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Appropriateness of Diagnostic Management and Outcomes of Suspected Pulmonary Embolism

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Background: International guidelines include several strategies for diagnosing pulmonary embolism with confidence, but little is known about how these guidelines are implemented in routine practice.

Objective: To evaluate the appropriateness of diagnostic management of suspected pulmonary embolism and the relationship between diagnostic criteria and outcome.

Design: Prospective cohort study with a 3-month follow-up.

Setting: 116 emergency departments in France and 1 in Belgium.

Patients: 1529 consecutive outpatients with suspected pulmonary embolism.

Measurements: Appropriateness of diagnostic criteria according to international guidelines; incidence of thromboembolic events during follow-up.

Results: Diagnostic management was inappropriate in 662 (43%) patients: 36 of 429 (8%) patients with confirmed pulmonary embolism and 626 of 1100 (57%) patients in whom pulmonary embolism was ruled out. Independent risk factors for inappropriate management were age older than 75 years (adjusted odds ratio, 2.27 [95% CI, 1.48 to 3.47]), known heart failure (odds ratio, 1.53 [CI, 1.11 to 2.12]), chronic lung disease (odds ratio, 1.39 [CI, 1.00 to 1.94]), current or recent pregnancy (odds ratio, 5.92 [CI, 1.81 to 19.30]), currently receiving anticoagulant treatment (odds ratio, 4.57 [CI, 2.51 to 8.31]), and the lack of a written diagnostic algorithm and clinical probability scoring in the emergency department (odds ratio, 2.54 [CI, 1.51 to 4.28]). Among patients who did not receive anticoagulant treatment, 44 had a thromboembolic event during follow-up: 5 of 418 (1.2%) patients who received appropriate management and 39 of 506 (7.7%) patients who received inappropriate management (absolute risk difference, 6.5 percentage points [CI, 4.0 to 9.1 percentage points]; $P < 0.001$). Inappropriateness was independently associated with thromboembolism occurrence (adjusted odds ratio, 4.29 [CI, 1.45 to 12.70]).

Limitations: This was an observational study without evaluation of the risk for overdiagnosis.

Conclusions: Diagnostic management that does not adhere to guidelines is frequent and harmful in patients with suspected pulmonary embolism. Several risk factors for inappropriateness constitute useful findings for subsequent interventions.

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Pulmonary embolism frequently presents a diagnostic challenge to emergency department physicians because the signs and symptoms are not specific and are very common (1). Both underdiagnosis and overdiagnosis are associated with substantial morbidity and mortality rates. Untreated pulmonary embolism can be fatal (2, 3), and overtreatment exposes the patient who does not have pulmonary embolism to an unjustified risk for major bleeding (4).

In latter decades, several noninvasive diagnostic tests have been validated for patients with suspected pulmonary embolism (5). No single noninvasive test is suitable in all cases, but the combination of clinical probability and 1 or several diagnostic tests allows the physician to differentiate pulmonary embolism from other conditions with confidence in most patients (6). However, the use of clinical probability, the numerous possible test combinations, and the complexity of several diagnostic algorithms may be confusing for clinicians and pose risk for inappropriate diagnoses (7).

Whether evidence-based diagnostic criteria are applied in routine clinical practice has not been extensively investigated (8). Therefore, we aimed to assess whether physicians in emergency departments routinely used evidence-based diagnostic criteria for managing patients with suspected pulmonary embolism. We also wanted to determine the risk factors for inappropriate diagnoses and whether the inappropriateness of the diagnostic criteria influenced the outcome of the patients.

METHODS

Patients and Study Design

We assessed consecutive patients with suspected pulmonary embolism who presented to 117 emergency departments (116 in France and 1 in Belgium) from 13 January 2003 to 16 February 2003 (**Figure 1**). All patients who underwent diagnostic testing for suspected pulmonary

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Context

A large body of high-quality medical literature supports guidelines for diagnosing pulmonary embolism.

Content

The authors studied 1529 patients with suspected pulmonary embolism who presented to 117 emergency departments. They compared each patient's data and the treating physician's final diagnosis with prespecified diagnostic criteria. When they diagnosed pulmonary embolism, physicians used appropriate diagnostic criteria in 92% of patients. When they ruled out pulmonary embolism, they used appropriate diagnostic criteria in only 43% of patients. Inappropriate management was strongly associated with thromboembolic events in a 3-month follow-up period.

