VALUE OF TRANSTHORACIC ULTRASONOGRAPHY IN DIAGNOSIS OF PULMONARY EMBOLISM

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ABSTRACT

Background: the diagnosis of pulmonary embolism (PE) is still a problem especially at emergency units. challenges remain regarding efficient, appropriate, and safe imaging methods for the diagnosis of suspected pulmonary embolism. **Aim of the study**: is to determine the diagnostic value of transthoracic ultrasonography (TUS) in patients with pulmonary embolism **.Patients and methods:** cross sectional study was conducted at Chest Department, Zagazig University Hospitals in the period from May 2017 to November 2017. The study was carried out on 48 patients clinically suspected PE. At the begining, TUS was performed by a chest physician, subsequently for definitive diagnosis computed tomography pulmonary angiography (CTPA) was performed to all cases as a reference method. Other diagnostic procedures were examination of serum d-dimer levels, echocardiography, and venous doppler ultrasonography of the legs. Diagnosis of PE was suggested if at least one typical pleural-based/subpleural wedge-shaped or round hypoechoic lesion with or without pleural effusion was reported by TUS. Presence of pure pleural effusion or normal sonographic findings were accepted as negative TUS for PE. **RESULTS :**PE was diagnosed in 31 patients. It was shown that TUS was true positive in 27 patients and false positive in 3 and true negative in 14 and false negative in 4. Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of TUS in diagnosis of PE for clinically suspected patients were 87.09%, 82.3%, 90%, 77.7%, and 85.4%, respectively. **CONCLUSIONS:**TUS with a high sensitivity and diagnostic accuracy, is a noninvasive, widely available, cost-effective method which can be rapidly performed. A negative TUS study cannot rule out PE with certainty, but positive TUS findings with moderate/high suspicion for PE may prove a valuable tool in diagnosis of PE at bedside especially at emergency setting, for critically ill and immobile patients, facilitating immediate treatment decision .

Keywords: Chest ultrasonography, hypoechoic shadow, pulmonary embolism.
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INTRODUCTION

Pulmonary embolism (PE) is a life-threatening clinical emergency. It is estimated that at least 600,000 cases are diagnosed per year in the United States. When treated, PE has a mortality rate of 2%- 8%, but when left untreated, the mortality rate is as high as 25%-30% **[1].** Timely diagnosis of PE is crucial because prompt appropriate managment can decrease mortality but is often confounded by nonspecific clinical presentation [2]. Moreover, actually there is no single noninvasive diagnostic test, that is sensitive enough for the diagnosis in all suspected cases.[3] The combination of clinical probability, ventilation-perfusion lung scanning, and lower extremity sonography has simplified the diagnostic approach. Although lung scanning, computed tomography pulmonary angiography (CTPA), and pulmonary angiography are important for the diagnosis, but they are not widespread enough and cannot be reached at the emergency units, also time factor is important. So, PE at the emergency units remains undiagnosed in the majority of patients, suggesting the need for alternative, easy, and widespread bedside diagnostic approaches.[4,5] The detection of thromboembolic lesions of the lung by thoracic ultrasonography (TUS) was first described 40 years ago.[6,7,8]. Mathis *et al*.,[9,10,11,12] reported their results more recently. Also, Reissig *et al*.,[13] suggested that transthoracic sonography of the lung and pleura may serve as additional method in the diagnostic workup of suspected PE. The most characteristic finding for PE in TUS is hypoechoic, pleural-based paranchymal lesion. Most of these lesions are wedge-shaped.[9,13] They may also have rounded or polygonal shape.

The aim of this study was to determine the sensitivity, specificity, positive predictive

value (PPV), negative predictive value (NPV), and diagnostic accuracy of TUS for diagnosing the PE in patients with moderate to high suspicion of pulmonary emboli.

PATIENTS AND METHODS

Study design

This cross sectional study was conducted at Chest Department in Zagazig Univesity Hospitals in the period from May 2017 to November 2017, in a total of 48 patients with clinical suspicion of PE, 31 patients diagnosed as PE while 17 patients were negative by CTPA. The main inclusion criteria were clinical suspicion of PE under consideration of risk factors. The risk factors were the presence of malignancy, lower extremity fracture, obesity, patients using contraceptive bills, postpartum period, and history of venous thromboembolism, operation, and PE, while pregnant women and patients with renal impairment were excluded from the study. . In the presence of risk factors for PE, the presence of unexplained dyspnea, tachypnea, pleuritic pain, and unexplained radiological findings and blood gas abnormalities are accepted as high clinical suspicion. In the presence of risk factors for PE, presence of dyspnea or hypoxemia which can be explained by conditions other than PE or the presence of unexplained dyspnea or hypoxemia without risk factors for PE are accepted as moderate clinical suspicion.

