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Acute pulmonary thromboembolism in emergency room: gray-scale versus color doppler ultrasound evaluation

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Abstract

Background: Pulmonary thromboembolism (PTE) remains under-diagnosed fatal disease at emergency units suggesting the need for alternative, easy, and noninvasive bedside diagnostic approaches.

Objectives: To determine the diagnostic role of gray-scale and color Doppler transthoracic ultrasonography (TUS) in patients with PTE.

Patients and Methods: Blinded to 64 multi-detectors CT pulmonary angiography (MDCTPA) examination as a gold standard, 60 patients with clinically suspected PTE underwent gray-scale and then color Doppler TUS examination. Results were compared and diagnostic accuracy of TUS was assessed.

Results: Forty patients proved to have PTE by MDCTPA. TUS showed typical lesions in 33 patients with the mean of 2 lesions per patient. Most lesions were hypoechoic, wedge- shaped, and pleural- based and the majority (80%) was located in the lower lobes. Consolidation with little perfusion was detected by Color Doppler ultrasound in 97% of lesions. Isolated central PTE was significantly higher in TUS negative patients. For gray –scale TUS, sensitivity, specificity, positive and negative predictive values and accuracy were 82%, 90%, 94%, 72%, and 85%. Meanwhile the sensitivity, specificity, positive and negative predictive values and accuracy of color Doppler TUS were 80%, 95%, 97%, 70% and 87%, respectively.

Conclusion: TUS is a reliable diagnostic bedside test for PTE in critically ill and immobile patients. Adding color Doppler to gray–scale TUS increases the specificity and accuracy and consequently the confidence in the diagnosis of peripheral pulmonary infarctions and differentiates them from other pulmonary lesions that allow initiation of anticoagulants.

KEYWORDS
pulmonary thromboembolism, gray- scale, color Doppler, ultrasonography

1 | INTRODUCTION

Acute pulmonary thromboembolism (PTE) is still a diagnostic problem especially at emergency units. It is frequently under diagnosed and consequently undertreated.[1]

Many deaths occur in hemodynamically unstable patients and the mortality rate in these patients is ranged from15% to 25%.[2] Early diagnosis of PTE is important because prompt appropriate management can decrease mortality but is often confounded by nonspecific clinical presentation.[3]

Computed tomography pulmonary angiography (CTPA) is considered the gold standard for the diagnosis. Unfortunately CTPA is expensive, not widespread enough cannot be reached at the emergency units, and also time factor is important. Furthermore, it has limitations in pregnancy and renal failure. So, PTE remains undiagnosed especially at the emergency rooms in the majority of patients, suggesting the need for alternative, easy, and widespread bedside diagnostic approaches.[4,5]

Transthoracic ultrasonography (TUS) is an emerging noninvasive diagnostic technique. It is gaining an increasingly important role in diagnosing many chest diseases including pulmonary embolism (PE).[6]

There are various sonographic diagnostic criteria which can be used in the diagnosis of PE. Hypoechoic, pleural-based parenchymal alteration is the most characteristic finding. More than 85% of these lesions are wedge-shaped. Also, they may have either polygonal or rounded configuration. In 20% of the patients, a single hyperechoic structure localized at the center of the lesion and indicates the presence of air-filled bronchiole may be present. Pleural effusion is another manifestation of PTE. Applying of color Doppler imaging may give additional diagnostic information. In pulmonary infarction, pulmonary arterial flow cannot be detected by color Doppler ultrasound, and this is called "consolidation with little perfusion". Also, congested thromboembolic vessel may be seen and this is called "vascular sign."[7–9] Despite its rising role, to the best of our knowledge, TUS has not been used or evaluated in our locality in the workup for diagnosis of PTE. Hence the aim of this study was to determine the diagnostic role of grayscale and color Doppler TSU in PTE in emergency situations where other diagnostic tests cannot be done or unavailable.

2 | PATIENTS AND METHODS

A total of 60 consecutive patients (27 women and 33 men; mean age 50.63 years) admitted to Medical Emergency Room or, Respiratory Intensive Care Unit (RICU), in a tertiary Hospital with suspected PE were enrolled in this prospective analytic cross- sectional study. The ethics committee approval was obtained and all enrolled patients completed a written consent form.

