Evaluation of Clinical, Instrumental and Laboratory Findings in Patients With Acute Pulmonary Embolism Diagnosed by Spiral CT Angiography

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Abstract

Objective: To investigate the correlations between spiral CT angiography and symptoms, signs, laboratory and instrumental findings in patients with suspected pulmonary embolism (PE).

Methods: Thirty-seven consecutive patients with suspicion of PE were included in the study. Electrocardiography, chest radiography, arterial blood gases analysis and D-dimer assay were performed in all patients. Five patients were excluded from the study due to low clinical probability and normal D-dimer levels. Spiral CT angiography and transthoracic echocardiography were applied to 32 patients with low clinical probability for PE and increasing D-dimer level (n=7), intermediate clinical probability for PE (n=5) and high probability (n=20). The patients were classified as group 1, those with PE (n=21) and group 2, those without PE (n=11).

Results: The two groups were similar in age and sex. Substernal pain (61.9%), dyspnea (100%) and syncope (28.6%) were significantly more frequent in group 1. Frequency of tachycardia (81%), tachypnea (95.2%), hemoptysis (47.6%) and circulatory collapse (28.6%) were also significantly higher in group 1. S1Q3T3 and sinus tachycardia were significant ECG findings and pleural effusion (81%), atelectasis (71.4%), pleural based opacity (71.4%) and prominent central pulmonary artery were also significant findings, in group 1. Mean values for pH, PaO_2, $PaCO_2$, O_2sat % and alveolar-oxygen gradient in groups 1 and 2, in respective order, were: 7.44±0.04 versus 7.40±0.007; 49.54±9.07 versus 63.34±16.05; 31.63±8.21 versus 37.32±9.74; 81.08±5.36 versus 88.58±8.61 and 60.92±14.96 versus 40.01±14.36. All echocardiographic abnormalities were of significantly higher frequency in group 1.

Conclusion: Spiral CT angiography can be used as a first line and safe diagnostic method in patients with suspected PE.

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Introduction

Because the symptoms and signs of pulmonary embolism (PE) are nonspecific or may be absent, it is difficult to make a diagnosis based on clinical symptoms. Conventional pulmonary angiography is the golden standard in the diagnosis of PE. While pulmonary angiography has a sensitivity and specificity greater than 95%, it is an invasive method and it has been reported to lead to a high mortality and morbidity. Also, difficulties are encountered in its interpretation (1). For the diagno-

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sis of PE, ventilation/perfusion (V/Q) lung scanning is frequently performed as the first diagnostic method. This method has a high negative predictive value when patients have a low clinical probability and a high positive predictive value when patients have a high clinical probability. However, only 34% of patients with PE fall into these two categories (2). For these reasons, a noninvasive and objective diagnostic imaging is needed in patients with suspected PE. Spiral CT technology has improved greatly since 1990 and it has been successfully investigated in the past ten years. Spiral CT angiography (SCTA) by giving contrast medium is well accepted as the first diagnostic approach in many centers for the diagnosis of PE. On the other hand, clinical and traditional instrumental findings such as a plain chest x-ray, although nonspecific, remain as valuable clues in selecting patients who need further diagnostic tests (3).

The aim of this study was to evaluate spiral CT angiography in the diagnosis of patients with suspected pulmonary embolism.

Materials and Methods

We included 37 consecutive patients (25 females, 12 males) with suspected PE to the study. Patients with a previous history of PE and those with findings considered as contraindication to contrast medium were not included in the study.