Written informed consent was obtained from all patients and study protocol was approved by the local ethics committee.

Methods : Included patients were subjected to the followings:

1-Thorough medical history, including history of :

Acute chest pain , dyspnea , tachypnea, tachycardia, hemoptysis. History of immobilization for more than three months, history of hormonal therapy(contraceptive pills) , herbal therapy ,operation and fracture .Presence of co-morbidities such as diabetes mellitus, cardiac, renal, hepatic disease , malignancy or collagen vascular disease and obesity with body mass index (BMI) ≥ 30 kg/m².

2- Clinical examination : including both general and local chest examination.

3. Laboratory investigations:

a) Complete blood count. b) Kidney function tests (Serum urea level & creatinine)
c) Liver function tests. d) Serum electrolytes (Na & K). e) Arterial blood gases analysis. f) Coagulation profile (INR, PT, and PTT).

4-Radiological analysis : including

- Plain chest and heart X-ray posteroanterior and lateral view.
- Transthoracic echocardiograghy
- Duplex of the lower limbs

Transthoracic ultrasound: was performed using **YD-9000A** digital ultrasonic diagnostic imaging system. And **sonoscape** ultrasound machine with double probe. The chest ultrasound was performed with the patient in a sitting position, arms raised and hands placed at the back of the head in order to extend the intercostal spaces and rotate the scapula outward. TUS was performed by an experienced chest physician who had completed a postgraduate thoracic ultrasonography course and trained by a radiologist.

Sonoscape ultrasound device with 3.5 MHz convex probe was used for sonographic examination. If the patient had chest pain, the physician began the sonographic examination from the painful area and intercostal areas were systematically examined in six vertical lines which were paravertebral, midscapular, posterior axillary, midaxillary, anterior axillary, and midclavicular [2].

- Patients were divided into five groups based on the following criteria of sonographic findings **(Comert. et al., 2013)**[2].

(1) Two or more wedge-shaped, triangular, or circular pleura-based hypoechoicareas with or without pleural effusion.

(2) One characteristic wedge-shaped, triangular, or circular pleura-based hypoechoic lesions with pleural effusion.

(3) One characteristic wedge-shaped, triangular, or rounded pleura-based hypoechoic lesions.

(4) Nonspecific subpleural lesions more than 5 mm in size or a free pleural effusion alone . (5) Normal sonographic image.

The diagnosis of PE was suggested if at least one or more typical pleural-based/subpleural

hypoechoic lesion with or without pleural effusion were reported by TUS (Groups 1, 2, and 3). In the presence of nonspecific subpleural lesions more than 5 mm in size, pure-free pleural effusion or normal sonografic findings, the diagnosis of PE was not supposed (Group 4 &5) .

- **CT pulmonary angiography :**was done for all patients in the study .

Statistical analysis

Data of the current study were collected, tabulated and analyzed statistically using Statistical Package for Social Science (SPSS version 19; SPSS, Inc., Chicago, IL). The variables in this study were presented as numbers and percentage or mean ± standard deviation (SD). The following tests were used t-test, Chi Square (x2), Fisher's exact and Logistic regression analysis. A P-value <0.05 was considered significant and P-value <0.001 was considerd highly significant. As regard crude odds ratio result, it was considered significant when number one not included in its range..

RESULTS

Table 1 showed that the most of studied patients were males (79.2%). The ages of studied patients ranged from 28 to 85 years with a mean of 51.7 ± 12.34 years. Current or former smoker presented (75%) among the patients in this study. The most frequent risk factor was prolonged immobility for more than 3 months (60.4 %),the most common symptom is dyspnea (100%) followed by chest pain (70.8%) , 24 cases (50%) have intermediate clinical probability and 22 (45.8%) cases have high probability.

Table (1): Demographic data of all studied cases

characters	NO.of patients N = 48	%
Age in years Mean (range)	51.7± 12.34 (28 – 85)	-
Sex male	38	79.2
female	10	20.8
Smoking smoker	36	75
Non smoker	12	25
Risk factor		
Immobility>3months	29	60.4
Hypertention	21	43.7
Malignancy	7	14.5
Obesity BMI>30kg/m²	12	25
Contraceptive bills	6	12.5
Diabetes mellietus	6	12.5
Postpartum (within 1month)	4	8.33
Cerebrovascular stroke (within the last 3months)	1	2
Symptoms		
Dyspnea	48	100
Chest pain	34	70.8
Cough	25	52
Expectoration	2	4.16
Wheeze	1	2
Hemoptysis	15	31.25
Signs		
Tachypnea.	29	60.4
Tachycardia.	32	66.6
Signs of deep vein thrombosis.	12	25
Fever		
crepitation	8	16.6
Rhonchi	14	29.1
Clinical propability of PE:	7	14.5
Low	2	4.2
Intermediate	24	50
High	22	45.8

Table 2 showed that 31 cases (64.5%) were diagnosed by CTPA as pulmonary embolism, while 17 cases (35.5%) were negative PE.