The main inclusion criteria were intermediate or high risk of PE as defined according to modified Wells score.[10]

All enrolled patients were subjected to

1. Detailed medical history and physical examination, making an attention to risk factors, signs and symptoms of PE.
2. Chest x- ray posteroanterior and lateral views.
3. Arterial blood gas analysis.
4. ECG and echocardiography.
5. Multidetector computed tomography with pulmonary angiography (MDCTPA) using Toshiba aquillion 64 MDCT, Otawara, Japan. It was considered as the reference gold standard test for diagnosis in all patients.[11–13] The images of all patients were evaluated by radiologists who do not know the result of TUS with respect to the diagnosis of PE. Image interpretation was performed with both soft tissue and pulmonary parenchymal window settings.[14] Central vascular zones included the main pulmonary artery, left and right main pulmonary arteries, left upper lobe trunk, the middle lobe artery and right and left lower lobe arteries. Peripheral vascular zones included the segmental and subsegmental arteries. Pulmonary embolism was considered to be present if intraluminal filling defect was detected in more than one slice in a well opacified scan. A CT scan was considered negative for PE if filling defect could not be seen in good quality scan.
6. Grayscale and Color Doppler TUS were performed at ultrasonography unit, chest department by an experienced chest physician who do not know the result of MDCTPA. Ultrasound was done by an ultrasound scanner (Aloka Echo Camera SSD-3500; Aloka Prosound; Japan).

For the sonographic examination of the lung and pleura, a 3.5 MHz convex scanner was used. In addition, a 7.5 MHz linear scanner was applied when a linear representation of the superficial parenchymal or pleural area was required. Sonographic examination of the chest was performed with the patient either seated or in a prone position to examine the dorsal and ventral aspects of the chest. The scanner was first applied in the intercostal areas where the patient localized the pain, followed by a systematic evaluation of the remaining intercostal spaces in six vertical lines which were paravertebral, midscapular, posterior axillary, midaxillary, anterior axillary, and midclavicular.

Examination was usually performed during tidal breathing. However, maximal inspiration and exhalation and placing the patient's hands behind the head with elevating the elbows may be required to gain access to areas covered by overlying bones of the thoracic cage and widen the intercostal space.[15] After complete gray-scale examination, all patients were examined by color-flow Doppler mode. Before the start of the color Doppler ultrasound examination, the Doppler filter was set at 50–100 Hz to avoid interference from respiratory and cardiac movement and to eliminate low-frequency signals from vessel wall motion. Also, color Doppler gain was adjusted until only a few noise specks were visible in the background.[16,17] The diagnosis of PE was considered if at least one or more typical pleural-based/subpleural hypoechoic lesions with or without pleural effusion were reported by TUS. Diagnosis of PE was very unlikely, in the presence of nonspecific subpleural lesions less than 5 mm in size, pure-free pleural effusion or normal

TABLE 1 Demographic data of 60 patients with suspected pulmonary embolism

	Total (n= 60)	PE[a] Positive (n= 40)	PE[a] Negative (n= 20)	*P*-value
Age (Mean ± SD)	50.63 ± 16.52	50.70 ± 17.34	50.50 ± 15.20	.965
Male (No, %)	33 (55)	24 (60)	9 (45)	.271
Female (No, %)	27 (45)	16 (40)	11 (55)	

[a]PE: Pulmonary embolism.

sonographic findings.[18] In pulmonary infarction, areas of pulmonary arterial flow could not be detected on color Doppler ultrasound, a phenomenon referred to as 'consolidation with little perfusion'. In addition, a congested thromboembolic vessel 'vascular sign' could be visible.[8,19]

2.1 | Exclusion criteria

1. Patients with allergy to contrast media.
2. Patients with severe renal impairment.
3. Patients who died or transferred to other hospitals before doing MDCTPA
4. Patients who refused to participate in the study.

2.2 | Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS-version 17) software. The results were expressed as mean ± standard deviation or frequencies. Proportions were compared with chi-square tests. The data was collected, analyzed and tabulated. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic value of the TUS in the diagnosis PE were calculated using the standard definitions.