Clinical findings of the patients, based on the clinical history and physical examination are given in Table 1. Chest radiographs were obtained in all patients before SCTA or pulmonary angiography. In most patients, the radiographs (in posterior-anterior and lateral projection) were taken while the patients were standing erect or seated, from a distance of 1.80 meter focus. However, in some patients, the posterio-anterior chest radiographs had to be taken in a semi-erect or supine position. Electrocardiograms were obtained within 24 hours before SCTA or pulmonary angiography. A 12-lead ECG was obtained in all patients. Abnormalities suggestive of right ventricular (RV) overload such as a S1Q3T3 or S1Q3 pattern, a S1S2S3 pattern, p-pulmonale, transient right bundle branch block (RBBB), pseudoinfarction and T wave inversion in the right precordial leads were recorded. Sinus tachycardia and nonspecific ST and T wave changes were other abnormalities noted. Arterial blood gases samples were taken from the femoral or radial artery in all patients while breathing room air and the measurements were performed within 5 minutes (Bayer Diagnostic Rapid Lab. 865, Fernwald, Germany). This analysis included pH, arterial oxygen partial pressure (PaO_2), arterial carbon dioxide partial pressure ($PaCO_2$), percent of arterial oxygen saturation (SaO_2 %) and alveolar-arterial oxygen gradient. Alveolar-arterial oxygen gradient was calculated as below (4):

[D (A-a) O_2 = 150 - (1.25 x $PaCO_2$ + PaO_2)]

Also, a 20 gauge cannule was placed in a medial antecubital fossa vein, and for D-dimer assay; 5 ml blood was drawn into a 0.09% sodium citrate sample bottle. The D-dimer assay was performed in all patients prior to other diagnostic investigations, using the latex-enhanced turbidimetric test (BCT, Dade Behring, Marburg, GMBH, Germany). Concentrations ≤500 µg/L were accepted as normal level and those over 500 µg/L as increased levels.

According to the initial evaluations, 37 patients were classified into three groups; as patients with low, intermediate and high clinical probability. Five patients having a normal D-dimer concentration level and low clinical probability were excluded. SCTA was applied to 32 patients who were evaluated as having 1) low clinical probability but with increased D-dimer concentration levels (n=7), 2) intermediate clinical probability (n=5), and 3) high clinical probability (n=20). There were some differences between the two radiologists on the interpretation of SCTA in 2 patients and therefore pulmonary angiography was applied to these patients. Thus, a diagnosis of acute PE was obtained in 21 patients by SCTA and in 2 patients by SCTA and pulmonary angiography. The diagnosis was excluded in 11 patients by SCTA (Figure 1). We also looked for pathological right heart findings by echocardiograph (Vingmed System Five, GE, Horten, Norway, with 2.5-MHz transducers). Findings indicative of pulmonary hypertension (systolic pulmonary artery pressure >30 mmHg), right ventricular dilatation without hypertrophy, paradoxical movement of interventricular septum and free wall hypochinesia of the right ventricle were noted.

The SCTA was performed in accordance with previously described technical methodology (5), by a single-slice spiral CT (X-vision, Gx, Toshiba, Nasu, Japan). Scenograp-

Table 1. Clinical findings in patients with positive (Group 1) and negative (Group 2) SCTA findings

	Group 1 (n=21) n (%)	Group 2 (n=11) n (%)	P value
Pleuritic chest pain	17 (81%)	6 (54.5%)	NS
Substernal pain	13 (61.9%)	2 (18.2%)	0.02
Sudden onset dyspnea	21 (100%)	7 (63.6%)	0.004
Cough	14 (66.7%)	7 (63.6%)	NS
Syncope	6 (28.6%)	-	0.05
Tachycardia (>100/min)	17 (81%)	2 (18.2%)	0.001
Tachypnea (>20 /min)	20 (95.2%)	5 (45.5%)	0.001
Hemoptysis	10 (47.6%)	1 (9.1%)	0.03
Circulatory collapse*	6 (28.6%)	-	0.05

