**Diagnostic performance of transthoracic ultrasound in patients with pulmonary embolism**

**Abstract:**

Background: Pulmonary embolism (PE) is an acute, significant and life threatening condition. Transthoracic ultrasound (TUS) is one of the non-invasive diagnostic modalities that has been presented for detection of numerous chest disorders as well as PE. Objectives: the aim of this work was to assess the accuracy, sensitivity and specificity of bedside transthoracic ultrasonography for the diagnosis of pulmonary embolism. Patients and methods: 50 patients with moderate or high clinical suspicion of PE were examined by TUS. Diagnosis of PE depended on clinical suspicion and confirmed by computed tomography pulmonary angiography (CTPA). Results: most of lesions related to PE and detected by US examination were in the right side (60%) and posterior lower lobe (70%) with predominance of A profile. Sensitivity, specificity, accuracy, negative and positive predictive values of TUS in diagnosis of PE were 93.3%, 65%, 82%, 86.7 and 80% respectively. Conclusion: TUS is an important diagnostic tool as a non-invasive bed side test in diagnosis of PE principally for critically ill or immobile patients with high sensitivity and specificity.

Keywords: Thoracic ultrasound, pulmonary embolism, CTPA

**Introduction**

Pulmonary embolism (PE) is an acute, significant and life threatening condition **(1).** PE is a usually undiscovered and untreated disorder. Since signs and symptoms are vague, the diagnosis of pulmonary embolism may be troublesome and requires high suspicion index. Recent technical advances, including D-dimer, computed tomographic pulmonary angiography (CTPA), ventilation/perfusion scintigraphy (V/Q) and spiral computed tomography (sCT) essentially affect PE diagnosis, increasing recognition rates particularly for segmental PE, however not without decrease specificity **(2).** Likewise, complications that may follow contrast dye injection and radiation exposure can occur. Consequently, alternative strategies could help doctors in certain settings**.** Likewise, PE is a possibly lethal disorder requiring instant anticoagulant treatment **(3)**.  Transthoracic ultrasound (TUS) is one of the non-invasive diagnostic modalities that have been presented for detection of numerous chest disorders as well as PE. To be recognizable by TUS, the lesions need to reach out to the pleural surface of a completely expanded lung. Moreover, parenchymal changes might be observable in lung separated from the chest wall when an acoustic window as atelectasis or pleural effusion is existing, permitting the ultrasound to enter into more profound tissue so that thromboembolic lesions become apparent to sonographic assessment whether pleural effusion presents or not **(4)**. PE-related changes are that the ‘pleural line’ comparing to the PE-related regions may lose its echogenicity and appear irregular or fragmented. Also, mechanical changes related to atelectatic lung tissue, and elevated capillary pressure in addition to high vessel wall permeability resulting from inflammatory mediators release may causes increased exudation of fluid into the pleural space **(5).** The goal of this work was to assess the accuracy, sensitivity and specificity of bedside transthoracic ultrasonography for the diagnosis of pulmonary embolism.

**Material and methods:**

**Ethics**

This prospective study was done in Benha University hospital in the period between November 2019 and July 2022. This study was approved by Ethical Committee of Benha University, Faculty of medicine (No. RC 17-9-2019). An informed and written consent were acquired from all participants.

**Study design**:

This study was performed in chest department and included 50 patients with moderate or high clinical supposition of PE. Pulmonary embolism diagnosis was depended on clinical suspicion on the basis of risk factors for venous thromboembolism, symptoms and signs of PE, including dyspnea of unknown etiology, chest pain, tachypnea either separately or together. Diagnosis was established by CTPA findings with a filling defect illustrated by contrast material and or by deep vein thrombosis (DVT) revealed by duplex sonography of lower limbs **(6).**

**Exclusion criteria**

Patients who had superficial lesions or diseases that interfere with using the US probe as subcutaneous emphysema or fractured ribs were excluded.