3 | RESULTS

The demographic data of the 60 patients with suspected PE included in this study were revealed in Table 1. Out of these, 40 patients were finally diagnosed as PE by MDCTPA. No significant difference between PE positive and PE negative cases as regard to patient's age and sex. Anatomical location of thromboemboli in MDCTPA was shown in Table 2. Chest ultrasonography gave positive results suggestive of PE in 33 patients where at least one typical subpleural hypoechoic lesion was found while in seven patients no typical lesions were detected. TUS demonstrated a total of 66 lesions in 33 patients with a mean ± SD of 2.00 ± 1.20 lesion/patient (range, 1- 6 lesions). The distribution, shape and size of these lesions were shown in Table 3. Central echo was found in 3 lesions (4.5%). When the lesions were examined using color Doppler imaging 64 out of 66 lesions (97%) showed consolidation with little perfusion sign.

Interestingly, five of the seven TUS negative patients had isolated central PE and showed acute cor-pulmonal in echocardiographic examination compatible with acute PE.

The two groups (TUS positive and TUS negative patients) were compared regarding the presenting symptom, chest X-ray findings and the location of the thrombus in MDCTPA as shown in Tables 4–6. The presence of pleuritic chest pain and hemoptysis were significantly higher in the presence of positive ultrasonographic findings consistent with PE ($P < .01$ and $P < .05$ respectively). Free chest X-ray was significantly higher in the chest ultrasonography negative patients ($P < .05$). Concerning the location of the thrombus as detected by MDCTPA, the presence of the thrombus on the right or left main pulmonary artery only, without the affection of lobar, segmental or subsegmental level, was significantly higher in chest ultrasonography negative patients ($P < .001$). However, the isolated lobar, segmental or subsegmental thrombus was significantly higher in chest ultrasonography positive patients ($P < .05$)

The sensitivity, specificity, PPV, NPV and accuracy of gray-scale TSU in patients with clinically suspected PE were 82%, 90%, 94%, 72% and 85% respectively. The addition of color Doppler examination to gray-scale examination increased specificity, PPV and the accuracy of TUS to 95%,

TABLE 2 Findings of MDCTPA in patients positive for pulmonary embolism

	No. (n= 40)	%
Location of thrombus:		
Right	13	32.5
Left	4	10.0
Bilateral	23	57.5
Affected artery:		
Main pulmonary artery	18	45.0
Lobar branches	9	22.5
Segmental branches	23	57.5
Sub-segmental branches	16	40.0

TABLE 3 Description of the lesions suggestive of pulmonary embolism in patients with positive tranthoracic ultrasonography findings (n = 33)

	No. (n= 66)	%
No. of lesions	66 in 33 patients	
Mean ± SD	2.00 ± 1.20	
Median (Range)	2 (1 – 6)	
Shape:		
Wedge	47	71.2
Rounded	8	12.1
Polygonal	11	16.7
Side:		
Right	34	51.5
Left	32	48.5
Location:		
Upper lobe	11	16.7
Middle lobe	2	3.0
Lower lobe	53	80.3
Depth:		
0.5-2 cm	52	78.8
> 2 cm	14	21.2
Central echo:	3	4.5
Colour Doppler (consolidation with little perfusion sign):	64	97.0

97%, and 87% respectively. Lesions suggestive of pulmonary embolism are shown in Figures 1–3.

4 | DISCUSSION

The diagnosis of PE remains a significant medical problem especially at the emergency departments. On the contrary, accurate diagnosis and early treatment of PE is important and potentially life-saving.[7] The decision about the PE suspected cases need to be made in real time and the time for making the decision is short. Thromboembolic occlusion of pulmonary artery causes intraalveolar hemorrhage, necrosis, atelectasis due to loss of surfactant, increased permeability because of mediator secretion and alveolar edema and these changes occur mostly in the subpleural area of lung periphery. These pathological situations, with or without pleural effusion, provide an ultrasonographic window so can be detected by ultrasonography. The early formation of these lesions within minutes, makes it possible to be identified with ultrasound in the early period.[7,20]

The criteria to diagnose PE with TUS applied in this study were the presence of at least one typical pleural-based/subpleural hypoechoic lesion with or without pleural effusion. In the presence of nonspecific subpleural lesions less than 5 mm in size, pure-free pleural effusion or normal sonographic findings, the diagnosis of PE was very unlikely. The studies of Reissig *et al.*,[1] Comert *et al.*,[18] and Pfeilet al.[21] adopted the same criteria.

