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

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Background: **The limitations of the current diagnostic standard, ventilation–perfusion lung scanning, complicate the management of patients with suspected pulmonary embolism. We previously demonstrated that determining the pretest probability can assist with management and that the high negative predictive value of certain D-dimer assays may simplify the diagnostic process.**

Objective: **To determine the safety of using a simple clinical model combined with D-dimer assay to manage patients presenting to the emergency department with suspected pulmonary embolism.**

Design: **Prospective cohort study.**

Setting: **Emergency departments at four tertiary care hospitals in Canada.**

Patients: **930 consecutive patients with suspected pulmonary embolism.**

Interventions: **Physicians first used a clinical model to determine patients' pretest probability of pulmonary embolism and then performed a D-dimer test. Patients with low pretest probability and a negative D-dimer result had no further tests and were considered to have a diagnosis of pulmonary embolism excluded. All other patients underwent ventilation–perfusion lung scanning. If the scan was nondiagnostic, bilateral deep venous ultrasonography was done. Whether further testing (by serial ultrasonography or angiography) was done depended on the patients' pretest probability and the lung scanning results.**

Measurements: **Patients received a diagnosis of pulmonary embolism if they had a high-probability ventilation–perfusion scan, an abnormal result on ultrasonography or pulmonary angiography, or a venous thromboembolic event during follow-up. Patients for whom the diagnosis was considered excluded were followed up for 3 months for the development of thromboembolic events.**

Results: **The pretest probability of pulmonary embolism was low, moderate, and high in 527, 339, and 64 patients (1.3%, 16.2%, and 37.5% had pulmonary embolism), respectively. Of 849 patients in whom a diagnosis of pulmonary-embolism had initially been excluded, 5 (0.6% [95% CI, 0.2% to 1.4%]) developed pulmonary embolism or deep venous thrombosis during follow-up. However, 4 of these patients had not undergone the proper diagnostic testing protocol. In 7 of the patients who received a diagnosis of pulmonary embolism, the physician had performed more diagnostic tests than were called for by the algorithm. In 759 of the 849 patients in whom pulmonary embolism was not found on initial evaluation, the diagnostic protocol was followed correctly. Only 1 (0.1% [CI, 0.0% to 0.7%]) of these 759 patients developed thromboembolic events during follow-up. Of the 437 patients with a negative D-dimer result and low clinical probability, only 1 developed pulmonary embolism during follow-up; thus, the negative predictive value for the combined strategy of using the clinical model with D-dimer testing in these patients was 99.5% (CI, 99.1% to 100%).**

Conclusion: **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.**

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Pulmonary embolism is a relatively common disease, with an estimated annual incidence in the United States of 23 cases diagnosed per 100 000 persons (1). More than 50% of cases are undiagnosed. Untreated pulmonary embolism has a high mortality, although risk for death is reduced significantly with anticoagulation (2). Because the clinical signs and symptoms of pulmonary embolism are not specific, timely diagnostic testing must be done to confirm the diagnosis. Ventilation–perfusion lung scanning is the most common imaging procedure for suspected pulmonary embolism. However, the result is frequently nondiagnostic, and additional testing is needed to confirm a diagnosis. Patients presenting to the emergency department with suspected pulmonary embolism present a challenge, particularly if diagnostic testing is not immediately available.

We recently validated a simple model (3), which we incorporated into a diagnostic algorithm, to classify pre-

test probability of pulmonary embolism by using clinical findings along with results on electrocardiography and chest radiography. We had not tested our model or the diagnostic algorithm in an emergency department setting. Another diagnostic test, D-dimer assay, may be useful in patients with suspected pulmonary embolism, but experience with this test to exclude pulmonary embolism diagnoses in an emergency department has been limited (4). In the current study, we used a diagnostic algorithm based on our clinical model and a non–enzyme-linked immunosorbent D-dimer assay in patients presenting to emergency departments with suspected pulmonary embolism. We sought to 1) demonstrate the safety of excluding the diagnosis of pulmonary embolism in an emergency department using diagnostic algorithms that were based on pretest probability and D-dimer assay results and 2) confirm the reliability of the pretest probability clinical model and D-dimer testing for pulmonary embolism in an emergency department.

METHODS

Patients

Data for this study were collected from September 1998 to September 1999 at four participating medical centers in Canada: The Ottawa Civic Hospital, Ottawa, Ontario; the London Health Sciences Centre, London, Ontario; the Queen Elizabeth II Health Sciences Centre, Halifax, Nova Scotia; and St. Paul's Hospital, Vancouver, British Columbia. The study was approved by the ethics review committees at each of the institutions.