**Inclusion criteria**

All patients suspected to have pulmonary embolism according to original and simplified Geneva criteria.

patients were subjected to thorough history taking, physical examination, plain chest X-ray (poster-anterior and left lateral view), arterial blood gases, laboratory investigations, echocardiography, CTPA which was investigated by radiologist who knew nothing about clinical findings and duplex lower limbs in suspected cases of DVT.TUS was carried out for all patients using ultrasound device (Philips Hd5 Color Doppler Ultrasound Machine, 2013 GE LOGIQ P5 Ultrasound Machine, made in Japan). TUS was performed via the convex probe (2.5–5 MHz frequency) and the linear probe (7.5–10 MHz) for lung and pleura examination respectively. TUS was done utilizing gray scale (B-mode), time- motion mode (M-mode) and color doppler mode.

Direct signs of PE were assessed including straddling clots at the bifurcation of pulmonary artery or suspended embolus in the right side of the heart **(7).**  Lung sliding was evaluated (the ‘‘to-and-fro” twinkling motion of the lung throughout breath that was noticeable at the pleural line), likewise artifacts types and lung profiles were identified and incorporated A profile (anterior overwhelming bilateral A lines (horizontal hyperechoic lines beneath and parallel to the pleural line and connected with lung sliding)), A´ profile (A profile with nullified lung sliding), B profile (anterior dominating bilateral B line) vertical hyperechoic lines emerging from the pleural line that extend the whole way to the boundary of the screen without disappearing)), B´ profile (B profile with abolished lung sliding), A/B profile (anterior dominant B lines at one side and A lines at the other), C profile (anterior lung consolidation) and PLAPS (posterior-lateral alveolar consolidation as well as pleural effusion syndrome). Abnormal sonographic discoveries of consolidation were checked out as sub pleural, echo-poor area or one with tissue-like echotexture, with air (dynamic hyper echogenic foci) and/or fluid bronchograms (anechoic tubular structures. pleural effusion was viewed as a homogeneous, anechoic space between the parietal and visceral pleura **(8)**. Patients were separated into five groups rely upon the accompanying characters of sonographic discoveries; group I (at least two typical wedge-formed, triangular or rounded pleura-based hypoechoic lesions ± pleural effusion), group II(One typical wedge-formed, triangular or rounded pleura-based hypoechoic lesions with pleural effusion), group III (One typical wedge-formed, triangular or rounded pleura-based hypoechoic lesions), group IV (Nonspecific subpleural lesions > 5 mm in size or pleural effusion only) and group V (Normal sonographic findings). PE diagnosis was suspected if one or more characteristic pleural-based/subpleural hypoechoic lesion ± pleural effusion were detected by TUS. In the existence of nonspecific subpleural lesions exceeding 5 mm in diameter, free pleural effusion or normal sonographic discoveries, PE diagnosis was not assumed. Patients were considered having PE sonographically if they had either A profile with positive DVT or multiple, hypoechoic, subpleural lesions mostly triangular, rounded or polygonal **(9).**

**Statistics :** Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) version 11.2 for Windows software (STATA Corporation, College Station, Texas). Continuous data were demonstrated as the mean ± SD and range, and categorical data were demonstrated as a number and percentage. Student t-test (t) and Mann Whitney test (z) were utilized to differentiate two groups of normally and non-normally distributed data respectively. One way analysis of variance (ANOVA; F) and Kruskal Wallis test (x2) were used to compare more than two groups as appropriate followed by post-hock tests using the Bonferroni method to detect differences in pairs. Percent of categorical variables were differentiated utilizing the Chi-square (χ2) test and Fisher’s Exact Test as appropriate. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic value of the TUS in the diagnosis PE were determined utilizing the standard definitions.

