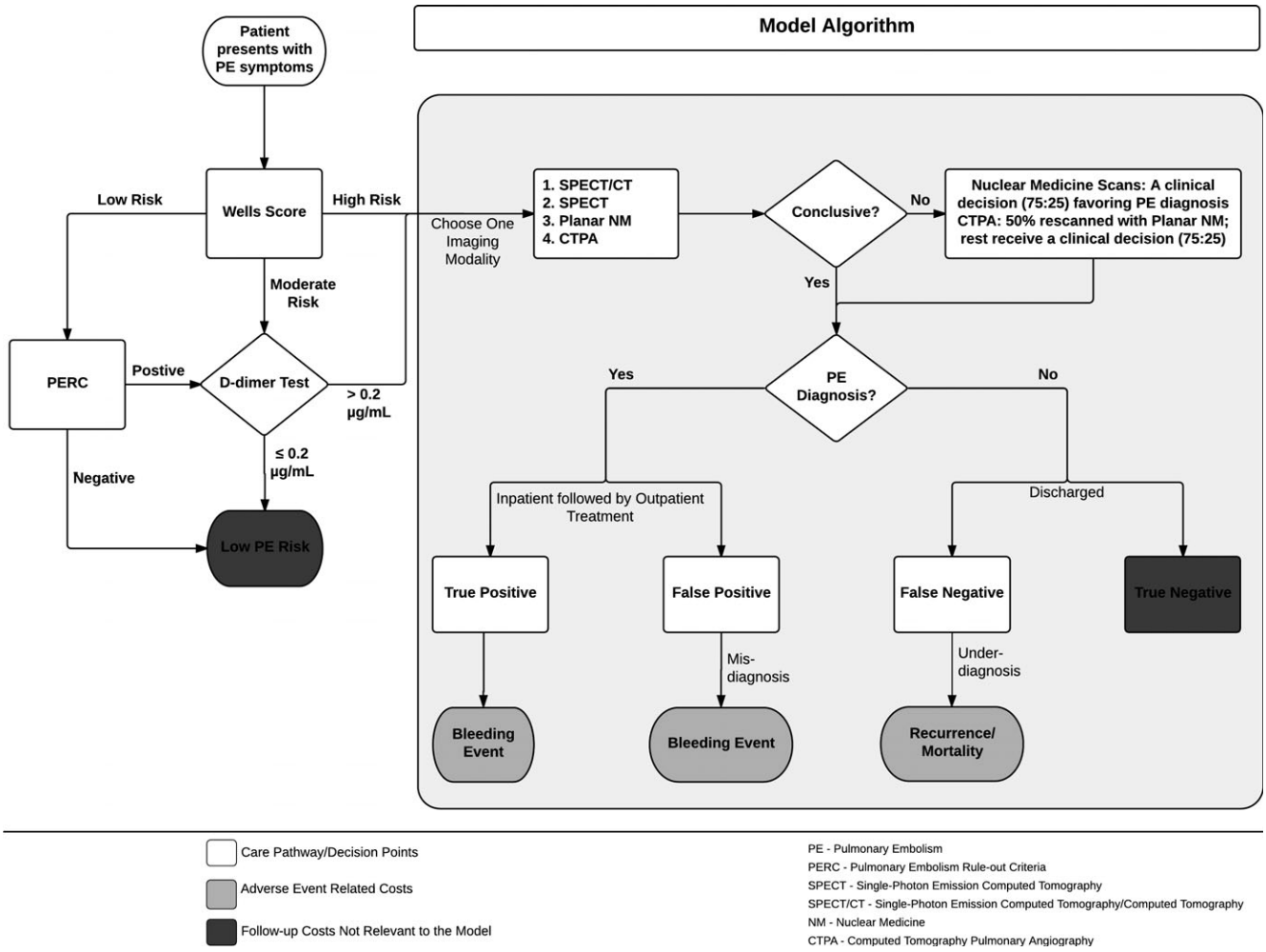

Figure 1. Model scaffold: proposed care pathway. CTPA = CT pulmonary angiography; NM = nuclear medicine; PE = pulmonary embolism; PERC = pulmonary embolism rule out criteria; SPECT = single-photon emission CT; SPECT/CT = single-photon emission CT with CT.

decision was made with the same 75%:25% empiric treatment allocation.