NS: Not significant, *Systolic arterial pressure <90 mmHg

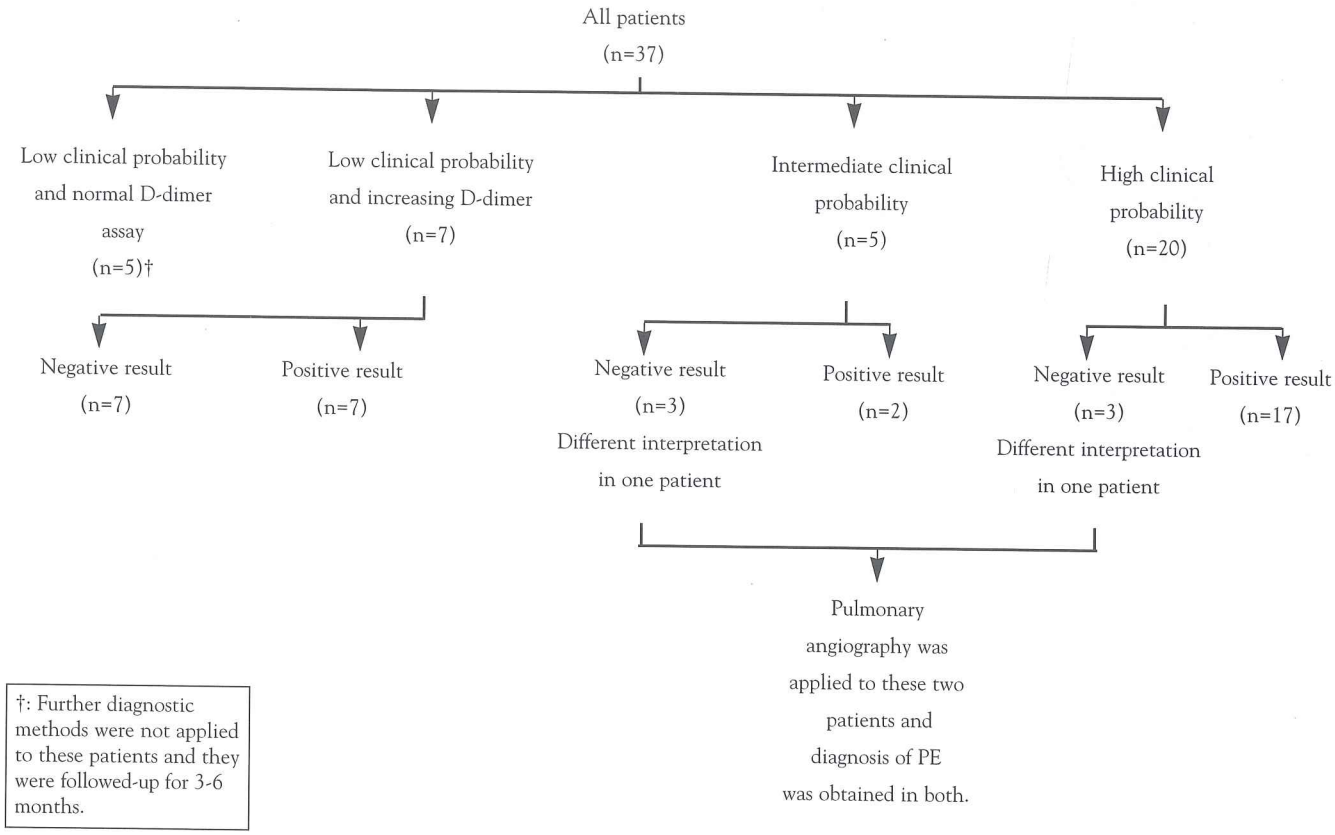

Figure 1. *Diagnostic algorithm.*

hical images were first established at supine position in all patients between the proximal of aortic arch and the diaphragm, and, if needed, parenchymal organs (e.g. liver and spleen) were also included in the imaging. A total amount of 120-140 ml contrast medium (300 mg iodine/ml, Omnipaque, Nycomed, Carrigtohill, Co. Cork, Ireland) was given to all patients by a venflon canule inserted in the antecubital vein. This was injected at a rate 2-4 ml/sec by using a power injector. The started delay was 18 to 20 sec and 25 to 30 sec for patients with normal hemodynamic status and with suspected pulmonary hypertension and right heart failure respectively. Other technical parameters were as follows: kV; 120, mA; 220, thin collimation; 3 mm, "Pitch"; 2:1. All SCTAs were interpreted by two senior radiologists who were blinded to the clinical data and one another's findings.

Finally, the SCTA applied patients were classified into two groups, namely, group 1; consisting of patients with positive SCTA results suggestive of acute PE (Figure 2) and group 2; those with negative SCTA results. Symptoms, clinical signs, laboratory and instrumental findings and echocardiography results were statistically compared between group 1 and group 2.