**Results:**

 The studied group included 50 patients; 21 female (42%) and 29 males (58%) with mean age 53.6±8.83. 72% of patients were obese (36 patients). The median Geneva score was 11 upon which patients divided into high clinical suspicion for PE (26 patients) and intermediate suspicion (24 patients) and the median pulmonary embolism severity index (PESI) score was 60 (45-67). Regarding ultra-sonographic findings among studied group, the percentage of US positive findings were more in males and more in obese patients. There was a high significant relation between positive lesions in US and high Geneva score, presence of risk factors as post-partum, post-operative, fracture, history of previous pulmonary embolism or DVT **(Table 1).** X-rays finding among the studied group included pulmonary infarction (90%), pleural effusion (24%), pulmonary oligemia (28%), enlarged pulmonary artery (20%) and normal chest x-rays in 8% of patients. While ultra-sonographic findings included wedge shape pleural based lesion among 52% of patients, rounded lesion (12%), pleural effusion (24%) and absence of flow perception in coloured Doppler examination of the infarcted area in 60% of patients. Most of lesions that found by US examination were in the right side (60%) and in the posterior lower lobe (70%) while left lung lesion and bilateral lesion represented 10% each. Most frequent lung profiles in ultrasound in pulmonary embolism suspected cases were A profile (94%). Mean pulmonary artery pressure (PAP) and right ventricular function were elevated in studied group (Table 2). Also there was significant positive correlation between pulmonary artery pressure (PAP) and PESI (Table 3). It was found that 8 patients had single parenchymal lesion, while the other 20 had multiple lesions (parenchymal lesion(s) + pleural effusion) those 28 patients also confirmed with CTPA to had pulmonary embolism (true positive cases) the remaining 7 cases that had ultrasonic picture suggesting PE were confirmed to be negative PE with CTPA (false positive cases). We had 2 cases show insignificant sonographic picture of PE but confirmed with CTPA to be PE (false negative) the remaining 13 cases were true negative with ultrasound and CTPA. So, the total number of patients with positive ultrasound findings (true & false positive) were 35 (Table 4) (Table 5). Chest US showed high sensitivity and specificity in diagnosis of PE compared to CTPA (Table 6) (Fig. 1)