Following PE diagnosis, it was assumed that all the patients would be hospitalized for inpatient monitoring and that a 6-month course of anticoagulant therapy would be initiated and continued postdischarge without discontinuation. In a separate scenario analysis, treatment for PE in an outpatient basis was also considered. The model did account for the in-hospital and 30-day mortality, attributable to PE, which averaged out to 12.8%.[18,19] The total cost burden, therefore, included hospitalization, outpatient therapy, and/or other follow-up healthcare costs (e.g., office and laboratory visits) reported by PE patients over a 6-month duration. All patients treated with anticoagulant therapy, regardless of whether therapy was received based on a true-positive or a false-positive diagnosis, were expected to have the same risk of experiencing anticoagulation complications. Only major bleeding events were considered, with 10% hypothesized to be fatal.[20] All patients who received therapy based on a true-positive diagnosis were assumed to have a complete resolution of PE symptomatology and were no longer considered to be at any further risk—fatal or otherwise—from recurrent PE in the subsequent model's follow-up time period of 6 months. The model also followed the untreated patients for 6 months and factored the increased risk for recurrent PE and/or deep venous thrombosis (DVT) event and/or PE-attributable death.

Clinical and Cost Parameters

All clinical parameters, including imaging test statistics (disease prevalence, scan sensitivity, specificity, and indeterminate rates) and treatment and complication (adverse events [AEs] and mortality) rates, were estimated from the published literature. In case of multiple sources, estimates were pooled and weighted by the sample sizes of the contributing studies.[15,16] The expected cost of any given event (or complication) was calculated by multiplying the event rate with its associated treatment cost. All cost estimates were also obtained from published evidence and government reports. These were inflated to the 2016 USD, using the Bureau of Labor Statistics' US Medical Care Consumer Price Index. For the imaging scans, reimbursement amounts were calculated based on the 2016 Medicare total payments (cumulative of technical and professional components) reported by the CMS for the codes 71260 (CTPA) and 78582 (nuclear medicine [NM] scans). The model assumed identical billing and payment for the different types of V/Q scans. Since the PE patient population in the United States is predominantly insured by commercial (non-Medicare) payers, the Medicare payments were adjusted by a conservative multiplier of 1.5 to appropriately represent a private payer's reimbursement amount.[21] An analysis performed using Medicare payments would be expected to yield similar results, as any introduced bias would be uniform across all groups. Table 1 summarizes the clinical and economic outcomes examined for each of the imaging options.

Study Outcomes

The model calculated the difference between SPECT/CT and CTPA, planar, and SPECT for each of the following outcomes defined below:

Total cost burden was defined as cumulative costs related to: 1) initial and secondary imaging, 2) hospitalization and outpatient therapy for the diagnosed patients, 3) imaging-related AE and treatment complications (e.g., contrast-induced anaphylaxis, nephropathy [CIN], and/or renal failure [RF]), 4) major bleeding episodes among patients receiving anticoagulation therapy, 5) PE/DVT recurrent events among untreated (false-negative) PE patients, and 6) end-of-life care due to fatal RF and untreated PE.

Potentially wasteful excess costs were defined as the sum of the costs attributable to: 1) secondary V/Q planar scans performed after initial nondiagnostic examinations, 2) Imaging-related AE and complication treatments (CIN and/or RF), (3) major bleeding event costs, 4) PE/DVT recurrent events among untreated (false-negative) PE patients, and 5) end-of-life care due to fatal RF and untreated PE.

Total lives lost was the cumulative of loss of life associated with the disease condition, subsequent treatment, and AEs in chosen imaging modality: 1) fatal RF associated with administration of contrast agent for patients undergoing CTPA, 2) PE attributable mortality (in-hospital + 30-day), 3) Fatal bleeding in any patient who receives anticoagulation, and (4) fatal cases of untreated PE (false negative).

