

Pulmonary embolism: diagnostic algorithms

Giuseppe Favretto, Paolo Stritoni*

Division of Cardiac Rehabilitation, Rehabilitation Hospital, Motta di Livenza (TV), *Division of Cardiology, General Hospital, Treviso, Italy

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In 90% of cases the clinical suspicion of pulmonary embolism (PE) is raised by clinical signs and symptoms, while in only 10% of cases PE is suspected on the basis of electrocardiographic, arterial blood gas analysis or radiological findings.

The combination of clinical signs and symptoms and the results of first-level diagnostic tests (electrocardiography, gas analysis and chest X-ray) allows a fairly accurate classification of patients with “clinical suspicion of PE” into three categories of clinical (or pre-test) probability: low, intermediate and high.

The clinical diagnosis of PE is very often inaccurate making the use of additional tests, including imaging techniques, mandatory.

The choice and the combination (= diagnostic algorithms) of second- and third-level diagnostic tests (D-dimer, venous ultrasound, echocardiography, lung scintigraphy, helical computed tomography and pulmonary angiography) depend primarily on the clinical conditions of patients and their pre-test probability.

We propose two diagnostic algorithms: 1) a diagnostic algorithm for patients with clinically suspected PE and critical clinical conditions (unstable patients), 2) a diagnostic algorithm for patients with clinically suspected PE and non-critical clinical conditions (hemodynamically stable patients).

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Address:

Dr. Giuseppe Favretto

U.O. di Cardiologia
Riabilitativa e Preventiva
Ospedale Riabilitativo
di Alta Specializzazione
Via Padre Bello, 3
31045 Motta di Livenza (TV)
E-mail:
giuseppe.favretto1@tin.it

Introduction

In 2005, the diagnosis of acute pulmonary embolism (PE) still remains a common, major, vexing and elusive clinical problem. The ideal diagnostic test should be accurate, safe, readily available, easy to interpret and cost-effective. Unfortunately, none of the available tests meets all these criteria. This holds true for pulmonary angiography as well, that has been generally considered the “gold standard” in the diagnostic work-up of PE.

Clinical suspicion of pulmonary embolism

In 90% of cases the “clinical suspicion of PE” is raised by clinical signs and symptoms, especially if patients present with clinical evidence of deep venous thrombosis or at risk for venous thromboembolism. Only in 10% of cases, PE is suspected because of incidental electrocardiographic or arterial blood gas analysis or radiological findings (chest X-ray or helical computed tomography).

Approximately 25-30% of patients with clinically suspected PE really have PE¹.

In the context of a recent trial² which enrolled 756 consecutive patients with clinically suspected PE collected from the emergency departments of three teaching hospitals, the prevalence of PE was 26%.

The clinical signs and symptoms alone of PE are non-specific; as a consequence the clinical diagnosis of PE is very often inaccurate. In order to improve clinical accuracy, it is therefore necessary to use additional tests which include imaging techniques.

First-level tests (first-line diagnostic tests), available in all hospitals, readily and easily performed, are the following: electrocardiography, arterial blood gas analysis, and chest X-ray. Unfortunately the diagnostic value of each test is poor (Table I)^{3,4}.

Clinical probability or pre-test probability

The combination of all these variables (risk factors for venous thromboembolism or documented deep venous thrombosis, signs or symptoms suggestive of PE, results of first-level tests) allows a fairly accurate stratification of patients with “clinical suspicion of PE” in

Table I. Diagnosis of pulmonary embolism (PE): first-level tests.

	Sensitivity	Specificity
ECG		
Versus PE	70%	Intermediate/high
Versus massive PE	95%	Intermediate/low
Arterial blood gas analysis		
Versus PE	85%	Low in COPD and elderly patients High in healthy and young subjects
Versus massive PE	95%	Low
Chest X-ray		
Patients without prior cardiopulmonary disease	High	Low
Patients with prior cardiopulmonary disease	Low	Very low
PIOPED ³	88%	Low
PISAPED ⁴	86%	High

COPD = chronic obstructive pulmonary disease.

three categories of clinical or pre-test probability: low, intermediate and high clinical probability or pre-test probability of PE.