Statistical evaluation was performed by Chi-Square (Fischer's exact test) and Mann-Whitney U tests. A p value < 0.05 was accepted as significant.

Results

In group 1 (12 females, 9 males) and group 2 (6 females, 5 males), mean ages were 54.04±17.33 and 47.72±17.20 years, respectively (p=0.33). The 5 patients who were evaluated as of low clinical probability and normal D-dimer assay and who did not undergo SCTA were followed-up for a period of 3-6 months. At the end of this period acute PE was established in one patient. The application of SCTA also provided us with data relating to other diseases which may present with symptoms and signs suggestive of PE (Table 2). A diagnosis of urolithiasis (by IVP) and coronary artery disease (by coronary angiography) was made in two patients who were initially evaluated to have an intermediate and a high clinical probability for PE.

Seventeen (81%) of 21 patients in group 1 and 6 (54.5%) of 11 patients in group 2 (p=0.12) had a history of pleuritic chest pain, while substernal chest pain was established in 13 patients (61.9%) in group 1 and in only 2 patients (18.2%) in group 2 (p=0.02). Unexplained sudden onset dyspnea had developed in all patients of group 1, but had occurred only in 7 (63.6%) of 11 patients in group 2 (p=0.004). There was no significant difference in frequency of cough between the two groups. Episodes of syncope were reported in 6 (28.6%) of 21 patients in group 1, but in no patients in group 2 (p=0.05). Tachypnea and tachycardia were the most frequent clinical signs in group

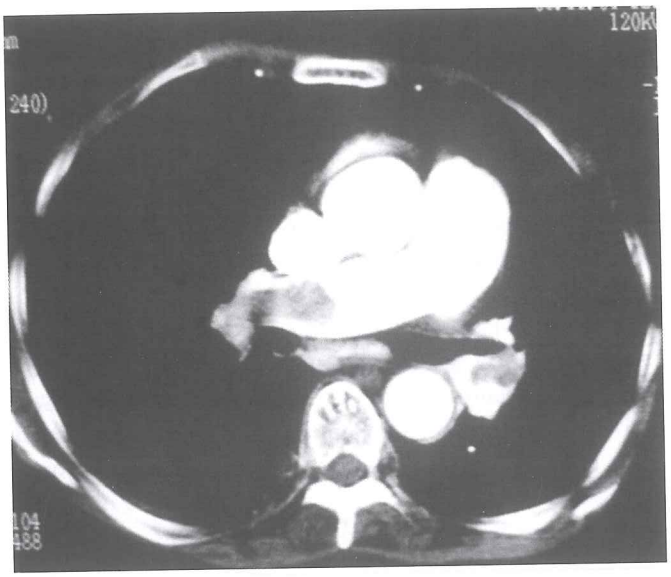

Figure 2. *In a patient with acute pulmonary embolism, spiral CT angiography showing the right main pulmonary artery and the pulmonary artery of the left lower lobe obstructed by a thrombus.*

1, present in 20 (95.2%) and in 17 (81%) of 21 patients respectively, whereas were present in only 5 (45.5%) and 2 (18.2%) of 11 patients in group 2 (p values; 0.001 for both signs). Hemoptysis occurred in 10 (47.6%) of group 1 patients and occurred only in one patient in group 2 (p=0.03). Circulatory collapse (shock or loss of consciousness) occurred in 6 (28.6%) patients in group 1, but in none of the patients in group 2 (p=0.05) (Table 1).

Electrocardiography (ECG) findings were abnormal in most patients with PE (group 1) (20 patients, 95.2%), and sinus tachycardia was the most common findings (17 patients, 81%). In group 2, the ECG was abnormal in 7 (63.6%) and the most common findings were nonspecific ST wave changes. S1Q3T3 was the only statistically significant ECG finding in 19 patients (76.2%) in group 1, 2 patients (18.2%) in group 2 (p=0.002). Other pathological ECG findings are shown in Table 3.