Table (2) : Final diagnosis of all studied cases according to computed tomography pulmonary angiography.

Studied cases	NO	%
PE positive cases	31	64.5
PE negative cases	17	35.5
Total	48	100.0

Table 3 showed that the most frequent symptoms in patients with PE is dyspnea (100%) followed by chest pain (77.4%), dry cough (61.3%) and hemoptysis (38.7%) with highly statistical significant difference between both groups as regard hemoptysis .

Table (3): Difference between studied groups as regard symptoms.

Symptoms	Patients with PE (N=31)		Patients without PE (n=17)		Test	P value
	No	%	No	%		
Chest pain	24	77.4	10	58.8	**χ 2 test** 2.02	0.33 NS
Dyspnea	31	100.0	17	100.0	------	-------
Cough	19	61.3	6	35.3	**χ 2 test** 2.97	0.084 NS
Expectoration	1	3.2	1	5.9	**Fisher's exact test** 0.19	0.65 NS
Hemoptysis	12	38.7	3	17.6	**Fisher's exact test** 13.59	0.001* S
Wheeze	0	0.0	1	5.9	**Fisher's exact test** 3.45	0.17 NS

***Highly statistical significant difference**

Variable	Patients with PE (N=31)		Patients without PE (N=17)		Test	P value
Age Mean ± SD	49.77± 13.51		55.23± 9.18		**T test** 1.48	0.14 NS
Sex	NO	%	NO	%	**χ 2 test**	
Male	7	22.6	3	17.6		**0.68**
Female	24	82.4	14	77.4	**0.16**	**NS**
Special habit					**χ 2 test**	**0.60**
-smoker	24	77.4	12	70.6		
-non smoker	7	22.6	15	29.4	**0.27**	**NS**
Risk factors					**Fisher's exact**	
• Immobility>3months	17	54.8	12	70.6	1.13	0.28
• Hypertention	16	51.61	5	29.41	2.19	0.13

• Malignancy	4	12.9	3	17.65	0.19	0.65
• Contraceptive bills	4	12.9	2	11.76	0.37	0.54
• Diabetes mellitus	4	12.9	2	11.76	0.37	0.54
Postpartum(within 1 month)	3	9.68	1	5.88	0.20	0.64
• Cerebrovascular stroke(within 3 months)	1	3.22	0	0.00	0.3	0.90
• Obesity (BMI>30kg/m²)	8	25.8	4	23.53	0.02	0.86

Table 4 shows that the most frequent risk factor among PE positive patients is prolonged immobility more than 3 months (54.8%) with no statistical significant difference between both groups of patients and other risk factors.

Table (5) *showed that 12 cases (38.7 %)of PE positive patients were confirmed with pulmonary embolism using TUS(have 2 or more hypoechoic shadows) so there was highly statistical significant difference between two maneuvers***.**

Table (5):distribution of transthoracic ultrasound shadow among pulmonary embolism positive and pulmonary embolism negative patients.

CTPA diagnosis / TUS findings	Patients with PE (N=31)		Patients without PE (n=17)		χ 2 test	P value
	No	%	No	%		
- 2 or more hypoechoic lesions	12	38.7	0	0.0	21.26	<0.001*
-1 hypoechoic lesion with effusion	10	32.3	0	0.0		
-1 hypoechoic lesion alone	5	16.1	3	17.6		
-Pleural effusion alone	1	3.2	9	52.9		
- normal	3	9.7	5	29.4		

Table (6) showed that TUS has high validity in suggestion cases with pulmonary embolism with sensitivity 87.09% and accuracy 85.41 % but with weak sensitivity in confirmation cases with PE in comparison to CTPA.

Table (6): Validity of US in diagnosis of Pulmonary embolism with use CT as gold standard.

	Sensitivity %	Specificity %	PVP %	PVN %	Accuracy %
***All PE cases by US (n=30)**	**87.09**	**82.35**	**90.0**	**77.78**	**85.41**
***Confirmed cases by US (n=12)**	**38.7**	**100.0**	**100.0**	**47.22**	**60.41**

DISCUSSION

In this study, the aim was to determine the role of bedside TUS for diagnosing the PE in patients with moderate/high clinical suspicion of PE, we concluded that pathological lesions such as consolidation, atelectasis, and local pleural effusion can be identified by TUS easily and TUS is a safe, cheap, and available method for the early diagnosis and treatment decision of PE[2].