**Discussion:**

PE is one of the significant cardiovascular emergencies that are habitually found in the clinical setting. Nonetheless, its detection is a challenge in many cases, conesquently an imaging confirmation is required for this reason. Numerous diagnostic procedures had been carried out in the diagnosis of PE, and each one had its own advantages and disadvantages including the gold standard CTPA **(10)**. Early management of PE is possibly lifesaving, and this requires the presence of a simple, harmless, and an exact imaging methodology that could be quickly carried out for immobile and critically ill patients as a bedside test. TUS might serve in such manner and recently utilized for this reason; additionally, it avoids the dangerous exposure to radiation and contrast media that could be utilized in CTPA **(11).**  In this study, the mean age of the studied group was found to be 53.6 ± 8.83 years with males 29 (58%) and females 21 (42%), 72 % of patients were obese. Geneva score median range is 11, 52% of the cases were high clinical suspicious andPESI median range is 60. This means that PE in our patients was more in patients above 50ys and in obese subjects, a feature of PE known for a long time **(12)**. This was nearly similar to Comert et al**.** who evaluated 100 patients with suspected PE. Of these patients, 54 were males and 46 were females. The mean age was found to be 64.1 ± 17.9 (range 19-85) years. 76 of cases interpreted as high clinical suspicion and 24 cases as intermediate clinical suspicion **(13).** We observed that DVT history was significantly elevated in PE positive group (P=0.001) and post-operative history was also observed significantly higher in PE positive group (P=0.006). Kagima and collagues evaluated the risk factors in their patient groups and found that at least one risk factor is present in 72% of their cases and DVT was noticed significantly higher in PE positive group (P < 0.05) **(14).** The habitual findings in chest X-ray of our patients were consolidation (90 %), and (8 %) of them were normal. This agrees withComert et al.who found pulmonary consolidation to bethehabitual chest X-ray findings (43.4%) in their PE positive group **(13).** According to distribution of ultra-sonographic finding in the studied group (shape of lesion) we found 26 (52%) hypoechoic, triangular, or wedge-shaped, subpleural lesions and 12 (24%) pleural effusions were detected by TUS. In a similar study done by Sayed and his coworkers**,** they found that the appearance of parenchymatous lesions in their PE cases were triangular in 55.6% which is similar to our results **(15).** In the current study, pleural effusion was detected in 24% of our cases, which agreed with Comert et al. who found basal pleural effusion in 19% of cases **(13).** Coloured doppler signal was absent in 60% of the suspected lesions of PE in this study, similarily Sayed and his coworkersfound that the colour flow signal was missed in 44.4% of patients **(15).** The majorities of the lesions (70%) were determined in the posterior lower part of lungs and were more in the right side (60%) in this work. In a comparable study done o patients with PE, themajority of the lesions (85.4%) in the lower part of lungs and 55.7% were on the right lung **(13).** The most frequent lung profiles in ultrasound in this study were A profile (94%). Profile A as the predominant profile seen in TUS was also found in 50% of patients studied by Sayed et al **(15).** Also, this was in consensus with Elkholy and his collagues who found that the common profile in PE group was A profile (55.6%) **(16).** The median range of PAP in patients with proved PE was 40 mmHg and other ECHO findings among patients with proved PE as TAPSE and FAC to assess right ventricular function all were suggestive for diagnosis of pulmonary embolism in suspected cases. Comert et al**.** found thatelevated PAP (>36 mmHg) as detected by echocardiographic examination in 43.4% of PE positive group **(13).** Also,Daley and his collaguesoptimized the measurement cut-off of TAPSE for the diagnosis of PE, using an abnormal cut-off of less than 2.0 cm and concluded that TAPSE has moderate diagnostic value in patients with suspected PE **(17).** Similarly**,** Karimialavijeh et al.examined66 patients of which 28 patients had positive CTPA. The mean TAPSE, was 16.36 ± 1.59 mm in the PE positive group and 21.68 ± 2.87 mm in the PE negative group (P-value = <.0001) **(18).** Also, KossaifymeasuredFAC to assess right ventricular function and concluded that a fractional area change <35% indicates of right ventricular systolic dysfunction **(19).** In this work, significant positive correlation between PAP&PESI was found which matched study done by Jiménez and his colleagueswho found thathigh risk patients with high pulmonary pressure had high PESI **(20).**The distribution of our patient groups depend on sonographic findings in PE and non-pulmonary embolism cases as follow; group I,II,III had 28 cases with positive US findings confirmed with CTPA and 7 cases had positive US findings but negative result with CTPA. In a study done byBitar et al.,theynoticed that a conclusion of PE was proposed if pleural-based/subpleural wedge-shaped or round hypoechoic lesion (regardless presence of pleural effusion) was descriped utilizing TUS **(4).** In this work true positive cases were 28 cases, false positive cases were 7, false negative cases were 2 and true negative were 13 cases.Nazerian and his coworkers evaluated 352 patients with suspected PE and found that PE was diagnosed in 194 patients. On the ultrasound, PE true-positive n = 144; PE false-positive n = 8; PE true-negative n = 150; and PE false-negative n = 50 **(21).** In the current study, sensitivity, specificity, accuracy, negative and positive predictive values of TUS in the detection of PE were 93.3%, 65%, 82%, 86.7 and 80% respectively. In a similar study done byReissig et al**.,** they compared TUS with CTPA in the detection of peripheral PE. A total of 33 patients with symptoms suggesting PE were registered in the study. TUS and CTPA were done within 24 h from the beginning of clinical signs. Reported the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of TUS as 80%, 92%, 95%, 72% and 84%, respectively **(9).** Also, Pfeil and his colleagues reported the sensitivity of TUS for PE diagnosis as 70% and specificity 69.6%, NPV and PPV were 84.25% and 50%, respectively **(22).** Similarly, another studyreported a sensitivity of 71.4%, specificity of 80.9% and accuracy of 87.1% **(15).** Also, Nazerian et al.found that Sensitivity of TUS for the diagnosis of PE (81.5%), while specificity was (95.4%) **(21).** Another similar study found that TUS had a sensitivity of 74%, a specificity of 95%, a PPV of 95%, a NPV of 75%, and an accuracy of 84%, Which match our results **(4).**

**Conclusion:** TUS is an important diagnostic tool as a non-invasive bed side test in detecting PE principally for critically ill or immobile patients with high sensitivity and specificity.