Consecutive patients presenting to the emergency departments of the participating centers were eligible if they had suspicion of pulmonary embolism with symptoms for less than 30 days and were experiencing acute onset of new or worsening shortness of breath or chest pain. Exclusion criteria were 1) suspected deep venous thrombosis of the upper extremity as a likely source of pulmonary embolism, 2) no symptoms of pulmonary embolism within 3 days of presentation, 3) anticoagulant therapy for more than 24 hours, 4) expected survival time less than 3 months, 5) contraindication to contrast media, 6) pregnancy, 7) geographic inaccessibility precluding follow-up, or 8) age younger than 18 years.

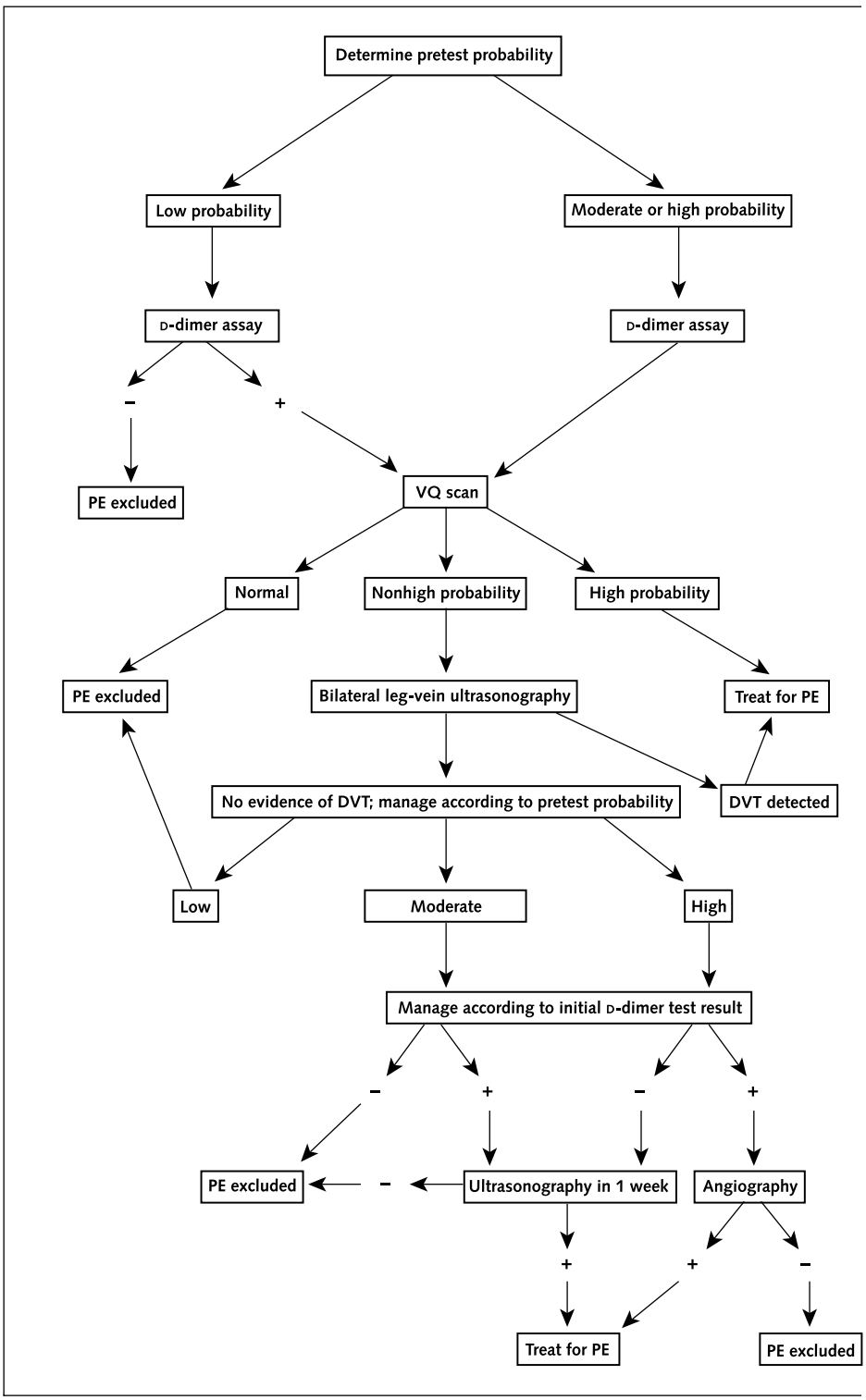
Interventions

After giving informed consent, patients were evaluated by 1 of 43 emergency department physicians, who used a simple clinical model to determine the clinical probability of pulmonary embolism (5). The physician assigned points for the following: clinical signs and symptoms of deep venous thrombosis (objectively measured leg swelling and pain with palpation in the deep-vein region), 3.0 points; heart rate higher than 100 beats/min, 1.5 points; immobilization (bedrest, except to access the bathroom, for $\geq$3 consecutive days) or surgery in the previous 4 weeks, 1.5 points; previous objectively diagnosed deep venous thrombosis or pulmonary embolism, 1.5 points; hemoptysis, 1.0 point; malignancy (patients with cancer who were receiving treatment, those in whom treatment had been stopped within the past 6 months, or those who were receiving palliative care), 1.0 point; and pulmonary embolism as likely as or more likely than an alternative diagnosis, 3.0 points (5). For the final variable, which was not strictly defined, physicians were told to use the clinical information (obtained by history and physical examination), along with results on chest radiography, electrocardiography, and whatever blood tests were considered necessary to diagnose pulmonary embolism. The pretest probability of pulmonary embolism was considered low in patients whose score was less than 2.0, moderate in patients whose score was at least 2.0 but no higher than 6.0, and high in patients whose score was greater than 6.0.