Interpretation

Failure to adhere to diagnostic guidelines for pulmonary embolism has consequences. Inappropriate management occurs more often when ruling out the condition.

—The Editors

embolism were prospectively included. Patients were excluded if 1) the diagnosis of thromboembolic disease was documented before admission; 2) pulmonary embolism was suspected during a hospital stay of more than 2 days' duration; or 3) diagnostic testing was canceled for ethical reasons, because of rapid death, or because the patient decided to leave the hospital against medical advice.

The physicians who examined the patients in the emergency department completed a standardized form to report each patient's characteristics, the clinical probability (if assessed), and the diagnostic tests that were ordered. Kidney failure was defined by a creatinine clearance of less than 0.50 mL/s (<30 mL/min) according to the Cockcroft–Gault formula (9). Because the aim of the study was to record the diagnostic management of patients with suspected pulmonary embolism in routine practice, we did not attempt to implement any recommendation for clinical evaluation, diagnostic testing, or treatment. The study coordinator in each center completed the form at the end of the patient's hospital stay to record all of the diagnostic tests performed and the final diagnostic decision. The coordinator checked the data and retrospectively reviewed the emergency department chart to assess the exhaustivity of the inclusions in the study. A standardized questionnaire was used to interview patients at the end of a 3-month follow-up period. If a patient was unavailable by telephone, the local study coordinator contacted the individual by mail or interviewed a family member or the patient's general practitioner. Whenever a possible event was disclosed, the general practitioner was contacted; we reviewed the results of diagnostic tests and the charts of those patients who were hospitalized.

According to French regulations, a participant's written consent is not required for observational studies. However, we requested that every patient orally consent to follow-up, and we informed all patients that they could request withdrawal of their personal data. The ethical committee of the University Hospital of Angers and the Société Francophone de Médecine d'Urgence research committee approved the study.

Classification of Diagnostic Strategies

The criteria for accurately confirming or excluding pulmonary embolism were defined prospectively on the basis of international guidelines and reviews published over the past 5 years (1, 5, 6, 10–14). Diagnostic criteria that were considered to be appropriate are shown in **Figure 2**; the results of other tests or combinations of tests were considered inappropriate. Two investigators independently analyzed each patient chart and classified the diagnostic criteria that were applied as appropriate or inappropriate. Discrepancies ($n = 4$) were resolved by consensus after asking the opinion of a third investigator. The test results were categorized as positive, negative, or inconclusive on the basis of the results mentioned in the patient charts.