Table 2. Diseases other than PE diagnosed with SCTA

	Probability of PE assessed clinically	n
Malign mesothelioma	Low	1
Mediastinal lymphadenopathy due to NSCLC	Low	2
Pneumonia and pleural effusion	Low	2
Only mediastinal lymphadenopathy due to TB	Low	1
Pneumonia	Low	1
Only pleural effusion	Intermediate	1
Liver abscess	High	1

Table 3. ECG abnormalities in group 1 and group 2 patients

	Group 1 (n=21) n (%)	Group 2 (n=11) n (%)	*P* value
Nonspecific ST changes	10 (47.6%)	4 (36.4%)	NS
Right precordial T inversion	6 (28.6%)	3 (27.3%)	NS
S1Q3T3	16 (76.2%)	2 (18.2%)	0.002
IRBBB†	6 (28.6%)	2 (18.2%)	NS
Pseudoinfarction	1 (4.8%)	1 (9.1%)	NS
S1S2S3	1 (4.8%)	3 (4.8%)	NS
P-pulmonale	5 (23.8%)	1 (9.1%)	NS
Sinus tachycardia	17 (81%)	3 (27.3%)	0.003

†: Incomplete transient right bundle branch block, NS: Not significant

The chest radiograph was abnormal in all patients in group 1, but only in about half of patients in group 2 (p=0.002). Atelectasis (15 patients, 71.4%) and pleural effusion (17 patients, 81%) were the most frequent abnormalities in group 1. The frequency of these abnormalities were 18.2% (2 patients) and 27.3% (3 patients) in group 2, respectively; (p values were 0.005 and 0.003). Pleural based opacity and prominent central pulmonary artery were significantly more frequent in group 1 than in group 2 (Table 4).

Arterial blood gases analysis results showed all parameters to be significantly lower in group 1 than in group 2. In group 1 and 2, pH of arterial blood were respectively 7.44±0.07 versus 7.40±0.07 (p=0.02). PaO_2 and $PaCO_2$, in group 1 and 2, were respectively 49.54±9.07 versus 63.34±16.05 (p values; 0.05 and 0.03). Arterial oxygen saturation (SaO_2%) was 81.08±5.36 versus 88.58±8.61 in group 1 and 2 (p= 0.01) respectively. Alveolar-arterial oxygen gradient [D (A-a) O_2 mmHg] was 60.92±14.96 ver-

Table 4. Abnormal findings in chest radiographs in the two groups

	Group 1 (n=21) n (%)	Group 2 (n=11) n (%)	*P* value
Atelectasis	15 (71.4%)	2 (18.2%)	0.005
Oligemia	4 (19%)	-	NS
Prominent central PA	7 (33.3%)	1 (9.1%)	0.01
Pleural based opacity	15 (71.4%)	1 (9.1%)	0.001
Elevated diaphragm	13 (61.9%)	5 (45.5%)	NS
Hilar artery amputation	2 (9.5%)	-	NS
Pleural effusion	17 (81%)	3 (27.3%)	0.003

NS: Not significant, PA: Pulmonary artery

Table 5. Arterial blood gases in the two groups			
Parameters	Group 1 (n=21) Mean±SD	Group 2 (n=11) Mean±SD	*P* value
pH	7.44±0.04	7.40±0.07	0.02
PaO_2	49.54±9.07	63.34±16.05	0.05
$PaCO_2$	31.63±8.21	37.32±9.74	0.03
O_2sat %	81.08±5.36	88.58±8.61	0.01
D(A-a)O_2 (mmHg)*	60.92±14.96	40.01±14.36	0.002
* Alveolar-arterial oxygen gradient			

sus 40.01±14.36 in group 1 and 2 (p=0.002) (Table 5). PaO_2 was lower than 80 mmHg in 20 (95.2%) of 21 patients in group 1, and it was lower than 80 mmHg in 9 (81.8%) of 11 patients in group 2, but the difference was not significant (p=0.22). $PaCO_2$ was lower than 37 mmHg in 17 (81%) of 21 patients in group 1 and 6 (54.5%) of 11 patients in group 2 (p=0.12). SaO_2% was lower than 90% in 20 (95.2%) of 21 patients in group 1 and 4 (36.4%) of 11 patients in group 2 (p=0.001).