Clinical probability may be estimated empirically or by a prediction score. The main advantage of a prediction score is to allow a standardized evaluation. The most prospectively valid scores are the simple clinical models devised by Wells et al.⁵ and the score of the Geneva Group⁶; the score system, of the PISAPED study⁴ has not been validated externally. A recent study which compared the performance of these three models in 215 consecutive patients with PE showed a very important difference in defining precisely the pre-test probability of PE⁷.

It has not been demonstrated yet that grading clinical probability by scoring systems represents a more accurate method than the empirical assessment undertaken by an experienced physician⁸.

In all patients with possible PE, clinical probability should be assessed and documented⁹. However, the positive predictive value of high clinical probability is approximately 70-75% whereas the negative predictive value of low clinical probability is approximately 85-90%. Therefore, it is necessary to use second- and third-level diagnostic tests.

Second-level diagnostic tests, available in all hospitals, are the following: laboratory assays (D-dimer, troponin, brain natriuretic peptide), venous ultrasound, and echocardiography.

Third-level imaging tests, not available in all hospitals, are the following: lung scintigraphy, helical (spiral) computed tomography, magnetic resonance angiography, and pulmonary angiography.

Diagnostic strategy

The choice and the combination of diagnostic tests (diagnostic algorithms, diagnostic work-up) depends on:

- 1) clinical conditions of patients with clinically suspected PE (critical or non-critical, presence or absence of prior cardiopulmonary disease);
- 2) clinical or pre-test probability (low, intermediate or high; rule out/rule in strategy);
- 3) suspected PE in outpatients or in hospitalized patients;
- 4) predictive accuracy of diagnostic tests as obtained by clinical evaluation ("virtual accuracy");
- 5) local availability of diagnostic tests;
- 6) local predictive accuracy of diagnostic tests ("real accuracy") as obtained by experienced professionals and equipments;
- 7) cost-effectiveness analysis of diagnostic strategies and risk-benefit ratio.

Diagnostic algorithms

Diagnostic algorithm for patients with clinically suspected pulmonary embolism and critical clinical conditions (unstable patients) (Fig. 1). The definition of critical clinical conditions is as follows¹⁰:

- patients with hemodynamic instability (cardiac arrest, shock, hypotension);
- patients without hemodynamic instability but with at least one of the following: a) important, persistent and worsening dyspnea; and b) recent syncope.

No absolute as well as validated algorithm is available for unstable patients with clinically suspected PE; diagnosis is influenced by the necessity to take urgent therapeutic measures.

Diagnostic algorithm for patients with clinically suspected pulmonary embolism and non-critical clinical conditions (hemodynamically stable patients) (Figs. 2 and 3). The diagnostic strategy and algorithm mainly depend on the pre-test probability:

- A) patients with clinically suspected PE and high pre-test probability of PE (approximately 20% of all pa-