The SimpliRED whole-blood agglutination D-dimer test (AGEN Biomedical, Ltd., Brisbane, Australia) was performed on citrated blood samples in a local coagulation laboratory. In all patients, the D-dimer test was performed only after the clinical model had been applied and the resultant probability had been recorded. Patients were to be managed as outlined in **Figure 1**. Pulmonary embolism was considered excluded if the patient had been assigned a low clinical pertest probability and had a negative result on D-dimer testing; no imaging procedures were performed in these patients. All other patients had ventilation–perfusion lung scanning. For patients who presented outside normal working hours (between 3:30 p.m. and 7:00 a.m.), a therapeutic dose (200 U/kg of body weight) of the low-molecular-weight heparin Dalteparin (Pharmacia-Upjohn, Mississauga, Ontario, Canada) was given subcutaneously, and diagnostic testing was done in the next 18 hours (6). Dalteparin was given to these patients only after the clinical model was applied and D-dimer testing was done.

Ventilation–perfusion scans were interpreted by nuclear medicine physicians who had no knowledge of the

Figure 1. **Diagnostic algorithm for initial evaluation of patients with suspected pulmonary embolism.**



Plus and minus signs indicate positive and negative test results, respectively. DVT = deep venous thrombosis; PE = pulmonary embolism; VQ = ventilation–perfusion lung scan.

clinical model outcome or D-dimer result. The scan interpretations were used to determine patient management. Ventilation–perfusion scans were interpreted as 1) normal, if no perfusion defects were found, 2) high probability, if at least one segmental (or larger) perfusion defect with normal ventilation or at least two large subsegmental perfusion defects (>75% of a segment) with normal ventilation were found, or 3) nondiagnostic, if ventilation–perfusion defects were detected but did not meet the criteria for high probability (7). A lung-segment reference chart was used to interpret ventilation–perfusion scans (8). Compression ultrasonography, when indicated, was performed on both lower extremities from the common femoral vein to the trifurcation of the calf veins, but the calf veins were not examined. Lack of vein compressibility was diagnostic of deep venous thrombosis (9). In patients with a history of deep venous thrombosis, diagnosis of recurrent thrombus required 1) the noncompressibility on ultrasonography to be in the previously uninvolved extremity or in an area previously unaffected by thrombus or 2) the clot diameter to be more than 4 mm greater than on previous measurement (10). In patients with previous pulmonary embolism, only new defects were considered. Patients were considered to have pulmonary embolism if they had abnormal results on ultrasonography or angiography, a high-probability result on ventilation–perfusion scan, or a venous thromboembolic event during the 3-month follow-up. In all other patients, a diagnosis of pulmonary embolism was considered excluded.