Echocardiography revealed that 20 of 21 patients with PE had at least one pathological finding. Pulmonary artery hypertension (PHT) was the most frequent finding (95.2%). Mean systolic pressure of PA was 53.71±12.88 mmHg versus 30.72±13.24 mmHg in group 1 and group 2, respectively (p<0.001). PHT was established in only two patients (18.2%) who did not have PE. Right ventricular dilatation, paradoxical movement of the interventricular septum and free wall hypochinesia of the right ventricle were found in 15 (71.4%), 9 (42.9%) and 9 (42.9%) of 21 patients with PE, respectively. Patients who did not have PE showed none of these findings (p<0.01).

Discussion

This study showed that SCTA was a safe procedure as a first and main diagnostic test in patients with suspected PE. A diagnosis of PE was safely excluded in patients who had normal SCTA results, including those patients who had a low clinical probability but an increasing D-dimer assay, and those with intermediate and high clinical probability for PE. The results indicate that there were very positive correlations between SCTA results and symptoms, clinical signs and other findings suggestive of PE and negative correlations between SCTA results and findings which are not suggestive of PE. On the other hand, the combination of a normal D-dimer assay and low clinical probability appears to be an adequate method for exclusion of a diagnosis of PE. SCTA also supplied information for diagnosis of diseases other than PE.

Kruip et al suggest that the combination of a normal D-dimer level and low clinical probability can safely exclude diagnosis of PE in patients with suspected PE and this diagnostic strategy is accepted by most clinicians (6). In this study, it was emphasized that anticoagulant therapy need not be given to such patients since the subsequent rate is only 0-6%. In our study, about 13% (5 patients) of the study population were within this group. At the end of a follow-up period of 3 and 6 months, PE developed in only one patient (2.7%). Van Strijen et al reported that false-negative spiral CT rates are 0.4% and sensitivity 99.6%, and recurrence of PE was noted in only 1 of 130 patients who were found to have an alternative illness diagnosed with spiral CT (7). Gottsater et al concluded that their study of negative spiral CT results in patients with suspected PE are warranted to confirm that clinically significant PE can be excluded with a high degree of accuracy and obviate the need for further diagnostic investigations and anticoagulation in the vast majority of patients (8). A weak aspect of our study was to include some patients who had pre-existing pulmonary diseases. However, Tillie-Leblond et al suggest that the presence of previous pulmonary diseases does not affect the negative predictive value of spiral CT (9).

In the patients with suspected PE, clinical features including symptoms, signs and laboratory findings, although nonspecific, usually point to a need for further diagnostic investigation when considered altogether (10). Pleuritic chest pain and sudden onset dyspnea are reported as the most frequent symptoms, and tachypnea and tachycardia are the most often clinical signs in patients with confirmed PE. However, the frequency of theose signs and symptoms are not significantly higher than that of patients who do have PE (3). Miniati et al suggest that sudden or gradual onset dyspnea, orthopnea, pleuritic or substernal chest pain and fainting are significantly higher in patients having PE (11). In the present study, sudden onset dyspnea was the most frequent and significant symptom (100%) in PE patients. Substernal chest pain and syncope with or without unconsciousness were other noteworthy symptoms. Tachypnea and tachycardia were the most frequent signs. These results are in agreement with previously reported results (10,11).

Our study indicates that one or more abnormal findings were present in the chest radiographs of patients with PE. The most significant abnormalities noted were pleural effusion, atelectasis and pleural based opacity. Others (10) also have reported that chest radiographs are usually abnormal in PE patients, and that parenchymal abnormality or atelectasis were the most frequent abnormalities, but that pleural effusions are small in patients who do not have a pre-existing cardiac or pulmonary condition. In yet another study (12), atelectasis and pleural effusion were reported as the most frequently encountered abnormalities in the chest radiographs of PE patients. All these studies

suggest that chest radiographs serve not only to exclude PE but also to diagnose other diseases that may mimic PE (3,12).