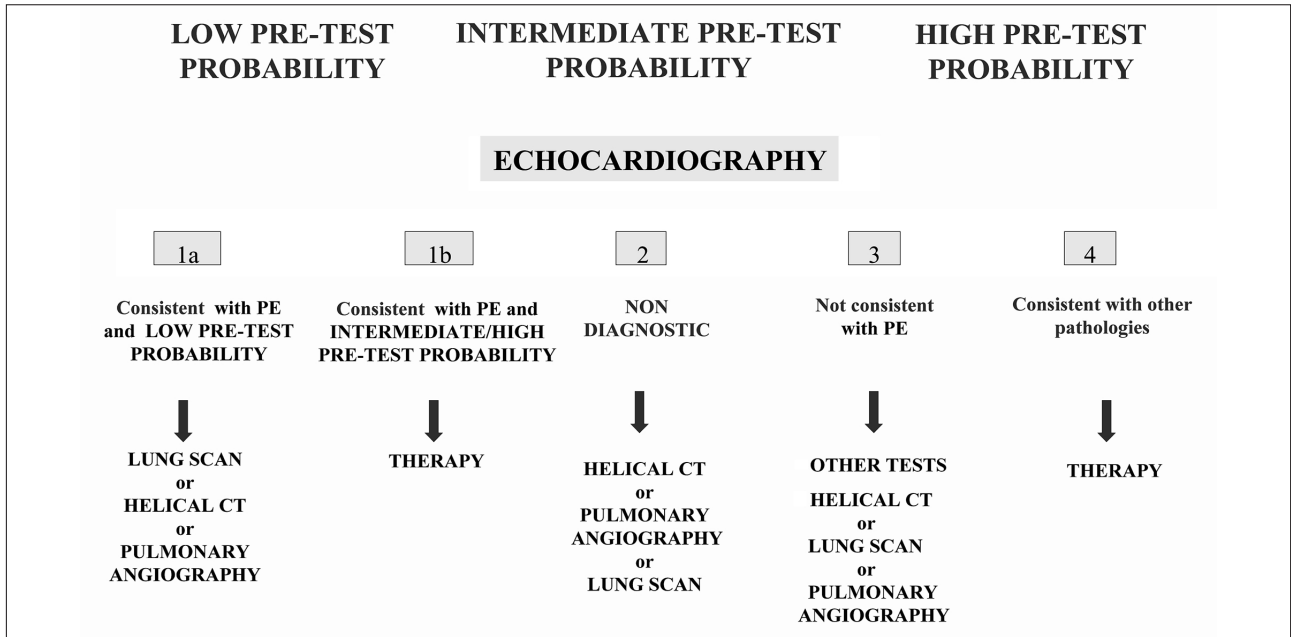


Figure 1. Proposed diagnostic algorithm for suspected pulmonary embolism (PE) in the presence of critical clinical conditions. CT = computed tomography.