One-way Sensitivity Analysis

To gauge the robustness of the results and to assess the impact of individual parameters, a one-way sensitivity analysis was conducted by varying each model parameter by ±25% of its default value.[15,16] The top three parameters found to be most critical to the model were reported along with tornado diagrams for each cost comparison of interest for additional details.

In addition to the above one-way sensitivity analysis, three scenario analyses were conducted as described below:

Scenario Analysis 1

The most recent 2016 American College of Chest Physicians guidelines provide a grade 2B recommendation for outpatient treatment for patients categorized as low-risk PE.[22] Unlike Canada and Europe, this is not the current management approach in the United States.[23] With an increasing number of risk scoring algorithms developed, we hypothesize that this cost-saving measure may soon see an increased use in the United States. One of the most recent algorithms identified approximately 30% of the PE population as a potential target for outpatient therapy.[18] Accordingly, it was assumed that 70% of our patient population diagnosed with PE would be initially hospitalized and receive treatment according to the previously described model. The balance of the diagnosed cohort would be categorized as "low risk" for PE-related adverse outcomes and discharged with a 6-month anticoagulant therapy prescription. The remaining parameters were left unchanged from their default values.

Scenario Analysis 2

The second scenario analysis evaluated an alternate reimbursement strategy for SPECT/CT as an acknowledgment that SPECT/CT may be billed using additional add-on CPT codes. Because a CT scan is not reimbursed in the current payment structure, a secondary CPT code (78599 for unlisted respiratory procedure, diagnostic NM) may be addended to the primary 78582 code. While the secondary code is reimbursed at a variable rate, for the purposes of this model, a 100% reimbursement was conservatively assumed [although reimbursement may be at other rates, such as 0 or 50%]). In such a scenario, the total reimbursement amount paid out by a commercial payer for a SPECT/CT scan was calculated to be $1,023. No other parameter was changed from its default value in this scenario analysis. This particular analysis was conducted to specifically assess the impact of potentially higher reimbursement rate for SPECT/CT.

Scenario Analysis 3

To address some of the inherent limitations arising from using data from multiple studies that encompassed different settings of care (high volume vs. low volume), patient populations (clinical trial vs. retrospective analysis), a third scenario analysis was performed wherein SPECT/CT was explicitly compared to CTPA, the most commonly used imaging modality, the caveat being that the key imaging parameters—sensitivity (97% vs. 67.7%), specificity (100% for both) and nondiagnostic rates (0% for each)—would be derived from head-to-head studies alone.[14] Similar to our study approach, these parameters would be required to be weighted by the studies' sample sizes in case of multiple studies with the remaining parameters kept the same as in our base-case analysis.

RESULTS

Total Annual Costs

The total cost of each strategy in our hypothetical cohort was the following: 3.2 million USD for SPECT/CT, 3.8 million USD for CTPA, 5.8 million USD for planar, and 3.6 million USD for SPECT (Figure 2). For every 1,000 suspected PE patients undergoing imaging, the incremental cost savings for a commercial payer when using SPECT/CT scan versus the other three imaging examinations were estimated to be $621,655 (vs. CTPA), $2,565,805 (vs. planar), and $435,038 (vs. SPECT). The budget impact of switching to first-line SPECT/CT imaging is expected to yield per-patient-per-month (PPPM) cost savings of $51.80 (vs. CTPA), $213.80 (vs. planar), and $36.30 (vs. SPECT), respectively (Table 2).

Potentially Wasteful Excess Costs

For every 1,000 suspected PE patients undergoing imaging, potentially wasteful excess costs associated with the imaging techniques were as follows: $182,293 (SPECT/CT), $1,177,070 (CTPA), $3,034,307 (planar), and $617,331 (SPECT; Table 2). Therefore, SPECT/CT scan avoids unnecessary costs of $994,777 (vs. CTPA), $2,852,014 (vs. planar), and $435,038 (vs. SPECT) per annum. The major component of these excess costs, for all the four modalities, was that related to hospitalization for false-positives cases ($144,027 for SPECT/CT, $409,923 for CTPA, $2,814,066 for planar, and $565,029 for SPECT, respectively). The substantially higher cost for planar imaging is primarily driven by its high indeterminate rate. Other drivers of cost included contrast-related AEs ($622,490) primarily composed of CIN