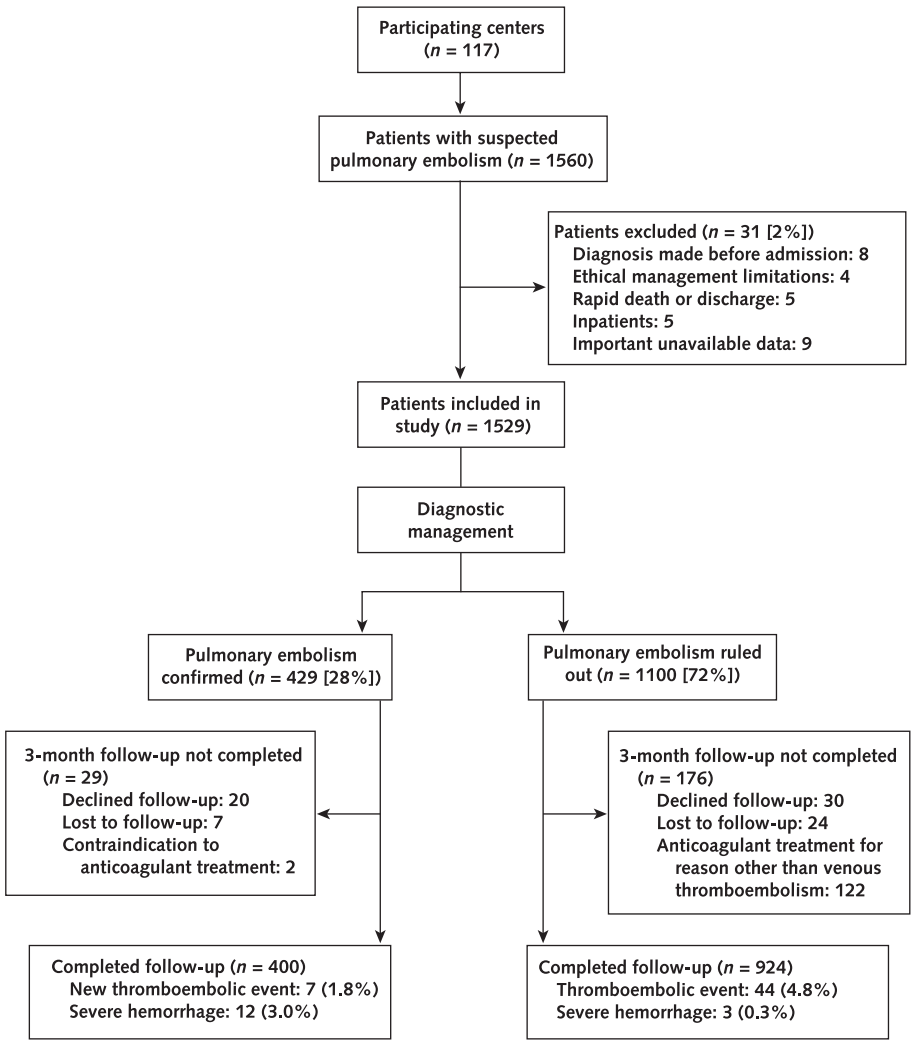
Follow-up Evaluations

Blinded to the diagnostic testing performed, we classified the nonfatal and fatal thromboembolic events that occurred during the 3-month follow-up period as definite thromboembolic events, possible thromboembolic events, or nonthromboembolic events. A thromboembolic event was considered to be definite if the diagnosis was objectively documented by high-probability ventilation–perfusion lung scan or spiral computed tomography (CT), if venous compression ultrasonography showed deep venous thrombosis, if results of pulmonary angiography were positive, or if an autopsy confirmed the diagnosis. Pulmonary embolism was considered to be a possible cause of sudden deaths that could not otherwise be explained (12). Severe hemorrhage was defined as any bleeding that resulted in disability, hospitalization, blood transfusion, or death. Patients in whom pulmonary embolism was confirmed according to initial diagnostic testing and who did not receive anticoagulant treatment were excluded from follow-up. We also excluded from follow-up those patients in whom pulmonary embolism was ruled out but who had received anticoagulant therapy for more than 5 days; therapeutic doses were defined as those intended to achieve an international normalized ratio of greater than 2.0 (oral anticoagulant therapy) or an activated partial thromboplastin time of 1.5 to 2.5 times greater than the control value (heparin) or adequate patient weight–related dose (low-molecular-weight heparin).

Statistical Analysis

All statistical analyses were performed by using SAS statistical software, version 8.2 (SAS Institute, Inc., Cary, North Carolina). We used a chi-square test and the Fisher exact test in cases of small samples to assess the association

Figure 1. **Flow chart summarizing the diagnostic process and 3-month outcomes.**



between the appropriateness of the diagnostic testing and categorical variables (**Table 1**). The adjusted odds ratios of inappropriateness were calculated according to a multivariable logistic regression model. We used SAS's GENMOD command to employ a generalized estimating equation model to adjust for the effect of clustering by hospital. Because emergency physicians did not measure serum creatinine levels in all patients, creatinine clearance determinations were missing in 17% of the patients; consequently, the variable of kidney failure was not included in the regression model. In patients in whom pulmonary embolism was ruled out, we used a similar method to investigate if inappropriate testing was an independent risk factor for a thromboembolic event during follow-up. For follow-up, we included in our model only those variables with a 2-sided significance level of less than 0.05; our goal was to have at least 10 outcomes for every variable in the model (15).