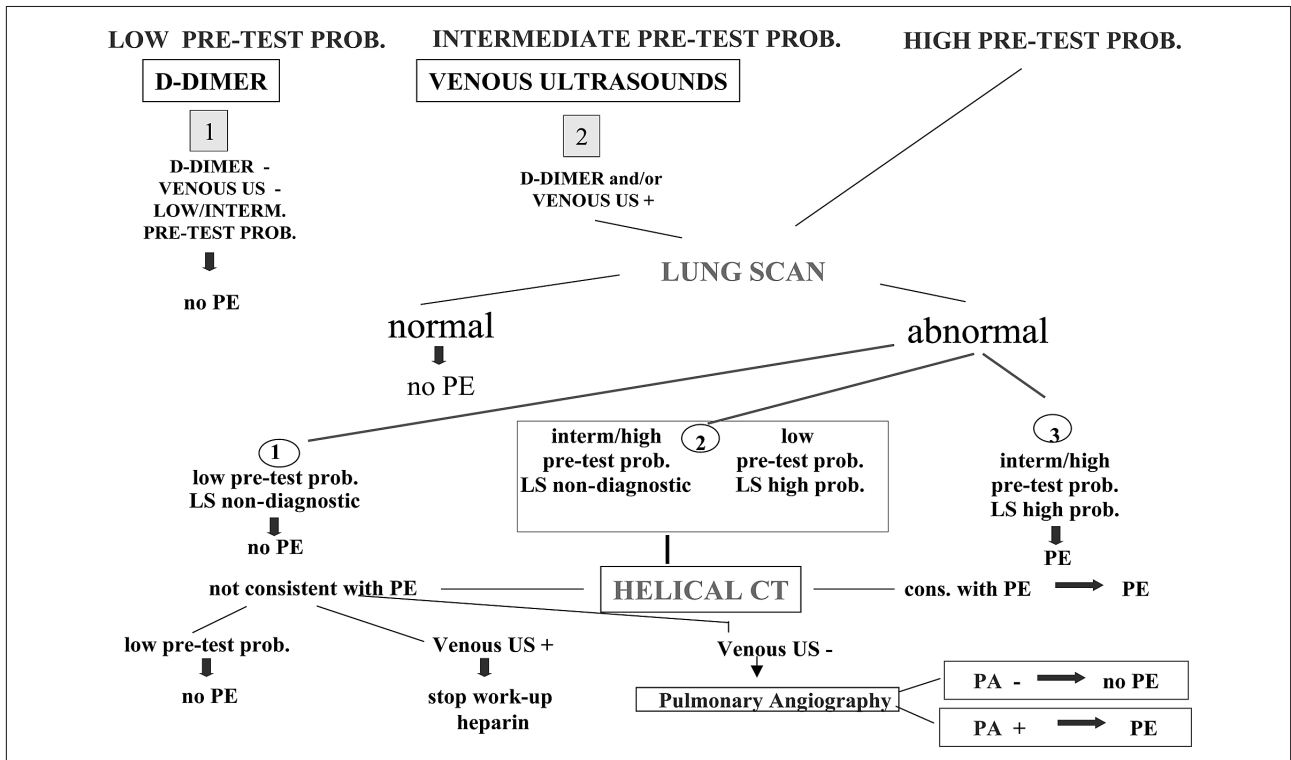


Figure 2. Proposed diagnostic algorithm for suspected pulmonary embolism (PE) in clinically stable patients in hospitals with all diagnostic tests available. CT = computed tomography; LS = lung scan; PA = pulmonary angiography; US = ultrasound.

tients with clinically suspected PE) have documented PE in 70% of cases (positive predictive value of high pre-test probability: 70%).

For those patients with high pre-test probability the following diagnostic tests are advised: lung scintigra-

phy, helical computed tomography, and echocardiography.

Patients with high pre-test probability, if necessary, may undergo pulmonary angiography for diagnosis of PE¹¹.