Treatment and Follow-up

Anticoagulant therapy was withheld in patients in whom a diagnosis of pulmonary embolism was excluded. These patients were given instruction cards and were directed to return at once if they developed new or worsening symptoms or signs suggesting pulmonary embolism or deep venous thrombosis. If at any time venous thromboembolism (deep venous thrombosis or pulmonary embolism) was suspected, patients were studied by using a standardized approach (3). Diagnoses of deep venous thrombosis and pulmonary embolism were excluded if results on ultrasonography and ventilation–perfusion scanning, respectively, were normal. Pulmonary embolism was diagnosed if a new ventilation–perfusion scan showed high probability, and deep venous thrombosis was diagnosed if results on ultrasonography were abnormal. Patients with nondiagnostic scans and equivocal ultrasonography results had gold-standard testing—pulmonary angiography and venography, respectively; the results were evaluated according to previously defined criteria (3). After 3 months, patients were followed up for development of thromboembolic events at a return appointment or by telephone contact. A committee blinded to all patient variables adjudicated suspected outcome events during follow-up.

Statistical Analysis

Our primary outcome was the proportion of patients who had a venous thromboembolic event during 3-month follow-up among patients in whom the diagnosis of pulmonary embolism had been excluded before follow-up (**Figure 1**). We and other authors have used this type of outcome in previous studies (3, 11, 12). Our primary analysis was an intention-to-treat analysis of all enrolled patients. We also planned a secondary analysis to evaluate the safety of our strategy in patients in whom the diagnostic algorithm was followed correctly. Because the SimpliRED test can rule out thromboembolism by yielding a negative result, we could also determine the negative predictive values of the D-dimer results in the three pretest-probability groups by determining thromboembolic event rates during the entire study period in those with negative D-dimer results. Before calculating the negative predictive values, we computed the total number of venous thromboembolic events diagnosed during the initial study period (the study period from presentation to follow-up) or follow-up to determine the overall event rates. Then, we determined the negative predictive value by dividing the number of patients with no diagnosis of venous thromboembolism by the number of patients with a negative D-dimer result. We calculated 95% CIs from the binomial distribution. For other secondary analyses, we compared the rates of pulmonary embolism between patients according to the pretest probability by using a 3×2 chi-square test and compared the proportion of patients requiring imaging tests to the proportion in our previous study (3).

We hypothesized that by combining the pretest clinical probability of pulmonary embolism with results on D-dimer testing, we could do fewer diagnostic tests in patients presenting with suspected pulmonary embolism in the emergency department and thus make the diagnostic approach simpler and less costly. We based our

Table 1. **Demographic Characteristics of Patients**

Characteristic	Total Patients ($n = 30$)	Patients with Pulmonary Embolism ($n = 86$)	Patients without Pulmonary Embolism ($n = 844$)
Mean age ± SD (range), *y*	50.5 ± 18.4 (16–93)	55.5 ± 17.0 (20–92)	50.0 ± 18.4 (16–93)
Men/women, *n/n*	347/583	46/40	301/543
Mean duration of symptoms ± SD, *d*	3.2 ± 5.2	4.0 ± 5.5	3.2 ± 5.2
Cancer, *n (%)*	67 (7.2)	19 (21.3)	48 (5.7)
Surgery, *n (%)**	78 (8.4)	17 (19.1)	60 (7.1)
Immobilized, *n (%)**	71 (7.6)	10 (11.2)	61 (7.2)
D-dimer assay result, *n*			
Positive	250	66	184
Negative	675	18	657
Not tested	5	2	3

* Within the previous 4 weeks.

sample size calculation on achieving a narrow 95% CI around the expected 3-month thromboembolic event rate in patients in whom pulmonary embolism had been excluded during the initial study period (before follow-up). On the basis of previous studies, we projected that the addition of the D-dimer test to the algorithm would result in a similar proportion of patients with venous thrombosis in follow-up (0.4%), with the added advantage of requiring fewer diagnostic imaging tests (3, 11). We chose an upper-range 95% CI of 1%, which required a sample size of 930 to test the safety of our strategy with respect to 3-month event rates. Analyses were done by using SPSS software, version 10.0 for Windows (SPSS, Inc., Chicago, Illinois).

Role of the Funding Source

The funding source had no role in the collection, analysis, and interpretation of the data or in the decision to submit the paper for publication.