**Conflict of interest: none**

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**Tables:**

**Table (1): Differences between ultra-sonographic findings among studied group regarding their sociodemographic characteristics and pulmonary embolism related data**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable**  | **Ultra-sonographic findings**  | **Chi Square Test**  | **P value**  |
| **Positive (No.)**  | **Negative (No).** |
| **Sex**  | **Male** | 20  | 9  | .035  | .85  |
| **Female**  | 15  | 6  |
| **Age (mean ±SD)** | 53.17 ± 9.0 | 54.87 ± 8.58  | **Student t-test =**.618  | .53  |
| **BMI** | **Normal**  | 11 | 3 | .68 | .409  |
| **Obese**  | 24 | 12 |
| **Geneva score** (Median (IQR)) | 11 | 9  | **Z mann-whitney test** 4.77 | **.001(HS)** |
| **Post-partum**  | 11  | 0  | 6.044  | **.014(S)** |
| **Post-operative** | 13  | 0  | 7.529  | **.006(HS)** |
| **History of previous pulmonary embolism or DVT** | 17  | 0  | 11.039  | **.001(HS)** |
| **Fracture**  | 9  | 6 | 4.704  | **.030(S)**  |

**BMI: body mass index, IQR: inter quartile range, DVT: deep venous thrombosis, HS: highly significant, S: significant.**

**Table (2):** **ECHO findings among** **patients with proved pulmonary embolism**

|  |  |
| --- | --- |
| **Variable**  | **Median (IQR)** |
| **PAP** | 40 (33-48) mmHg |
| **RV FAC**  | 20% (17-23) |
| **TAPSE** | 1-1.5 cm |

**IQR: inter quartile range, PAP: pulmonary artery pressure, RV: right ventricle, FAC: fractional area change, TAPSE: tricuspid annular plane systolic excursion.**

**Table (3): Spearman correlation between PAP &PESI of the studied group**

|  |  |  |
| --- | --- | --- |
|  | **Spearman** **rs=** | **P value**  |
| **PESI and PAP** | 0.328 | **0.02 (s)** |

PESI: pulmonary embolism severity index, PAP: pulmonary artery pressure, S: significant.

**Table (4): Distribution of groups based on sonographic findings in pulmonary embolism and non-pulmonary embolism cases**

|  |  |
| --- | --- |
| **Sonographic findings**  | **Pulmonary embolism**  |
| **Positive confirmed with CTPA****(No.)** | **Negative confirmed with CTPA****(N0.)**  |
| **Group I: Two or more typical wedge-shaped lesions with or without pleural effusion** | 12 | 3 |
| **Group II:** **One wedge-shaped lesion with pleural effusion** | 8 |  3 |
| **Group III: One hypoechoic lesion** | 8 |  1 |
| **Group IV: Nonspecific subpleural lesions > 5 mm in size or a free pleural effusion only** | 1  | 3 |
| **Group V: Normal sonographic findings** |  1  | 10 |

CTPA: computed tomography pulmonary angiography, No.: number.

**Table (5): Distribution of true positive and true negative findings by ultrasonography in the studied group**

|  |  |  |
| --- | --- | --- |
|  | **CTPA** | **Total**  |
| **Positive No. (%)** | **Negative N0. (%)** |
| **Ultrasonography**  | **Positive** | 28 (93.3) | 7 (35) | 35 |
| **Negative**  | 2 (6.7) | 13 (65) | 15 |
| **Total**  | 30 | 20 | 50 |

CTPA: computed tomography pulmonary angiography, No. number.

**Table (6**): **Sensitivity, specificity, positive, negative predictive values and accuracy of ultrasonography**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Ultrasonography** | **AUC** | **95% CI** | **Sensitivity****%** | **Specificity**% | **PPV** | **NPV** | **Accuracy** **%** |
| **Pulmonary embolism** | .792 | .651 - .932 | 93.3 | 65 | 80 | 86.7 | 82 |

AUC: area under the curve, CI: confidence interval, PPV: positive predictive value, NPP: negative predictive value



**,Figure (1): ROC curve of ultrasonography findings among studied group**