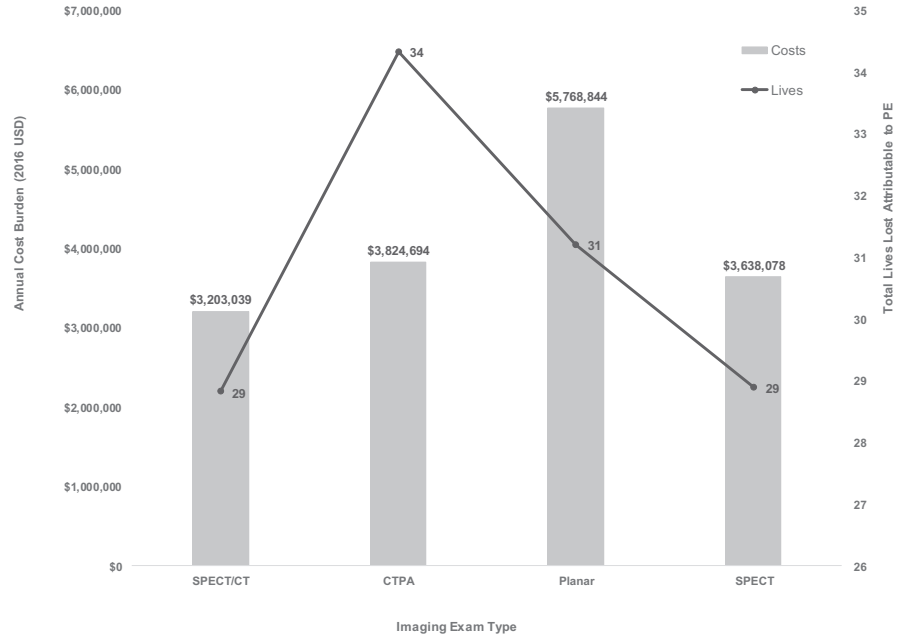

Figure 2. OVERALL Pulmonary Embolism Economic Burden, by Imaging Type. CTPA = CT pulmonary angiography; PE = pulmonary embolism; SPECT = single-photon emission CT; SPECT/CT = single-photon emission CT with CT.

Table 2
PE Total Cost Burden Summary

Cost Component	SPECT/CT	CTPA	Planar	SPECT
Initial scan cost	$525,000	$346,500	$525,000	$525,000
Rescan cost*	$0	$13,650	$0	$0
Contrast allergy treatment cost*	$0	$25	$0	$0
CIN treatment cost*	$0	$515,760	$0	$0
RF treatment cost*	$0	$55,980	$0	$0
RF mortality cost*	$0	$71,392	$0	$0
PE hospitalization cost–FPs*	$144,027	$409,923	$2,814,066	$565,029
Bleeding risk costs–FPs*	$4,802	$13,667	$93,823	$18,838
Recurrent event costs–FNs*	$2,676	$7,732	$10,111	$2,676
Mortality event costs–FNs*	$30,787	$88,941	$116,307	$30,787
PE hospitalization cost–TPs	$2,415,222	$2,226,879	$2,138,247	$2,415,222
Bleeding risk costs–TPs	$80,525	$74,245	$71,290	$80,525
Total costs	$3,203,039	$3,824,694	$5,768,844	$3,638,078
In-hospital + 30-day PE mortality–TPs	26.56	24.49	23.51	26.56
Fatal bleeding–TPs	0.44	0.40	0.39	0.44
RF mortality*	0.00	4.17	0.00	0.00
Fatal bleeding–FPs*	0.03	0.07	0.51	0.10
Undiagnosed mortality–FNs*	1.80	5.20	6.80	1.80
Total lives lost	28.82	34.34	31.21	28.90

*Potentially wasteful (and avoidable) excess costs/lives lost.
CIN = contrast induced anaphylaxis, nephropathy; CTPA = CT pulmonary angiography; FN = false negative; FP = false positive; PE = pulmonary embolism; RF = renal failure; SPECT = single-photon emission CT; SPECT/CT = single-photon emission CT with CT; TP = true positive.