Role of the Funding Source

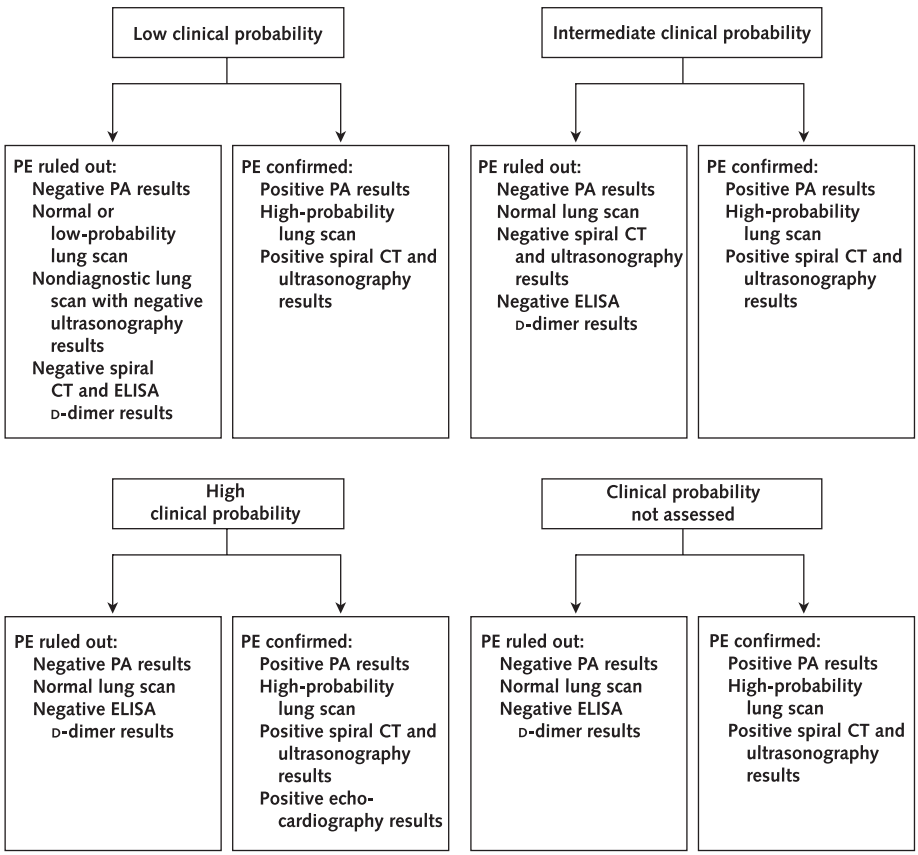
The study was supported by a grant provided by the clinical research department of Pays de la Loire (Projet régional Hospitalier de Recherche Clinique). The funding source provided feedback regarding study design but had no role in data collection, data analysis, data interpretation, or writing of the report.

RESULTS

Centers and Patients

The study was conducted in 117 emergency departments (23 university hospitals and 94 community hospitals). Of the participating centers, 39% admitted fewer than 20 000 patients annually whereas 27% admitted more than 40 000 patients annually. All centers were capable of performing plasma D-dimer measurements; 47% used quantitative enzyme-linked immunosorbent assays, 50%

Figure 2. **Judgment criteria used to classify each diagnostic process as appropriate or inappropriate according to international guidelines.**



A diagnostic process was considered to be appropriate when the results of the tests performed corresponded to those mentioned in the box. All other strategies were considered to be inappropriate. Positive ultrasonography results are defined as incompressibility of a proximal leg vein (popliteal or supra); positive echocardiography results refer to the presence of acute right ventricular dilatation. CT = computed tomography; ELISA = enzyme-linked immunosorbent assay; PA = pulmonary angiography; PE = pulmonary embolism.

used quantitative latex assays, and 3% used semiquantitative assays. At least 5 days per week, venous compression ultrasonography of the lower limbs was available in 80% of the centers; spiral CT was also available in 80% of centers, of which 45% used a multidetector spiral CT scanner. Ventilation–perfusion lung scans could be performed in 33% of participating centers, pulmonary angiography could be performed in 44%, and echocardiography could be performed in 91%. Written guidelines were available in 29% of the emergency departments: Eight percent used a diagnostic algorithm that included clinical probability scoring, 13% used an algorithm without clinical probability scoring, and 8% used clinical probability scoring alone.