Despite the new improvements in technology such as multislice CTPA, since it is costly and cannot be available at every medical center also it is associated with potentially harmful radiation and application of contrast medium, diagnosing PE still remains a significant medical problem especially at the emergency departments. On the contrary, accurate diagnosis and early treatment of PE is important and potantially life-saving.[13] The decision about the PE suspected cases need to be made in real time and the time for making the decision is short.

Table 4 shows that the mean age of cases of pulmonary embolism is younger than that in cases negative for PE but this difference was statistically insignificant. These results are in agreement with **Nandita** & **Rakesh 2008[**14**]**. In contast , **Stein et al.,2008[**15**],**who noted that pulmonary embolism is associated with advancing age due to the cumulative effect of risk factors that patients acquire with aging such as immobility, hypertention, obesity , trauma, and surgery.

Table (4) in this study also shows that (77.4%) of the proved PE cases by CTPA were males while (22.6%) were females. This is in agreement with **Tapson2008**[16] and **Nataliia et al.,2012[**17**]** who noted that PE is more common among men than women and this can be explained by the more exposure of men to risk factors for PE such as smoking and trauma .

In the present study table (4) shows no significant relation between smokers and pulmonary embolism, but there was increase in percent of smokers with Pulmonary embolism.

This is coincised with **Cheng Y et al., 2013[**18**]** who noted that pulmonary embolism incidence is more with smokers due to the following causes, reduced fibrinolysis, inflammation, and increased blood viscosity.

Table (4) in this study shows no significant difference between occurance of PE and multiple risk factors but percent of patients with embolism are high with immobility 54.8% followed by hypertention 51.6%.

This was concised with (**Reyad et al., 2012)[**19**]** who was in agreement with **(Samama,2000)[**20**]** who noted that prolonged immobility and resting in bed are associated with increased incidence of VTE. This is explained by prolonged immobility leads to local venous stasis resulting in accumulation of clotting factors and fibrin, resulting in thrombus formation.

In contrast, **Coon &Willis 1997[**21**]** found that previous history of DVT is the strongest predisposing factor in pulmonary embolism (present in 74%), followed by smoking , anathesia and surgery and then immobility, this difference could be explainedby the difference in the selected population, as their study was conducted only to detect the prevelance of pulmonary

embolism in patients with different malignancies, and this population is well known to be more susceptible to the risk of recurrent VTE.

In this study **table (3)** shows that the most frequent symptom among PE cases is dyspnea (100%), chest pain (73.3%), cough (61.3%) and hemoptysis (38.7%) with statistical significant difference between patients with and without embolism as regard hemoptysis and fever , but there was no statistical significant difference in chest pain , cough, dyspnea, expectoration and wheeze.

This is concised with **Tapson (2008**)[17] who concluded that the most frequent symptoms in PE is breathlessness and chest pain.

This is due to ventilation perfusion (V/Q) mismatch and release of mediators that cause bronchoconstriction **(Tapson 2008)[**17**]**.

In this study ***table 5& table 6*** *show that 38.7 % of patients were confirmed with pulmonary embolism using TUS.*

According to the TUS findings when Groups 1,2 and 3 were discussed, in the presence of two or more subpleural, characteristic, hypoechoic lesions (only Group 1) the sensitivity of TUS for diagnosing PE was 38.7% and specificity 100%, Whereas in addition to two or more hypoechoic lesions (Group 1), one lesion together with localized pleural effusion (Group 2) and one characteristic lesion without pleural effusion (Group 3), sensitivity increased significantly up to 87.09 % but specificity decreases to 82.3 %, Negative predictive value was 77.78 %, if groups 1, 2, and 3 were considered together and 47.22 % if only group 1 was taken into consideration.

This is in agreement with **Comert S et al.,2013[**2**]** who found that TUS findings when Groups 1,2 and 3 were discussed, in the presence of two or more subpleural, characteristic, hypoechoic lesions (only Group 1) the sensitivity of TUS for diagnosing PE was 43.3%, specificity was 75%. But with addition of (group 2 and 3) sensitivity increases significantly up to 90% but specificity decreases to 60% . Negative predictive value was 80%, if Groups 1, 2, and 3 were considered together, 46.8% if only Group 1 was taken into consideration.

CONCLUSIONS

Transthoracic ultrasonography is non invasive and does not employ radiation and contrast material; the method may be applied on patients, irrespective of their age, during pregnancy, under conditions of renal failure, or in patients with allergy to contrast material. Finally, portable sonographic equipment also allows ultrasound evaluation at any time and in any place (patients in ICU and those on mechanical ventilation).

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