($515,760) for CTPA and end-of-life care costs for fatal RF and "false-negative" cases among CTPA ($88,941) and planar ($116,307) scan patients.

Total Lives Lost

The model also estimated the annual number of lives lost attributable to PE, its treatment and associated

AEs. It was calculated that a total of 28.8 lives (SPECT/CT), 34.3 lives (CTPA), 31.2 lives (planar), and 28.9 lives (SPECT) would be lost under each strategy (Figure 2). Taken together, SPECT/CT was associated in saving an additional 5.5 lives versus CTPA, 2.4 lives versus planar, and 0.1 lives versus SPECT for every 1,000 cases of suspected PE patients receiving the compared imaging scans.

Sensitivity analyses

One-way sensitivity analysis found that the model was most sensitive to the following: 1) scan parameters including image reimbursement costs, sensitivity/specificity, and/or nondiagnostic rates; 2) proportion of PE patients getting hospitalized following diagnosis and related costs; and 3) PE prevalence (Figure 3).

Scenario Analysis 1

When roughly 30% of patients diagnosed with PE were deemed "low risk" and were treated with outpatient anticoagulation therapy without an inpatient admission, the total cost burden varied between a low value of 2.5 million USD for SPECT/CT to a high value of 4.5 million USD for planar imaging. PPPM cost savings of employing SPECT/CT as first-line imaging were estimated as follows: $50.10 (vs. CTPA), $161.90 (vs. planar), and $27.10 (vs. SPECT), respectively. Furthermore, SPECT/CT imaging is projected to lead to avoidance of wasteful excess costs totaling $925,499 (vs. CTPA), $2,156,343 (vs. planar), and $325,348 (vs. SPECT) in this hypothetical cohort.

Scenario Analysis 2

In a scenario where SPECT/CT was reimbursed $1,023, and CTPA ($347), planar, and SPECT scans ($525) received their standard disbursements, SPECT/CT's imaging burden increased to 3.7 million USD; however, the incremental cost savings were maintained between SPECT/CT and CTPA ($123,655) and planar imaging ($2,067,805) leading to delta PPPM reductions of $10.30 (vs. CTPA) and $172.30 (vs. planar). However, SPECT/CT led to an additional $5.20 PPPM impact versus SPECT in this scenario.

Scenario Analysis 3

SPECT/CT versus CTPA comparison using the study by Gutte et al.[14] imaging parameters, our findings demonstrate the total cost burden to be approximately 3.1 million USD for SPECT/CT versus 3.0 million USD for CTPA, leading to an additional PPPM of $3.8 million for SPECT/CT. In a similar cohort of patients, however, increased sensitivity for SPECT/CT (97%) versus CTPA meant that the hybrid technology also saved an additional 18 lives. The incremental cost per life saved was thus calculated to be $4,554, indicating SPECT/CT to be a very cost-effective modality.

DISCUSSION

Computed tomography pulmonary angiography, planar, and SPECT scans are the three most widely available scanning techniques used in the investigation of acute PE diagnosis.[24] Yet there is still an enduring debate as to which test is the most accurate, appropriate, and optimal for this indication. Seeking an effective and efficient means of diagnosing PE is both desirable and an important barometer for improving patient outcomes. Our study found that the diagnostic accuracy of SPECT/CT meant that it is the most economical imaging option. When measured in terms of overall cost burden, for every 1,000 suspected PE cases who received imaging services, dollars saved were estimated to be $0.6 million (vs. CTPA), $2.6 million (vs. planar), and $0.4 million (vs. SPECT), respectively. This translated to incremental PPPM cost savings ranging between $36.30 (vs. SPECT) and $213.80 (vs. planar). In addition to a higher number of lives saved due to optimal PE detection and treatment, SPECT/CT scan was also found to have the lowest amount of potentially wasteful expenditures compared to the other three imaging examinations.