ECG is one of the first tools used in the assessment of patients having suspected PE (13). ECG may be of value in the diagnosis of PE, especially for massive PE, although its specificity and sensitivity are not very high. Perhaps, ECG is most useful in assessing the severity of PE since the findings, particularly the presence of an anterior ischemic pattern in the right precordial leads, show positive correlations with the severity of the condition. A previous study suggests that ECG abnormalities, especially an anterior ischemic pattern, are of value not only in the diagnosis of PE but also for evaluation of response to thrombolytic treatment (14). In our study, negative T waves in the right precordial leads were present only in 6 patients with PE (28.6%) and this finding was not significantly higher in group 1 patients than in those who did not have PE. But, severe PE was present in all these 6 patients, confirming that negative T waves are associated with the severity of PE. In our series of PE patients, S1Q3T3 and sinus tachycardia were also found to be significant ECG findings (Table 3).

Assessment of arterial blood gases may be useful in the diagnosis of PE when these are considered together with clinical, electrocardiographic and radiographic findings (3,10). Some early studies suggest that PaO_2 may be normal in patients who have submassive or massive PE and no pre-existing cardiac or pulmonary diseases (15,16). However, a diagnosis of PE is not excluded in patients who have suspected PE and a normal level of alveolar-arterial oxygen gradient (17). Although nonspecific, arterial blood gases analysis should be done as a first diagnostic approach in patients with suspected PE (18). In the PIOPED study it was demonstrated that PaO_2 is lower than 80 mmHg in 81% of patients with PE (19). In the PISA-PED study, PaO_2 and $PaCO_2$ were found to be respectively lower than 82 mmHg and 37 mmHg in 90% of PE patients (11). However, it must be remembered that significant arterial hypoxemia and hypocapnia may occur in some clinical conditions other than PE (3). Our study shows that mean values for all arterial blood gases parameters were significantly lower in patients with PE as compared to patients who did not have PE (Table 5). PaO_2 and $PaCO_2$ were lower than 80 mmHg and 37 mmHg in 95.2% and 81% of PE patients, respectively.

Early studies performed with the transthoracic echocardiograph in the diagnosis of PE focused on the direct observation of thrombus in the right heart cavities (20,21). Subsequent studies investigated the relationships between the degree of pulmonary vascular obstruction and echocardiographic findings in massive or submassive PE cases (22,23). In another study, in which the diagnostic accuracy of transthoracic echocardiograph in patients with suspected PE was investigated, it was found that two or more abnormal echocardiographic findings were present in 56% of patients with PE, but only in 10% of patients without PE, and consequently, that this method and these criteria could be used in the diagnosis of acute PE (24). In our study, pulmonary artery hypertension (PHT) was the most frequent finding in patients who have PE (20 of 21 patients, 95.2%). There were at least three echocardiographic abnormalities (right ventricular dilatation, paradoxical movement of the interventricular septum and free wall hypokinesia of the right ventricle) in about half of the patients with PE. The frequencies of these abnormalities, in respective order, were 71.4%, 42.9% and 42.9% in the 21 patients with PE, significantly higher compared to patients who did not have PE.

In conclusion, this study suggests that SCTA may be considered as a first line diagnostic method in patients with suspected PE. In addition, negative SCTA findings may serve to exclude the diagnosis of PE.