During the study, 268 704 patients were referred to the 117 emergency departments, and 1560 patients with suspected pulmonary embolism were prospectively included (**Figure 1**); review of emergency department charts indicated that 75% of all patients with suspected pulmonary embolism were included in the study. The number of patients included at each site varied between 1 and 98 (median, 9; mean [± SE], 13.4 ± 14.3). Of 1560 potential participants, 22 patients were excluded because of predefined reasons and 9 were excluded because the results of a diagnostic test were missing. The remaining 1529 patients were eligible for analysis (**Table 1**). According to patient reports, 68% had dyspnea, 57% had chest pain, 22% had syncopic episodes or dizziness, and 5% had hemoptysis. Signs of deep venous thrombosis were observed in 13% of the patients. The emergency physician assessed the level of clinical probability in 1100 (72%) patients; the probability of pulmonary embolism was determined to be low in 475 (31%) patients, intermediate in 363 (24%) patients, and high in 262 (17%) patients.

Diagnostic criteria were appropriate in 867 (57%) patients and inappropriate in 662 (43%) patients. The independent risk factors for inappropriateness of diagnostic management and the adjusted odds ratios are shown in **Table 1**.

Table 1. **Characteristics of Participating Patients and Centers**

Variable*	All Patients (n = 1529), n (%)	Patients Managed according to Appropriate Criteria (n = 867), n (%)	Patients Managed according to Inappropriate Criteria (n = 662), n (%)	Adjusted Odds Ratio† (95% CI)	P Value
Patients					
Age					
≤50 years	384 (25)	266 (31)	118 (18)	1	
>50 and ≤75 years	586 (38)	348 (40)	238 (36)	1.32 (0.92–1.88)	0.130
>75 years	559 (37)	253 (29)	306 (46)	2.27 (1.48–3.47)	<0.001
Sex					
Men	597 (39)	321 (37)	276 (42)	1	
Women	932 (61)	546 (63)	386 (58)	0.94 (0.72–1.23)	0.66
Allergic disorder					
No	1368 (91)	769 (90)	599 (93)	1	
Yes	134 (9)	86 (10)	48 (7)	0.93 (0.59–1.47)	0.75
Currently receiving anticoagulation‡					
No	1421 (93)	838 (97)	583 (88)	1	
Yes	108 (7)	29 (3)	79 (12)	4.57 (2.51–8.31)	<0.001
Known heart failure					
No	1254 (83)	763 (89)	491 (75)	1	
Yes	263 (17)	98 (11)	165 (25)	1.53 (1.11–2.12)	0.010
Chronic lung disease					
No	1347 (88)	781 (90)	566 (85)	1	
Yes	182 (12)	86 (10)	96 (15)	1.39 (1.00–1.94)	0.048
Active malignant disease					
No	1419 (93)	812 (94)	607 (92)	1	
Yes	110 (7)	55 (6)	55 (8)	1.29 (0.78–2.16)	0.32
Lower-limb paralysis					
No	1475 (97)	840 (97)	635 (97)	1	
Yes	45 (3)	24 (3)	21 (3)	0.89 (0.50–1.60)	0.70
Surgery within past month					
No	1463 (96)	831 (96)	632 (95)	1	
Yes	66 (4)	36 (4)	30 (5)	1.45 (0.87–2.41)	0.160
Plaster cast on a lower limb within past month					
No	1487 (97)	838 (97)	649 (98)	1	
Yes	42 (3)	29 (3)	13 (2)	0.47 (0.21–1.02)	0.056
Bed rest or long travel§					
No	1226 (81)	695 (81)	531 (81)	1	
Yes	287 (19)	165 (19)	122 (19)	0.93 (0.66–1.32)	0.70
Previous thromboembolism					
No	1174 (77)	652 (75)	522 (79)	1	
Yes	355 (23)	215 (25)	140 (21)	0.63 (0.47–0.85)	0.002
Current or recent pregnancy					
No	1513 (99)	862 (99)	651 (98)	1	
Yes	16 (1)	5 (1)	11 (2)	5.92 (1.81–19.30)	0.003
Kidney failure‖					
No	1151 (91)	685 (94)	466 (87)		
Yes	112 (9)	40 (6)	72 (13)		
Centers					
Emergency department admissions per year					
≥40 000	613 (40)	427 (49)	186 (28)	1	
<40 000 and ≥20 000	522 (34)	252 (29)	270 (41)	1.39 (0.91–2.12)	0.130
<20 000	394 (26)	188 (22)	206 (31)	1.30 (0.76–2.23)	0.34
Test availability					
Ventilation–perfusion lung scan or spiral computed tomography, ultrasonography, and pulmonary angiography	751 (49)	493 (57)	258 (39)	1	
Ventilation–perfusion lung scan or spiral computed tomography, ultrasonography; no pulmonary angiography	301 (20)	163 (19)	138 (21)	1.07 (0.69–1.67)	0.75
Ventilation–perfusion lung scan or spiral computed tomography; no ultrasonography	310 (20)	139 (16)	171 (26)	1.26 (0.74–2.14)	0.39
No ventilation–perfusion lung scan or spiral computed tomography	167 (11)	72 (8)	95 (14)	1.41 (0.75–2.62)	0.29
Written guidelines					
Algorithm included clinical probability score	251 (16)	195 (22)	56 (8)	1	
Incomplete guideline	291 (19)	179 (21)	112 (17)	2.12 (1.18–3.80)	0.012
No guideline	987 (65)	493 (57)	494 (75)	2.54 (1.51–4.28)	<0.001