The aim of imaging for suspicion of PE is to accurately confirm or rule out the diagnosis. A false-positive diagnosis of PE exposes the patient to the costs and risks associated with anticoagulation therapy. Furthermore, anticoagulation requires frequent blood tests, dietary changes, and an increased risk of bleeding. In addition, overdiagnosis can cause patients needless inconvenience, anxiety, and distress of having a potentially life-threatening disease.[25] Additional downstream impact could plausibly involve higher premiums. On the other hand, a false-negative diagnosis exposes the patient to a potential recurrent event and the possibility of death due to untreated PE. The imaging technologies themselves also expose the patient to additional complications. This is especially relevant to CTPA, which has been associated with CIN. Although modern CTPA and V/Q scans maintain similar whole-body radiation exposure, CTPA may result in a higher organ-specific exposure to the breast, especially concerning in young

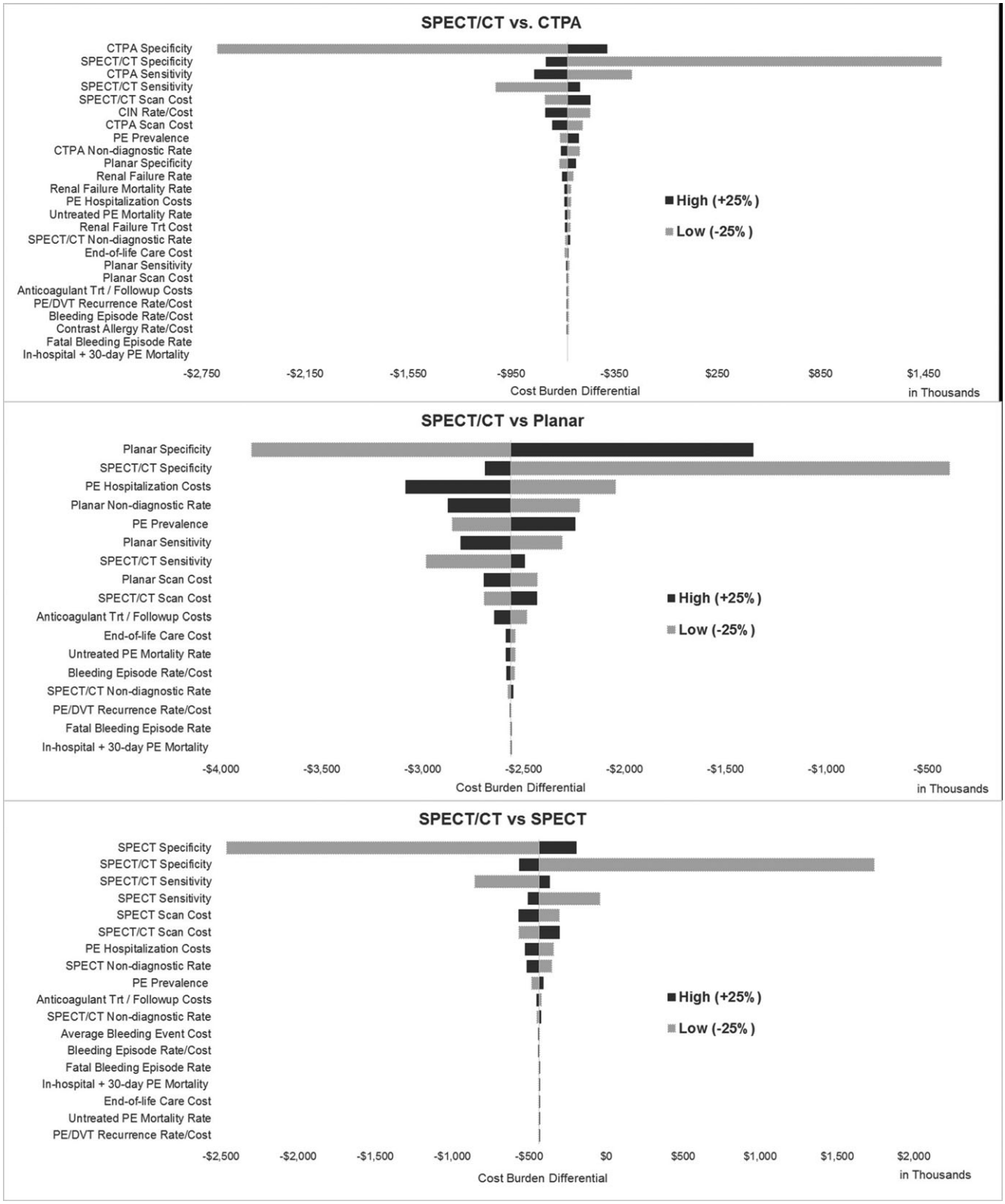

Figure 3. Tornado diagram: one-way sensitivity analysis results: SPECT/CT versus CTPA, SPECT/CT versus planar, and SPECT/CT versus SPECT. CIN = contrast-induced anaphylaxis, nephropathy; CTPA = CT pulmonary angiography; DVT = deep venous thrombosis; PE = pulmonary embolism; SPECT = single-photon emission CT; SPECT/CT = single-photon emission CT with CT.

and pregnant women who have more radiosensitive breast tissue, especially if multiple follow-up CTPA scans are required.[5,26]

A 2005 US survey of ED physicians indicated that most consider CTPA to be the first-line test for PE.[25] Its extensive use was attributed to round-the-clock

availability, fast scan times, low cost, high frequency of conclusive results, and capability of providing alternative diagnoses.[5] Yet, this must be weighed against the incidence of contrast-related complications. Our analysis shows that the CTPA arm of our model accumulated in excess of $600,000 (12%) in treatment costs. CTPA may be a financially suboptimal choice if employed as the first-line imaging choice for the entire imaging population. Furthermore, some studies have estimated that CTPA may be contraindicated in up to 50% of the suspected PE imaging directed population because of an underlying clinical condition including renal insufficiency, recent myocardial infarction, grave arrhythmia, allergy, etc.[27] Without this contrast-related burden, CTPA fares very well against planar and SPECT with incremental PPPM cost savings of $2,587.30 and $456.50, respectively. However, this benefit was not extended to SPECT/CT, the latter costing approximately $1.80 less than CTPA PPPM. Therefore, even after discounting the effects of CIN, SPECT/CT was found to be cost saving.