RESULTS

A total of 946 consecutive, symptomatic patients were evaluated. Sixteen patients were lost to follow-up because of relocation outside the study region. Our analysis comprised data on the remaining 930 patients, who had a mean (±SD) age of 50.5 ± 18.4 years and mean symptom duration of 3.2 ± 5.2 days. Eighty-six (9.5% [95% CI, 7.5% to 11.3%]) of these 930 patients received a diagnosis of pulmonary embolism during the entire study period. In the patients in whom diagnostic imaging was indicated, pulmonary embolism occurred in 16.9%. **Table 1** shows other demographic data for the participants according to diagnosis of pulmonary embolism. **Figure 2** outlines the outcomes of the diagnostic algorithm. The initial pretest probabilities were determined, according to the clinical model, to be high in 64 patients (7%), moderate in 339 patients (36%), and low in 527 patients (57%). Including follow-up events, pulmonary embolism was diagnosed in 24 of 64 (40.6% [CI, 28.7% to 53.7%]) patients with high pretest probability, 55 of 339 (16.2% [CI, 12.5% to 20.6%]) patients with moderate pretest probability, and 7 of 527 (1.3% [CI, 0.5% to 2.7%]) patients with low pretest probability. The difference in the prevalence of pulmonary embolism among the three pretest-probability groups was statistically significant ($P < 0.001$).

In the intention-to-treat analysis, 81 patients initially received a diagnosis of pulmonary embolism (6 of 527, 52 of 339, and 23 of 64 patients with low, moderate, and high probability, respectively). Among the 81 patients who received diagnoses of pulmonary embolism before the follow-up period began, the diagnosis was based on test results in 7 patients who had undergone more tests than were called for by the algorithm. Among these 7 patients, 2 had low pretest probability along with a negative D-dimer result but high probability on ventilation–perfusion scanning that was done on the day of presentation; in the remaining 5 patients, all of whom

Plus and minus signs indicate positive and negative test results, respectively. *Two patients had pulmonary embolism diagnosed according to high-probability ventilation–perfusion scanning, which had been done despite a negative D-dimer test result. †Deep venous thrombosis on day 46. ‡Deep venous thrombosis on day 11 in a patient with high clinical pretest probability. §One patient had no D-dimer testing and showed pulmonary embolism on spiral computed tomography. CT = computed tomography; DVT = deep venous thrombosis; PE = pulmonary embolism; VQ = ventilation–perfusion lung scan.