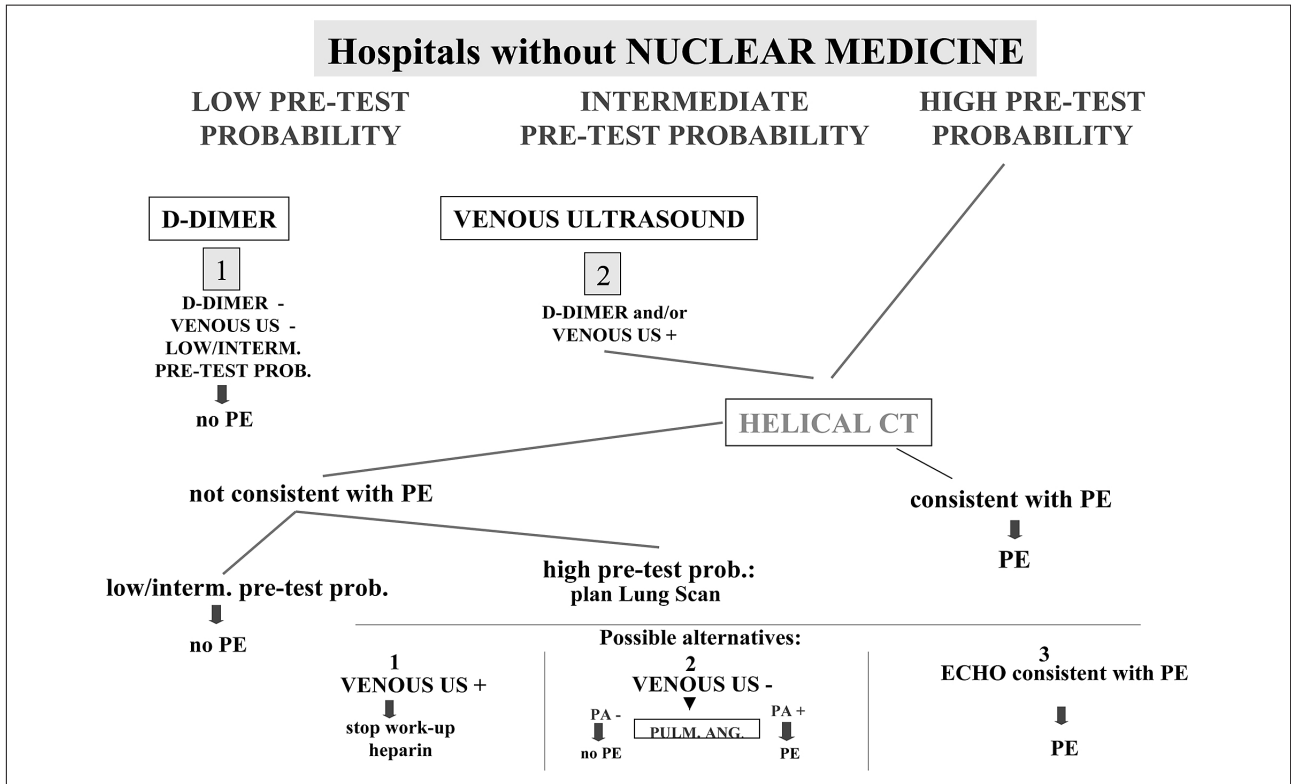


Figure 3. Proposed diagnostic algorithm for suspected pulmonary embolism (PE) in clinically stable patients in hospitals without Nuclear Medicine. CT = computed tomography; PA = pulmonary angiography; US = ultrasound.