TABLE 4 Distribution of the presenting symptoms in chest ultrasonography positive and chest ultrasonography negative cases among patients with pulmonary embolism (n = 40)

	Positive TUS[a] (n= 33)		Negative TSU[a] (n= 7)		*P*-value
	No.	%	No.	%	
Dyspnea	29	87.9	7	100.0	.781
Pleuritic chest pain	27	81.8	1	14.3	.002
Retrosternal chest pain	4	12.1	4	57.1	.029
Hemoptysis	21	63.6	1	14.3	.049

[a]TUS, Transthoracic ultrasonography.

TABLE 5 Distribution of Chest X-ray findings in chest ultrasonography positive and chest ultrasonography negative cases among patients with pulmonary embolism (n = 40)

	Positive TUS[a] (n= 33)		Negative TUS[a] (n= 7)		*P*-value
	No.	%	No.	%	
Free	6	18.2	5	71.4	.016
Consolidation	13	39.4	0	0.0	.115
Pleural effusion	14	42.4	0	0.0	.089
Raised copula	8	24.2	1	14.3	.940
Hampton hump sign	6	18.2	0	0.0	.522
Westernmark sign	1	3.0	1	14.3	.775
Atelectasis	1	3.0	1	14.3	.775

[a]TUS: Transthoracic ultrasonography.

In the current study, TUS demonstrated subpleural hypoehoic lesions suggestive of PE in 33 out of 40 patients finally diagnosed as PE by MDCTPA. Sixty-six lesions with a mean of two lesions per patient were observed in those patients. This result was in agreement with several studies[18] which reported a mean of 2.14 lesions per patient and Ref. [22] which reported 2.3 lesions per patient. However, the mean in our study was lower than that detected in other studies[1] which detected a mean of 2.6 lesions per patient and higher than other studies[21] which detected a mean of 1.6 lesions per patient.

Regarding the location of the lesions, the majority of the lesions were detected in the lower lobe (53 lesions, 80.3%) followed by the upper lobe (11 lesions, 16.7%) and the middle lobe (2 lesions, 3%). The majority of the lesions (59.1%) were located in the posterior lower part of lungs. These results can be explained by the hemodynamic properties of the lungs where pulmonary arteries have a large axial trunk that branches off at an angle and terminates in the posterior basal segments so PE lesions as hemorrhages and infarctions have a pleural base and mainly placed in the lower lobes. In addition the lower lobes are easily viewed by TUS, while the upper lobes can only be inspected by an experienced investigator.[19] Several studies reported the same results.[18,21,22]

As regard to the shape of the lesions, the present study demonstrated that most lesions (71.2%) were wedge shaped. This may be explained by the anatomy of lung tissue. The triangular configuration corresponds to an increased attenuation within several affected secondary pulmonary lobules and has a broad base abutting the pleural surface with a truncated apex towards the hilum. Pulmonary infarction is often localized at the peripheral lung surface, an area that can be well visualized by TUS. These results were in agreement with previous studies regarding the shape of the lesions detected by TUS. Comert *et al.*[18] stated that the majority of lesions were wedge-shaped (63%) by TUS. Mathis *et al.*[22] reported that sonographic morphology was mainly triangular toward the hilum of lung in 58% and rounded or mixed in 42%. Reissig *et al.*[1] reported that most of the hypoechoic lesions (78 lesions; 85.7%) were wedge shaped and 10

TABLE 6 Location of embolus in MDCTPA in chest ultrasonography positive and chest ultrasonography negative cases among patients with pulmonary embolism (n= 40)

Affected artery	Positive TUS[a] (n= 33)		Negative TUS[a] (n= 7)		*P*-value
	No.	%	No.	%	
Main pulmonary artery only	3	9.1	6	85.7	.000
Main pulmonary artery with lobar, segmental or sub-segmental affection	9	27.3	0	0.0	.284
Isolated lobar, segmental or subsegmental affection	21	63.6	1	14.3	.049

[a]**TUS**: Transthoracic ultrasonography.