* Data were missing for the following variables: allergic disorder (27 patients), known heart failure (12 patients), lower-limb paralysis (9 patients), bed rest or long travel (16 patients), and kidney failure (266 patients).
† After adjustment, 1479 patients were included in this calculation.
‡ Use of therapeutic doses of anticoagulant agents for more than 5 days.
§ Bed rest of more than 48 hours or long travel of more than 6 hours within 1 month.
‖ Kidney failure was defined as a creatinine clearance of less than 0.50 mL/s (<30 mL/min) according to the Cockcroft–Gault formula. Serum creatinine levels were not measured in all patients (representing 17% of missing data); therefore, the kidney failure variable was not included in the multivariable analysis of the adjusted odds ratio.

Table 2. **Inappropriate Diagnostic Work-ups***

Variable	Patients (*n* = 662)
Pulmonary embolism suspected	
Total, *n*	36
Incomplete strategy, *n (%)*	34 (94)
Distal venous thrombosis, inconclusive ventilation–perfusion lung scan or spiral CT, *n*	10
Distal deep venous thrombosis, no ventilation–perfusion lung scan or spiral CT, *n*	9
Inconclusive ventilation–perfusion lung scan or spiral CT, normal ultrasonogram or no ultrasonogram, *n*	8
Positive D-dimer assay results; no ventilation–perfusion lung scan, spiral CT, or ultrasonography, *n*	7
Inadequate clinical probability, *n (%)*	2 (6)
Positive echocardiographic results, *n*†	2
Pulmonary embolism excluded	
Total, *n*	626
Incomplete strategy, *n (%)*	353 (56)
Inconclusive results on spiral CT or ventilation–perfusion lung scan, *n*	6
Spiral CT and ventilation–perfusion lung scan with discordant results, *n*	6
Normal D-dimer assay results and patient receiving anticoagulant treatment, *n*	18
Normal ultrasonogram, positive or negative echocardiographic findings, no ventilation–perfusion lung scan, no spiral CT, *n*	120
Negative echocardiographic findings, no ultrasonography, no ventilation–perfusion lung scan, no spiral CT, *n*	61
No echocardiography, no ultrasonography, no ventilation–perfusion lung scan, no spiral CT, *n*	142
Inadequate clinical probability, *n (%)*	273 (44)
Normal results on spiral CT, normal ultrasonogram, *n*‡	27
Low-probability ventilation–perfusion lung scan, *n*§	7
Intermediate-probability ventilation–perfusion lung scan and normal ultrasonogram, *n*§	16
Normal results on spiral CT, *n*§	119
Negative results on quantitative latex or semiquantitative D-dimer assay, *n*§	104

* CT = computed tomography.
† In patients with low or intermediate clinical probability of pulmonary embolism or when the clinical probability was not evaluated.
‡ In patients with high clinical probability of pulmonary embolism or when the clinical probability was not evaluated.
§ In patients with intermediate or high clinical probability of pulmonary embolism or when the clinical probability was not evaluated.

Pulmonary Embolism Confirmed

The diagnosis of pulmonary embolism was confirmed at the end of the diagnostic work-up in 429 (28%) patients (**Figure 1**). Diagnostic criteria were appropriate for 393 (92%) patients and inappropriate for 36 (8%). The inappropriate work-ups are listed in **Table 2**.