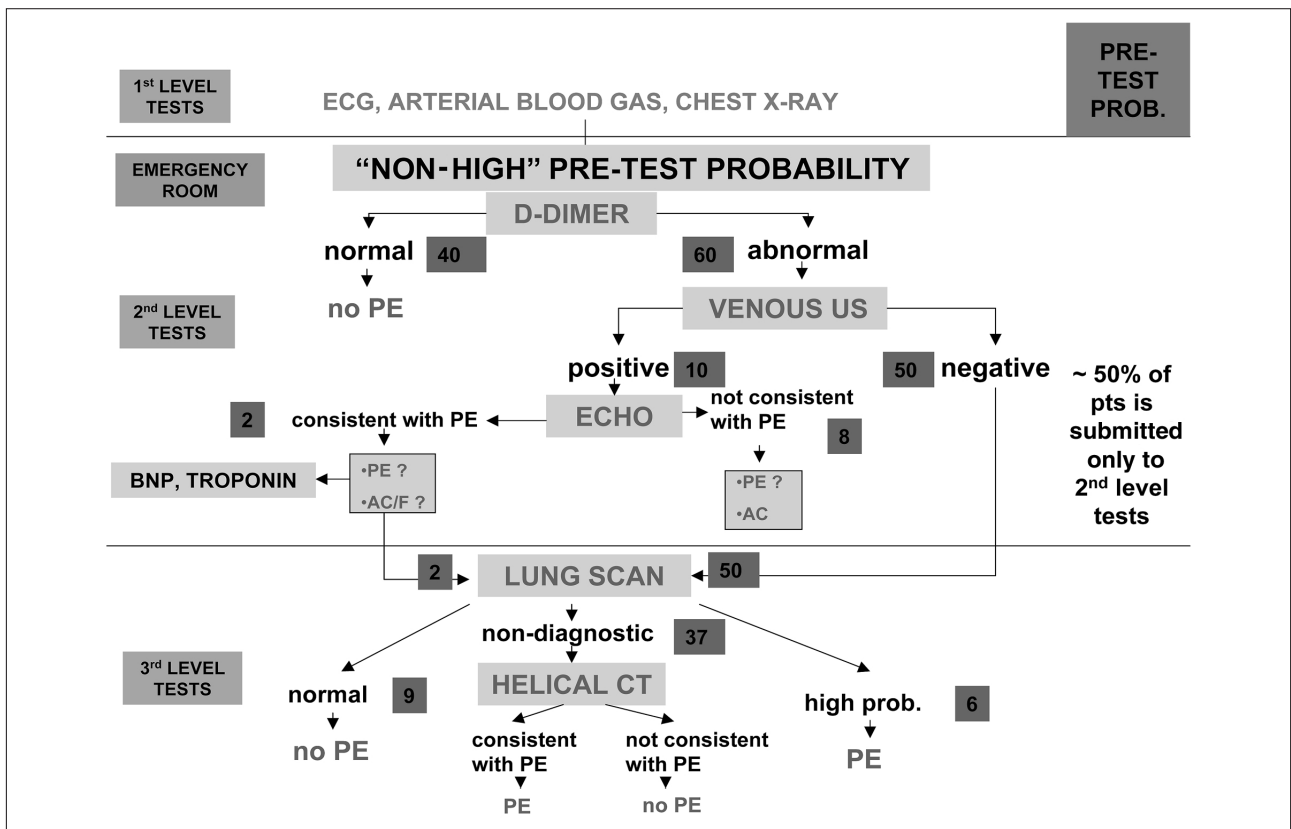


Figure 4. Proposed diagnostic algorithm for suspected pulmonary embolism (PE) in clinically stable Emergency Room patients with non-high pre-test probability. AC = anticoagulants; BNP = brain natriuretic peptide; CT = computed tomography; ECG = electrocardiography; F = fibrinolytics; US = ultrasound.