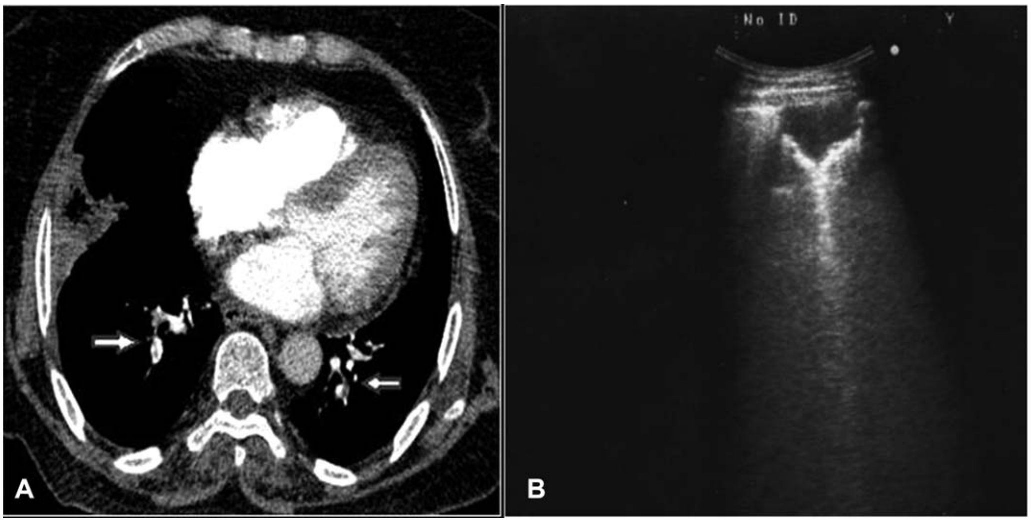

FIGURE 1 (A) Multidetector CT pulmonary angiography showed filling defects in segmental pulmonary arteries on both lower lobes and peripheral consolidation in the right lower lobe corresponding to.pulmonary infarction. (B) Transthoracic ultrasongraphy on the right infrascapular area showed a pleural based hypoechoic lesion representing wedge shaped pulmonary infarction.

lesions (11%) were rounded, and 3 lesions (3.3%) had polygonal configurations.

Central echo localized at the center of the lesions was found in 3 lesions (4.5%) in 3 different patients. The central hyperechoic structure indicates the presence of air inside the patent bronchiole in the affected segment and is considered as a sign of segmental involvement.[8] Our results were near that of Mathis *et al.*[22] who found central echo in 7% of the patients and lower than the study of Reissig *et al.*[1] that found central echo in 17.1% of patients.

In the current study, we found that PE patients who presented by pleuritic chest pain or haemoptysis were more likely to have positive ultrasonographic findings consistent with PE. This can be explained by the fact that pleuritic chest pain is caused by pleural irritation due to distal emboli causing pulmonary infarction which can be detected by TUS.[23] The presence of haemoptysis with peripheral infarctions may be resulted from an intra-alveolar haemorrhage in the infracted area caused by thromboembolic occlusion of a pulmonary artery. This may cause tissue destruction (incomplete infarction) or haemorrhage with necrosis of lung parenchyma (complete infarction).[24,25] On the other hand, we found that PE patients who presented by dyspnea or retrosternal chest pain were less likely to have positive ultrasonographic findings consistent with PE and the explanation could be that retrosternal chest pain is possibly reflecting RV ischemia in central PE. TUS was negative as this type of embolism is usually not accompanied by peripheral infarctions.

Regarding chest x-ray, the finding of free chest x-ray was significantly higher in the TUS false negative cases. The explanation of this might be that plain x-ray findings in PE are due to occurrence of peripheral infarctions manifested as consolidations, Hampton hump sign, atelectasis or pleural effusions which could be easily detected by TUS.