Figure 2. **Algorithm for patients with suspected pulmonary embolism.**

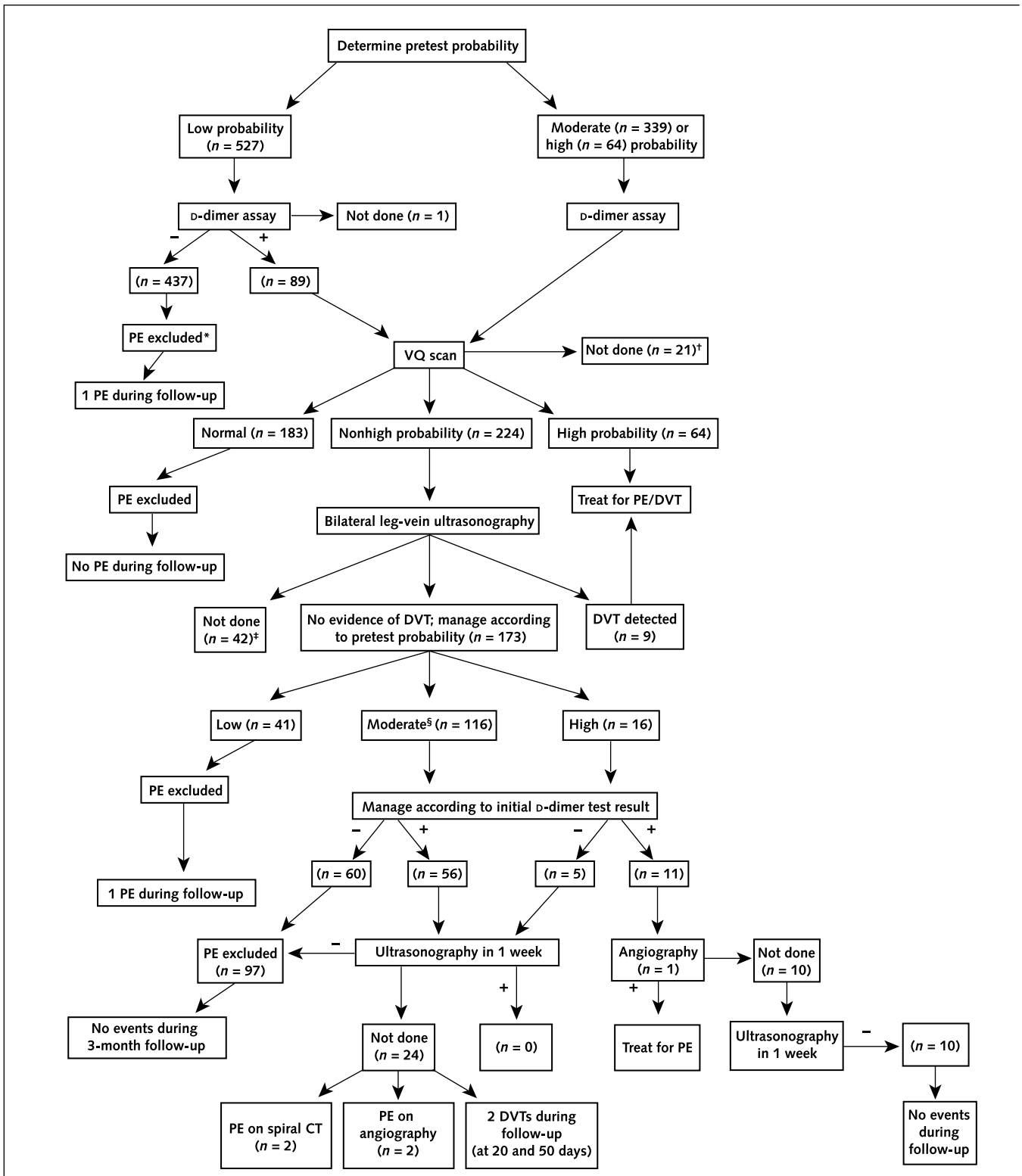


Table 2. **Cause of Death in Patients according to Initial Diagnosis**

Cause of Death	Patients in Whom Pulmonary Embolism Was Initially Diagnosed	Patients in Whom Pulmonary Embolism Was Initially Excluded	Total Patients
	← *n* →		
Metastatic cancer	1	5	6
Congestive heart failure	0	3	3
Renal failure	0	1	1
Sepsis	2	0	2
Chronic obstructive pulmonary disease	0	2	2
Pulmonary embolism	2	0	2
Stroke	0	1	1

had moderate pretest probabilities, spiral computed tomography ($n = 3$) or pulmonary angiography ($n = 2$) was done (**Figure 2**). Overall, the diagnosis of pulmonary embolism had been excluded during the initial diagnostic investigation (before follow-up) in 849 patients. Seventeen of these 849 patients presented with suspected events during follow-up—6, 9, and 2 patients with low, moderate, and high probability, respectively, according to the pretest clinical model; suspected events were confirmed in 5 (0.6% [CI, 0.2% to 1.4%]) of these patients. During follow-up, of 4 suspected pulmonary emboli and 2 suspected cases of deep venous thrombosis in patients with low pretest probability, 1 pulmonary embolus (on day 16 of follow-up) was confirmed; of 4 suspected pulmonary emboli and 5 suspected cases of deep venous thromboses in the moderate-probability group, 3 cases of deep venous thrombosis (days 20, 46, and 50 of follow-up) were confirmed; and of 2 suspected pulmonary emboli in the high-probability group, 1 (day 34 of follow-up) was confirmed.

Overall, 92 patients had fewer tests done than required by the algorithm, and 4 of the 5 confirmed events during the follow-up period occurred in these 92 patients. Nineteen patients with moderate pretest probability, nonhigh probability on ventilation–perfusion scans, and negative results on initial ultrasonography did not undergo serial (at 1 week) ultrasonography; 2 of these patients developed deep venous thrombosis (on days 20 and 50 of follow-up). Sixteen moderate-probability patients had no diagnostic imaging procedures, and 1 of these patients had deep venous thrombosis during follow-up on day 46. The fourth confirmed event during follow-up in the 92 patients with insufficient imaging testing occurred in a patient with high pretest probability and a non–high-probability ventilation–perfusion scan in whom no initial ultrasonography was performed. This patient returned on day 34 with worsening symptoms, and pulmonary embolism was diagnosed by spiral computed tomography.