Some guidelines recommend planar imaging as an alternative for patients contraindicated for CTPA due to severe renal insufficiency, multiple myeloma, or allergy to intravenous contrast agents or those with an inconclusive CT scan.[28] Yet the relatively high rate of indeterminate (low and intermediate probability) planar scan results limit their clinical and economic utility. Our analysis shows that the economics of the current model support an imaging strategy involving SPECT, rather than conventional planar scans, when CTPA should be avoided due to the above-mentioned reasons. In our study, SPECT versus CTPA and planar scanning found per-patient incremental cost savings of $186.60 and $2,130.80 respectively. Unlike SPECT/CT, SPECT scanners are available in many NM departments and the PE diagnostic imaging can be performed in almost all patients since there are no definitive contraindications. However, their use is currently hindered by relative unfamiliarity by the referring physicians or inaccessibility during off hours.[12,29] This study highlight the need for SPECT to be considered as an alternative to planar scans that can be immediately implemented in many hospitals.

The scenario analyses also highlight a couple of key considerations. First, the costs imposed by the improper hospitalization for false-positive diagnosis of PE is significant. The cost is lower if these patients are treated in an outpatient setting, but the excess costs remain an issue. SPECT/CT appears to alleviate this burden by substantially reducing the number of false positives as well as by having the highest diagnostic accuracy among the compared imaging modalities. The second scenario was created to address the issue of alternative reimbursement for SPECT/CT. This is important because there are a number of perceived barriers to broader SPECT/CT utilization, namely, that CTPA is faster, low cost, and not constrained by a typical NM's daytime working hours. Improved reimbursement for SPECT/CT would encourage capital investment in SPECT/CT equipment and staffing, which would address some of these barriers. The second scenario shows that even under improved SPECT/CT reimbursement for the provider, the cost savings to the payer under the SPECT/CT strategy continue to exist compared to all other strategies and, in particular, versus CTPA.