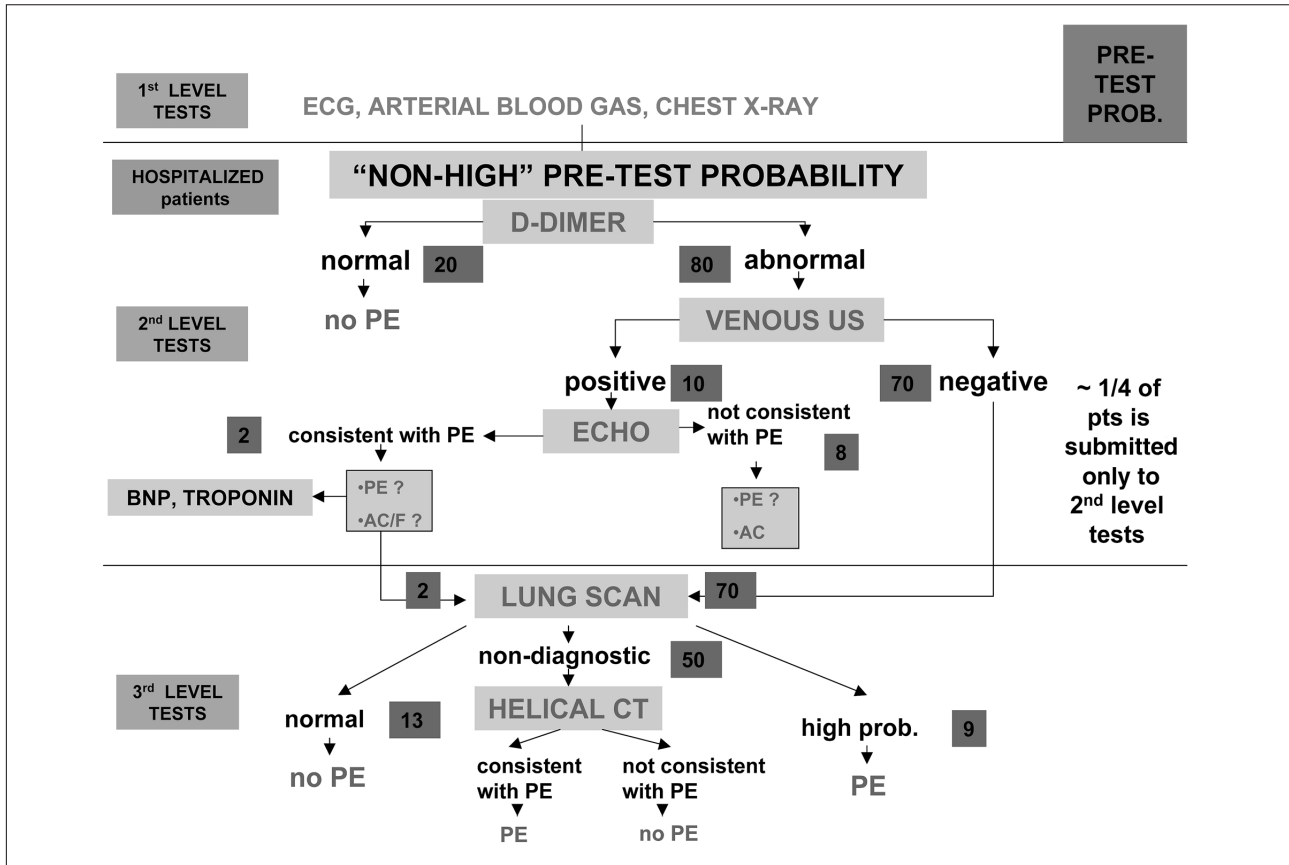


Figure 5. Proposed diagnostic algorithm for suspected pulmonary embolism (PE) in clinically stable hospitalized patients with non-high pre-test probability. AC = anticoagulants; BNP = brain natriuretic peptide; CT = computed tomography; ECG = electrocardiography; F = fibrinolytics; US = ultrasound.

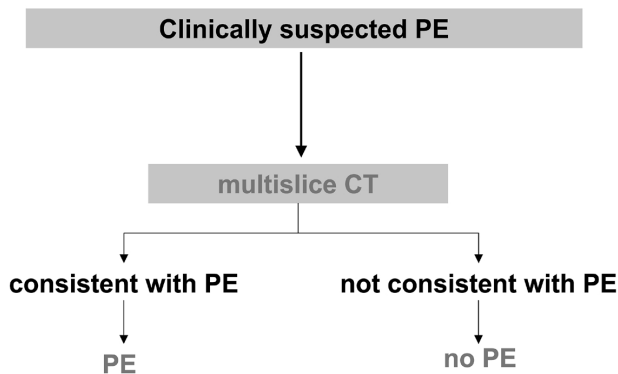


Figure 6. Diagnostic algorithm for clinically suspected pulmonary embolism (PE) which should not be applied. CT = computed tomography.

The D-dimer assay should not be performed in patients with high pre-test probability because also normal D-dimer levels obtained using highly sensitive techniques (VIDAS or turbidimetrics) do not rule out PE⁹.

In patients with high pre-test probability echocardiography consistent with PE may be diagnostic of PE¹⁰.

B) Patients with clinically suspected PE and “non-high” (“non-high” means low or intermediate pre-test

probability) pre-test probability of PE (approximately 80% of all patients with clinically suspected PE) represent only 20% of PE (negative predictive value of non-high pre-test probability: 80%). In these patients the following diagnostic tests are advised: D-dimer assay, lung scintigraphy, and helical computed tomography.

Patients with non-high pre-test probability should not undergo pulmonary angiography for diagnosis of PE.

In patients with non-high pre-test probability a normal D-dimer test at high sensitivity as well as a negative rapid quantitative ELISA (VIDAS) test may rule out PE^{9,11,12}.

First- and second-level diagnostic tests (available in all hospitals), permit the management of most patients with clinically suspected PE; therefore, even in hospitals missing nuclear medicine facilities and helical computed tomography a partial management of clinically suspected PE is possible. An example is provided in figures 4 and 5:

1) outpatients with clinically suspected PE, non-critical clinical conditions and non-high pre-test probability in emergency room (Fig. 4): approximately 50% of outpatients with clinically suspected PE may be appropriately managed with tests available in all hospitals;

2) hospitalized patients with clinically suspected PE, non-critical clinical conditions and non-high pre-test probability (Fig. 5): approximately 25% of inpatients with clinically suspected PE may be appropriately managed in all hospitals.

In conclusion, even if helical multislice computed tomography will soon become the gold standard for diagnosis of PE, we believe that the application of the diagnostic algorithm shown in figure 6 is still premature.

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