We had also planned to analyze the results in the patients in whom the algorithm was correctly followed. In 759 of the 849 patients in whom pulmonary embolism was not found during the initial investigational evaluation (before follow-up), the diagnostic protocol was followed correctly. Only 1 (0.1% [CI, 0.0% to 0.7%]) of these 759 patients developed pulmonary embolism or deep venous thrombosis during follow-up. This event, pulmonary embolism on day 46, occurred in a patient with low pretest probability and test results that were positive on D-dimer, nondiagnostic on ventilation–perfusion scanning, and negative on ultrasonography. The negative predictive value of the D-dimer test was 97.3% (CI, 95.8% to 98.4%) in the entire patient cohort and 99.5% (CI, 98.4% to 99.9%) in the low-probability group, 93.9% (CI, 89.8% to 96.7%) in the moderate-probability group, and 88.5% (CI, 69.9% to 97.6%) in the high-probability group. No imaging tests were required in 47% of patients, serial ultrasonography was indicated in only 7% of patients and angiography was indicated in 1.1% compared with 0%, 57%, and 3.7%, respectively, in our previous study, in which the D-dimer test was not used in the diagnostic algorithm.

Seventeen patients died during the study. During the initial study period, pulmonary embolism had been diagnosed in 5 of these patients and excluded in the other 12 patients. Of the 12 patients who died but in whom pulmonary embolism initially had been excluded, none were judged to have died of an undiagnosed pulmonary embolism. Of the 5 deaths in patients with a diagnosis of pulmonary embolism, 3 occurred in patients with metastatic cancer (of 7 total patients with metastatic cancer); no autopsy was done. Two patients who had had idiopathic pulmonary embolism died of recurrent disease during treatment (**Table 2**).

DISCUSSION

Our study represents an advance over previous studies that used diagnostic algorithms. We demonstrated

that by combining consideration of pretest clinical probability, which was determined according to a clinical model, and results on the SimpliRED D-dimer test, pulmonary embolism can be diagnosed or ruled out safely, with a dramatic reduction in the need for imaging procedures. No patients in whom pulmonary embolism was excluded on the basis of our diagnostic algorithms subsequently died of pulmonary embolism in follow-up, and thromboembolic events during follow-up were rare. In contrast to our previous study, only about half of the patients required imaging tests, 93% of patients had a diagnosis of pulmonary embolism made or ruled out within 24 hours of presentation, and angiography was rarely indicated. Furthermore, this study demonstrated that the clinical model can be applied by emergency physicians to accurately categorize patients' clinical probability of pulmonary embolism and that diagnostic algorithms based on pretest probability and D-dimer test results are feasible in an emergency department.

Diagnosis and exclusion of pulmonary embolism remain problematic. The gold standard, pulmonary angiography, is invasive and expensive, with limited availability and serious potential effects (13). Ventilation–perfusion scanning provides a definitive diagnosis in fewer than 40% of cases (6, 14). These limitations may explain why clinicians often do not pursue definitive objective tests for suspected pulmonary embolism (15–17). When patients have a nondiagnostic ventilation–perfusion scan, two validated options are pulmonary angiography or serial noninvasive imaging of the leg veins. However, use of these options can be limiting because ideally, diagnostic studies in patients who present to the emergency department should be done on the day of presentation. In addition, pulmonary angiography is invasive, limited in availability, and expensive. Our earlier studies suggested that we could overcome these limitations by identifying patients with low clinical probability of pulmonary embolism in whom a negative result on the SimpliRED D-dimer test should exclude the diagnosis without the need for imaging tests; further testing would be necessary in higher-risk patients, but angiography should rarely be required. We succeeded because our strategy was safe and limited the need for diagnostic imaging tests to 53% of patients. Only 16% (55 of 339) and 25% (16 of 64) of patients with moderate and high probability of pulmonary embolism, respectively, would require testing beyond the day of presentation with our strategy. Overall, only 7.6% of 930 patients required diagnostic testing beyond the day of presentation, and our strategy virtually eliminates the need for pulmonary angiography. Similarly, our strategy could limit the requirement for spiral computed tomography.