Of 400 patients who completed follow-up, 7 (1.8%) experienced venous thromboembolism recurrence. Deep venous thrombosis was diagnosed in 1 of these 7 patients, and the other 6 died suddenly, possibly as a result of fatal pulmonary embolism. A total of 12 (3.0%) patients who completed follow-up had severe hemorrhage; 3 had intracranial bleeding, 5 had gastrointestinal bleeding, and 4 had muscular hematomas that required blood transfusion. In total, 29 patients died during the 3-month follow-up period. The deaths were attributed to initial pulmonary embolism ($n = 10$), a possible recurrence of pulmonary embolism ($n = 6$), severe hemorrhage ($n = 3$), or an underlying disease (malignant tumor [$n = 5$], respiratory failure [$n = 1$], septic shock [$n = 1$], cardiac failure [$n = 2$], and stroke [$n = 1$]).

Pulmonary Embolism Excluded

The initial diagnostic work-up excluded pulmonary embolism in 1100 (72%) patients (**Figure 1**). Diagnostic criteria were appropriate for 474 (43%) patients and inappropriate for 626 (57%) patients. The inappropriate diagnostic studies are listed in **Table 2**.

Of 924 patients who completed follow-up and who did not receive anticoagulation, 44 (4.8% [95% CI, 3.5% to 6.4%]) had a thromboembolic event during the 3-month follow-up. Twelve of these 44 patients had a nonfatal thromboembolic event (6 had pulmonary embolism and 6 had deep venous thrombosis), and 32 patients died of a possible pulmonary embolism. Thirty-four deaths were attributed to causes other than venous thromboembolism: malignant disease ($n = 12$), respiratory failure ($n = 8$), septic shock ($n = 6$), cardiac failure ($n = 4$), metabolic disorder ($n = 2$), stroke ($n = 1$), and liver disease ($n = 1$).

Thromboembolic events occurred in 39 of 506 (7.7% [CI, 5.6% to 10.5%]) patients in whom pulmonary embolism was excluded on the basis of inappropriate diagnostic criteria. Inappropriate criteria consisted of a normal ultrasonogram but no thoracic imaging performed ($n = 12$), normal echocardiographic findings but no ultrasonography or thoracic imaging performed ($n = 5$), and positive results of D-dimer assay but no additional diagnostic testing performed ($n = 13$). Thromboembolic events also occurred in 1) patients with intermediate, high, or undetermined clinical probability and normal results on spiral CT ($n = 7$) or a combination of a nondiagnostic ventilation–perfusion lung scan and a normal ultrasonogram ($n = 1$) and 2) in a patient with high or undetermined clinical probability and a combination of normal results on spiral CT and a normal ultrasonogram ($n = 1$). Conversely, only 5 events occurred in the group of 418 (1.2% [CI, 0.4% to 2.9%]) patients with appropriate criteria (**Table 3**). The relative risk for

Table 3. **Patient Outcomes at 3 Months after Exclusion of Pulmonary Embolism***

Diagnostic Work-up	Patients Receiving Appropriate Management (*n* = 418)	Patients Receiving Inappropriate Management (*n* = 506)	*P* Value
Total thromboembolic events, *n* (%)	5 (1.2)	39 (7.7)	<0.001
Nonfatal thromboembolic event, *n*	2	10	0.045
Unexplained sudden death, *n*	3	29	<0.001

* Patients who received anticoagulation for reasons other than thromboembolic disease were excluded from follow-up analysis.

venous thromboembolism during follow-up was 6.4 (CI, 2.6 to 16.2) for patients who were managed inappropriately, and the absolute risk increase was 6.5 percentage points (CI, 4.0 to 9.1 percentage points). In multivariable analysis, the inappropriateness of diagnostic criteria was the only independent risk factor for venous thromboembolism ($P = 0.009$). The odds ratio was 4.29 (CI, 1.45 to 12.70) after adjusting for age and known heart failure and chronic lung disease.

DISCUSSION

In our nationwide study of emergency departments, routine diagnostic practice for suspected pulmonary embolism differed greatly from evidence-based guidelines, and the appropriateness of the diagnostic criteria strongly correlated with patient outcomes. In a majority of patients in whom pulmonary embolism was excluded by the initial evaluation, diagnostic criteria did not adhere to guidelines. The risk for thromboembolism during follow-up was 6-fold higher in these patients than in those who received appropriate management. Of note, proper management was found to be hampered in institutions that lacked a written diagnostic algorithm that included a method for scoring the clinical probability of pulmonary embolism.