Concerning the location of the thrombus as detected by MDCTPA, the presence of the thrombus on the right or left main pulmonary artery only, without the affection of lobar, segmental or subsegmental level, was significantly higher in TUS false negative cases. However, isolated thrombus in lobar, segmental or subsegmental level was significantly higher in TUS true positive cases. This could be explained by the fact that embolism-associated lesions can be detected by TUS only when they extend to the lung periphery which is not the case in isolated central PE.

In the present study, the sensitivity, specificity, PPV, NPV and accuracy of TUS in clinically suspicious PE cases were presented as 82%, 90%, 94%, 72% and 85% respectively. These results agree with that of Reissig *et al.*[1] that reported the sensitivity, specificity, PPV, NPV, and accuracy of TUS to be 80%, 92%, 95%, 72%, and 84%, respectively. In contrary to our results, Pfeil *et al.*[21] reported the sensitivity of TUS for detecting PE 70% and specificity 69.6%. This could be explained by the small numbers included in their study (33 patients with only 10 diagnosed as PE).

In our study, seven cases were considered false negative where they had negative TUS scan while their MDCTPA were positive for PE. Six of these seven cases had isolated central PE with only affection of the main right or left pulmonary arteries. This one of the limitations of TUS in the detection of isolated central PE with no peripheral extension. Interestingly, five of these six cases showed acute corpulmonal by echocardiography. This finding made us to believe that the combination of TUS and echocardiography as a two bedside tests with the same device may markedly increase the sensitivity to detect PE in emergency

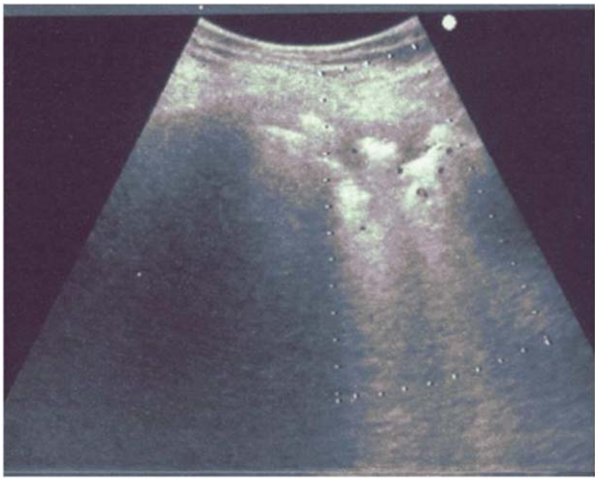

FIGURE 2 Transthoracic ultrasound showed pleural based hypoechoic lesion with a single centrally located echo representing peripheral infarction. By the colour doppler examination the infarction was vascularized only at the margin and not in the center (consolidation with little perfusion sign)

situations. Further studies should be done to clarify this point. The last false negative case showed isolated subsegmental PE in the upper lobe with peripheral infarction seen in MDCTPA behind the scapula which couldn't be reached by TUS. This showed another limitation of TUS as it didn't have access to the whole surface area of the lungs but fortunately the majority of the lesions occur in the lower lobe due to anatomical considerations and were easily accessible by TUS.

To the best of our knowledge the role of color Doppler TUS in diagnosis of PE wasn't largely studied before. Mathis *et al.*[22] stated that Color-coded duplex sonography is a problematic procedure for diagnosing peripheral PE since many lesions tend to reperfuse early so the value of color Doppler sonography as one tool in the diagnostic work of PE needs to be investigated further. In our study, when the lesions were examined using color Doppler imaging 64 out of 66 lesions (97%) showed consolidation with little perfusion sign. However, the vascular sign with characteristic circulation stop wasn't found in any lesion which could be attributed to number of factors concerning this sign and the study itself. Yuan *et al.*[26] and Mathis *et al.*[22] stated that, in very few cases, the investigator was able to visualize, on color-coded duplex sonography, a circulation stop caused by embolism. This limitation has several reasons. First, patients with dyspnea cannot hold their breath long enough, which causes several artifacts on colour-coded duplex sonography. Second, it is difficult to locate the supplying vessel at the right level. Third, when reperfusion occurs rapidly, the lesion is revascularized early. There were also factors concerning our study that might cause this result as the relatively limited number of patients if compared to the study of Mathis *et al.*[22] for example which include 352 patients. Meanwhile, "vascular sign" is not a reliable sign for the diagnosis of PE in many literatures.