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References

1. Blachere H, Latrabe V, Montaudon M, et al. Pulmonary embolism revealed on helical CT angiography: comparison with ventilation-perfusion radionuclide lung scanning. Am J Roentgenol 2000;174:1041-7.
2. Worsley DF, Alavi A. Comprehensive analysis of the results of the PIOPED Study. J Nucl Med 1995;36:2380-7.
3. Miniati M, Pistolesi M. Assessing the clinical probability of pulmonary embolism. Q J Nucl Med 2001;45:287-93.
4. Masotti L, Ceccarelli E, Cappelli R, et al. Pulmonary embolism in the elderly: Clinical, instrumental and laboratory aspects. Gerontology 2000;46:205-11.
5. Remy-Jardin M, Remy J. Spiral CT angiography of the pulmonary circulation. Radiology 1999;212:615-36.
6. Kruip MJ, Slob MJ, Schijen JH, et al. Use of a clinical decision rule in combination with D-dimer concentration in diagnostic workup of patients with suspected pulmonary embolism: a prospective management study. Arch Intern Med 2002;162:1631-5.
7. Van Strijen MJ, de Monye W, Schiereck J, et al. Advances in New Technologies Evaluating the Localisation of Pulmonary Embolism Study Group. Single-detector helical computed tomography as the primary diagnostic test in suspected pulmonary embolism: a multicenter clinical management study of 510 patients. Ann Intern Med 2003; 138: 307-14.
8. Gottsater A, Berg A, Centergard J, et al. Clinically suspected pulmonary embolism: is it safe to withhold anticoagulation after a negative spiral CT? Eur Radiol 2001;11:65-72.
9. Tillie-Leblond I, Mastora I, Radenne F, et al. Risk of pulmonary embolism after a negative spiral CT angiogram in patients with pulmonary disease: 1-year clinical follow-up study. Radiology 2002;223: 461-7.
10. Stein PD, Terrin ML, Hales CA, et al. Clinical, laboratory, roentgenographic, and electrocardiographic findings in patients with acute

pulmonary embolism and no pre-existing cardiac or pulmonary disease. Chest 1991;100:598-603.
11. Miniati M, Prediletto R, Formichi B, et al. Accuracy of clinical assessment in the diagnosis of pulmonary embolism. Am J Respir Crit Care Med 1999;159:864-71.
12. Worsley DF, Alavi A, Aronchick JM, et al. Chest radiographic findings in patients with acute pulmonary embolism: observations from the PIOPED Study. Radiology 1993;189:133-6.
13. Stein PD, Dalen JE, McIntyre KM, et al. The electrocardiogram in acute pulmonary embolism. Prog Cardiovasc Dis 1975;17:247-57.
14. Ferrari E, Imbert A, Chevalier T, et al. The ECG in pulmonary embolism. Predictive value of negative T waves in precordial leads-80 case reports. Chest 1997;111:537-43.
15. National Cooperative Study. The Urokinase Pulmonary Embolism Trial. Circulation 1973;47/48 (Suppl II):II-18-II-21 and II-81-II-85.
16. Stein PD, Willis PW III. Diagnosis, prophylaxis and treatment of acute pulmonary embolism. Arch Intern Med 1983;143:991-4.
17. Overton DT, Bocka JJ. The alveolar-arterial oxygen gradient in patients with documented pulmonary embolism. Arch Intern Med 1988; 148:1617-9.
18. Masotti L, Ceccarelli E, Cappelli R, et al. Arterial blood gas analysis and alveolar-arterial oxygen gradient in diagnosis and prognosis of elderly patients with suspected pulmonary embolism. J Gerontol A Biol Sci Med Sci 2000;55;761-4.
19. Stein PD, Saltzman HA, Weg JG. Cilinical characteristics of patients with acute pulmonary embolism. Am J Cardiol 1991;68:1723-4.
20. Armstrong WF, Feigenbaum H, Dillon JC. Echocardiographic detection of right atrial thromboembolism. Chest 1985;87:801-6.
21. Farfel Z, Shechter M, Vered Z, et al. Review of echocardiographically diagnosed right heart entrapment of pulmonary emboli-in-transit with emphasis on management. Am Heart J 1987;113:171-8.
22. Metz D, Chapoutot L, Ouzan J, et al. Doppler echocardiograph assessment of the severity of acute pulmonary embolism. Am J Noninvas Cardiol 1991;5:223-8.
23. Mastora I, Remy-Jardin M, Masson P, et al. Severity of acute pulmonary embolism: evaluation of a new spiral CT angiographic score in correlation with echocardiographic data. Eur Radiol 2003;13:29-35.
24. Miniati M, Monti S, Pratali L, et al. Value of transthoracic echocardiography in the diagnosis of pulmonary embolism: results of a prospective study in unselected patients. Am J Med 2001;110:528-35.