Multiple surveys have corroborated the role of defensive medicine behind the ordering of unnecessary and "low-yield" CT examinations. A recent survey of physicians ordering CTPA scans for diagnosing PE found that defensive behavior (e.g., fear of missing PE, threat of malpractice litigation) was a factor in nearly three of five scans. These factors kept pace with other evidence-based medicine factors for driving the post-imaging clinician decision making.[30] A 2005 survey of Pennsylvania ED physicians found that 63% ordered radiologic tests that were not indicated, while 93% of physicians, in general, practice defensive medicine.[31] A Massachusetts-based survey revealed that 23% of all types of CTs were ordered for defensive reasons.[32] While the role of defensive medicine in driving up healthcare costs is controversial, these behaviors are estimated to cost the US healthcare system up to $45 billion to $100 billion annually and are thought to account for 5% to 25% of all US medical care costs.[30] While behavior modification in dealing with physician risk aversion has a definite role to play in using imaging resources judiciously and efficiently, this also highlights an unmet need that SPECT/CT can potentially fill as a result of its superior diagnostic accuracy and efficiency, which reduces the overall cost burden.

LIMITATIONS

We acknowledge that there were several limitations to the current study. The parameters were generated from published literature and represented a mix of randomized controlled trial and real-world settings and diverse

populations as well as physicians, clinicians, and/or technicians with varying degrees of technology experiences. The model did not account for any costs and/or resource use unrelated to the acute PE episode (either additional to PE or an alternate diagnosis, e.g., pleural effusions, heart failure). While this may underestimate the benefits associated with differential non-PE diagnoses, since CTPA and SPECT/CT share similar advantages, this does not bias our current results between the new intervention and the most prevalent imaging modalities. Next, the model assumes that all patients who were prescribed anticoagulants did not prematurely self-discontinue their therapy for any reason, which may not be reflective of real world. In addition, the model did not differentiate between single and the superior multidetector CT scanning methods. Also, the long-term impact of radiation exposure was not estimated owing to the study's shorter follow-up time frame. The impact of rarer events (contrast-related mortality) was not considered. Finally, this economic evaluation will evolve with the addition of further evidence from larger controlled trials that are currently needed to corroborate the benefits of SPECT/CT scan over other available imaging modalities.

CONCLUSION

The accurate diagnosis of pulmonary embolism continues to challenge both clinicians and imaging specialists. Misdiagnosis is problematic because untreated pulmonary embolism can be fatal, and on the other hand unnecessary treatment with anticoagulation places the patient at risk of bleeding. Our results indicate that lung scintigraphy performed with single-photon emission computed tomography in combination with low-dose computed tomography without contrast enhancement could be considered as a potential first-line imaging test in the diagnostic workup of pulmonary embolism, especially in cases where computed tomography pulmonary angiography is contraindicated. Annual economic burden was estimated to be reduced with a switch to the hybrid scan with PPPM cost savings estimated at $51.80 (vs. computed tomography pulmonary angiography), $213.80 (vs. planar), and $36.30 (vs. single-photon emission computed tomography), respectively, for a commercial payer or health system for every patient eligible for diagnostic imaging of suspected pulmonary embolism. This translates to $0.6 million (vs. computed tomography pulmonary angiography), $2.6 million (vs. planar), and $0.4 million (vs. single-photon emission computed tomography) in overall savings per annum for every 1,000 imaging patients. Switching to single-photon emission computed tomography with computed tomography is expected to avoid potentially wasteful excess per patient costs averaging between $435 (vs. single-photon emission computed tomography) and $2,852 (vs. planar) mainly via reduction in pulmonary embolism hospitalization costs of the false positives. It is also expected that the higher sensitivity/specificity of single-photon emission computed tomography with computed tomography and absence of contrast-related complications may help avoid loss of life compared to computed tomography pulmonary angiography (approximately six lives) and planar (approximately three lives). Taken together, compared to the currently available scanning technologies for diagnosing suspected pulmonary embolism, single-photon emission computed tomography with computed tomography appears to confer superior economic value, primarily via improved sensitivity and specificity and low nondiagnostic rates. In turn, the improved diagnostic accuracy accorded single-photon emission computed tomography with computed tomography the lowest ratio of expenses attributable to potentially avoidable complications, misdiagnosis, and underdiagnosis. This simulation analysis further highlights the need for well-designed head-to-head clinical studies to confirm this study's results.

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