Our study has some limitations. Pulmonary embolism remains a complex diagnosis despite our simplified strategy, and in 92 patients (about 10% of our total sample) the protocol was not followed exactly. Of these 92 patients, 5% (4 of 92) developed deep venous thrombosis or pulmonary embolism during follow-up compared with 0.4% (1 of 759) of patients in whom the protocol was followed completely to exclude pulmonary embolism. On the other hand, 7 patients had extra tests done that resulted in a diagnosis of pulmonary embolism, and one could consider that 1% (8 of 759) could have had events in follow-up; however, we do not hold this opinion. In two patients, both with negative D-dimer results and low clinical probability, pulmonary embolism was diagnosed according to a high-probability lung scan on the day of presentation. We are uncertain how the physicians in these cases could have considered the clinical probability to be low and yet ordered a ventilation–perfusion scan, which was then read as high probability. Perhaps the concept of "pulmonary embolism is as likely as or more likely than an alternative diagnosis" was misunderstood in these cases. Otherwise, the clinician would not have ordered the scan. According to our model, if pulmonary embolism is as likely as or more likely than any other diagnosis to cause the patient's symptoms, the patient should not be assigned low clinical probability. Furthermore, if the patients truly had low pretest probability, then the post-test probability of pulmonary embolism after a high-probability ventilation–perfusion scan is only 40%; thus, pulmonary embolism may not have been present. In the group with moderate pretest clinical probability, we attempted to decrease the requirement for serial ultrasonography by recommending this test only in patients for whom results are nondiagnostic on ventilation–perfusion scanning, normal on initial ultrasonography, and positive on the D-dimer test. Regardless, the attending physicians and patients were not always comfortable with this approach, as reflected by spiral computed tomography in 3 patients (1 of whom was not even sent for ultrasonography), pulmonary angiography in 2 patients (both of which were diagnostic of pulmonary embolism), and the patient's or

physician's decision to decline the use of serial testing in 19 cases. This does not mean the algorithm failed or that these patients would not have been given a diagnosis if the algorithm had been followed. Apparently, use of serial testing is safe but inconvenient.

A possible limitation to our study is the low prevalence of pulmonary embolism in our sample; this may suggest that the patients were at lower risk. For the many patients who present to the emergency department with undifferentiated, often pleuritic, chest pain with normal chest radiographic findings, pulmonary embolism must be considered and investigated by using electrocardiography and physical examination. In addition, we believe this low prevalence reflects what will be seen in practice as use of D-dimer tests increases because of wider availability. As with all new and easier diagnostic tests, initial accuracy studies describe high prevalence of disease, but as the test becomes more widely available, the rates decrease. For a potentially fatal disease such as pulmonary embolism, this is not inappropriate. With more widespread testing and use of D-dimer tests as a screening tool, tests with a higher specificity, such as the SimpliRED, become more important. It is possible that the results of our study may not apply to a patient population with a higher prevalence of thromboembolic disease.

We deliberately chose to use a D-dimer test with a higher specificity and lower sensitivity than enzyme-linked immunosorbent assay D-dimer tests to maximize the proportion of patients with suspected pulmonary embolism in whom the diagnosis could be excluded without using imaging procedures. This decision necessitates the use of the D-dimer in conjunction with pretest clinical probability, because the overall negative predictive value of such a D-dimer test is insufficient to rule out pulmonary embolism independently. On the other hand, Perrier and colleagues (12) demonstrated the utility of using D-dimer testing without clinical probability in patients presenting to the emergency department with suspected pulmonary embolism when a D-dimer test with a higher sensitivity than the SimpliRED is used (12). However, in that study, only 36% of the patients had pulmonary embolism excluded on the basis of a normal D-dimer result; furthermore, 11% of patients required pulmonary angiography. The combination of the clinical prediction rule score of less than 2 and a negative result on SimpliRED D-dimer assay excluded pulmonary embolism in 47% of the patients enrolled in our study, and angiography was indicated according to study protocol in about 1% of patients.

Two other studies have used the SimpliRED D-dimer test to determine management of patients with suspected pulmonary embolism. In one study, in an emergency department setting, D-dimer had no benefit (4). However, this study had many limitations, including a small number of patients ($n = 173$), the recruitment of patients with suspected pulmonary embolism or deep venous thrombosis, a high prevalence of disease (suggesting inclusion bias), noteworthy proportion of patients lost to follow-up, lack of confirmation of thromboembolic events during follow-up, and diagnosis of pulmonary embolism based only on a high-probability lung scan. The other study described a small sample of hospitalized and ambulatory patients (18); treatment was safely withheld in 66 of the patients with lung scans of nondiagnostic probability, nondiagnostic clinical probability, and negative D-dimer results. New noninvasive imaging tools for diagnosing pulmonary embolism have been examined, including spiral computed tomography of the thorax and magnetic resonance imaging (19, 20). However, these are expensive and not widely available in many countries; most important, their use has not been validated in large studies. Indeed, in the only management study using spiral computed tomography, more than 5% of patients in whom pulmonary embolism was excluded on the basis of computed tomographic findings subsequently had pulmonary embolism during 3-month follow-up (21). A randomized trial comparing a management strategy such as ours with spiral computed tomography is needed.

If adopted, the application of our bedside method in emergency department patients may save health care resources, reduce inconvenience to patients, and limit risks to patients by averting unnecessary presumptive treatment and further diagnostic testing.

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