We observed that "consolidation with little perfusion sign" as detected by color Doppler TUS is helpful in the diagnosis of PE and in differentiating subpleural lesions caused by PE from those caused by pneumonia, metastasis or peripheral lung mass.

When chest ultrasonographic scan was considered positive only in cases with positive color Doppler examination (the presence of consolidation with little perfusion sign) in addition to the finding of the subpleural hypoechoic lesion consistent with the presence of PE, the sensitivity, specificity, PPV, NPV and accuracy of TUS in clinically suspicious PE cases were presented as 80%, 95%, 97% and 70.4% respectively. So adding color Doppler to gray-scale examination increased specificity from 90% to 95%, increased PPV from 94% to 97% and increased accuracy from 85% to 87%. So color Doppler US increase the confidence that these hypoechoic lesions were due to pulmonary infarction and not caused by other lesions as consolidation, atelectasis or lung mass so increase the value of TUS in diagnosis of PE.

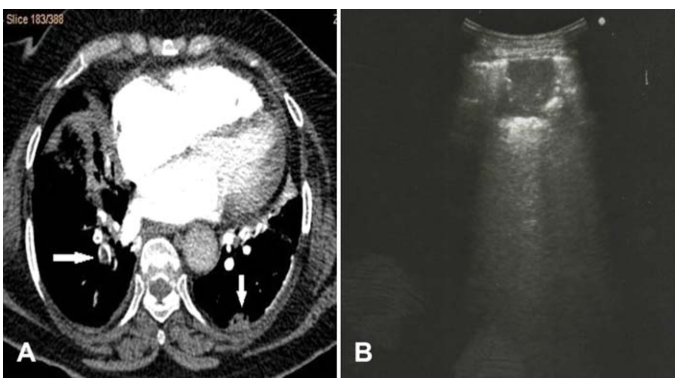

FIGURE 3 (A) MSCTPA showed filling defects on segmental and subsegmental branches in both lower lobes and peripheral consolidation in the left lower lobe corresponding to.the infarction detected by TUS. (B) TUS on the left infrascapular area showed a pleural based hypoechoic lesion representing polygonal shaped pulmonary infarction

However, ultrasound cannot replace CT in the emergency diagnostic. Using CT some perilous differential diagnosis can be excluded, which is not possible for TUS.

Pfeil *et al.*[27] reported that by using MDCT vascular signs and wedge-shaped opacities were associated with PE and so may be predictors of PE. Moreover, using MRI after a single injection of gadofosveset trisodium is more sensitive in detecting DVT compared to standard DUS, and is able to detect PE in asymptomatic patients.[28]

There are several limitations for the use of TUS in diagnosis of PE. First, TUS is operator dependent and depends on the experience of the examiner. Second, about 35% of the peripheral lung areas are covered by bony structures so not accessible by TUS. Third, embolism related lesions can be detected only when they extend peripherally to the lung surface.

5 | CONCLUSION

TUS is a reliable screening technique for diagnosing PTE with high specificity but relatively low sensitivity. Adding color Doppler to gray–scale TUS increases the specificity and accuracy and consequently the confidence in the diagnosis of peripheral pulmonary infarctions and differentiates them from other pulmonary lesions.

6 | CLINICAL IMPLICATION

TUS, in trained hands, has high specificity and diagnostic accuracy following its use as bedside screening method in emergency –based situations, especially for critically ill and immobile patients that allow initiations of anticoagulants.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

AUTHOR CONTRIBUTIONS

All authors participated in the conception and study design. They performed grayscale and color Doppler Transthoracic ultrasonography. Also they participated in data collection, statistical analysis and interpretation of data. They have drafted and participated in the final approval of the submitted manuscript and revised it.

ETHICS

The ethics committee approval was obtained and all enrolled patients completed a written consent form.

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