For patients with confirmed pulmonary embolism, an inappropriate diagnostic work-up was unusual (9%); in these cases, the diagnosis was generally retained after leg vein ultrasonography revealed a distal venous thrombosis without further testing. Conversely, most exclusion criteria did not conform to guidelines. Pulmonary embolism was frequently ruled out solely on the basis of a normal leg vein ultrasonogram or without performing any further testing after a positive D-dimer test result. In other cases, physicians made inappropriate management decisions after applying a diagnostic test result (normal spiral CT results or negative results on latex D-dimer assay) to an inadequate clinical probability category.

We identified several risk factors for inappropriate management. Clinicians may be prompted to stop the diagnostic process prematurely under 2 circumstances: when thoracic imaging and the use of contrast media may carry increased risk (for example, in pregnant or elderly patients) and when symptoms suggestive of pulmonary embolism can also be ascribed to an underlying disease (for example, heart failure or chronic lung disease) (16). The lack of a diagnostic testing facility did not appear to limit proper diagnostic evaluations. However, the unavailability of a written diagnostic algorithm and a clinical probability score in the emergency department was an independent risk factor for inappropriate work-up. Recent guidelines for managing pulmonary embolism underscore the importance of estimating pretest probability of the disease to ensure that a proper work-up is performed (1, 5, 6, 10–14). Clinical observations and results of diagnostic evaluations can be combined either implicitly or by applying explicit rules to stratify patients into 3 categories (low, intermediate, and high clinical probability) that correspond to an increasing likelihood of pulmonary embolism (17). In our study, 40% of the inappropriate diagnostic strategies were at least partially related to physicians not properly factoring clinical probability into their diagnostic decision. However, only 16% of our participants presented in an emergency department that had no written guidelines for the diagnostic evaluation of patients with suspected pulmonary embolism. This observation confirms that written guidelines are necessary but not sufficient for implementing evidence-based strategies (18).

The strengths of our study are the quantity of centers and the large number of patients who completed follow-up, allowing an analysis of the causes and clinical consequences of everyday diagnostic practice for suspected pulmonary embolism. Nevertheless, our research also has some limitations. Renal function was not evaluated in 17% of the patients, which precluded an assessment of the role of kidney failure as a confounder in the multivariable analysis of independent risk factors. Our appropriateness criteria may be debatable because some strategies are not universally accepted (**Figure 2**) (1, 5, 6, 10–14). The rate at which physicians managed patients inappropriately would have been even higher if we had adopted a more stringent definition (1). Although some authorities consider normal results on spiral CT to be an accurate means for excluding pulmonary embolism in all patients (10), we did not adhere to this guideline on the basis of our findings from earlier research (19, 20). Our results confirm that the risk for venous thromboembolism after normal results on spiral CT is still high; however, this finding might be attributed to the proportion of centers in our study that still use a single-detector spiral CT scanner (21). We did not review the local test interpretations or assess the rate of false-positive results. As is common in outcome studies (19, 20, 22, 23), unexpected deaths were adjudicated by blinded investigators who attributed them to possible pulmonary embolism. Although this may be an overestimation because few autopsies were performed, inappropriate diagnostic management was associated with an increased risk for nonfatal and proven thromboembolic events.

During the past decade, many clinical studies regarding the diagnosis of pulmonary embolism have been published. Our study shows that evidence-based diagnostic strategies have a similar level of confidence in both clinical and research settings (19, 20, 22, 23), and the exclusion of pulmonary embolism on the basis of inappropriate criteria exposes patients to an increased risk for venous thromboembolism. Consequently, we believe that future research should focus on determining how to implement evidence-based guidelines in everyday clinical practice. Institutions should concentrate their efforts on establishing written diagnostic guidelines that include a clinical probability scoring system. Physicians, in turn, should pay more attention to elderly patients; patients with heart failure, chronic lung

disease, and current or recent pregnancy; and patients receiving anticoagulation because they are at high risk for receiving inappropriate management for suspected pulmonary embolism.

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