American Journal of Emergency Medicine (2012) **30**, 317–324

The American Journal of Emergency Medicine

www.elsevier.com/locate/ajem

Original Contribution

A comparison of different diagnostic tests in the bedside evaluation of pleuritic pain in the ED

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Received 13 October 2010; revised 24 November 2010; accepted 24 November 2010

Abstract

Purposes: Bedside lung ultrasound (LUS) is useful in detecting radio-occult pleural-pulmonary lesions. The aim of our study is to compare the value of LUS with other conventional routine diagnostic tools in the emergency department (ED) evaluation of patients with pleuritic pain and silent chest radiography (CXR).

Methods: Ninety patients consecutively admitted to the ED with pleuritic pain and normal CXR were retrospectively (n = 49) and prospectively (n = 41) studied. All patients were blindly examined by LUS and submitted to clinical examination and blood samples. The ability of blood tests and symptoms to predict any radio-occult pleural-pulmonary condition confirmed by conclusive image techniques and follow-up was evaluated and compared with LUS.

Results: In 57 cases, the final diagnosis was chest wall pain. The other 33 patients were diagnosed with a pleural-pulmonary condition (22 pneumonia, 2 pleuritis, 7 pulmonary embolism, 1 lung cancer, 1 pneumothorax). Lung ultrasound showed a sensitivity of 96.97% (95% confidence interval [CI], 84.68%-99.46%) and a specificity of 96.49% (95% CI, 88.08%-99.03%) in predicting radio-occult pleural-pulmonary lesions and significantly higher area under the curve (AUC) of receiver operating characteristic analysis (AUC, 0.967; 95% CI, 0.929-1.00) than D-dimer (AUC, 0.815; 95% CI, 0.720-0.911) and white blood cell count (AUC, 0.778; 95% CI, 0.678-0.858). None of the other routine tests considered or a combination between them better predicted the final diagnosis.

Conclusions: Chest radiography and blood tests may be inadequate in the diagnostic process of pleuritic pain. In case of silent CXR, LUS is critical for identifying patients with pleural-pulmonary radio-occult conditions at bedside and cannot be safely replaced by other conventional methods.

1. Introduction

Pleuritic pain is felt as a sharp pain, usually well localized by the patient to a precise chest area, that worsens by forceful breathing movements, such as taking a deep breath, talking, coughing, or sneezing. It represents a common presenting symptom in the emergency department (ED). Ancillary testing is frequently relied upon to aid in sorting out the differential diagnosis between a parietal muscoloskeletal condition, very often with spontaneous recovery, or an irritation of the parietal pleura due to a pleural-pulmonary disease, requiring precise differential diagnosis, specific

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doi:10.1016/j.ajem.2010.11.035

treatment, and follow-up. Conventionally, the diagnostic process relies mainly on the visualization of pleural and pulmonary lesions, corresponding to the painful chest area, by plain film chest radiography (CXR). However, in a significant number of cases, pleuritic pain may be caused by radio-occult lesions occurring as a presenting complaint for pneumonia, pulmonary embolism, cancer, or pneumothorax [1-3]. Hence, very often, when CXR is silent, the diagnostic process in the ED is inconclusive. Most patients presenting with isolated pleuritic pain are discharged from the ED with a diagnosis of "chest wall pain," not otherwise specified [4]. In a previous study, we have demonstrated that bedside lung ultrasound (LUS), a noninvasive approach easily performed in a few minutes, is highly accurate in detecting radio-occult conditions, being of value even in the differential diagnosis of lesions due to pneumonia, pulmonary embolism, or cancer [3]. Without great sonographic skill, the attending emergency physician (EP) may easily identify those patients who need further imaging by detection of any abnormal sonographic pattern at LUS, whereas negative examination allows safe discharge with a diagnosis of chest wall pain [3]. In the daily practice, other clinical parameters, such as symptoms, physical signs, and blood examinations, are commonly used in the decision-making process in the ED, and the exact role of LUS has not yet been explored.

This study was designed to compare the value of LUS with other conventional diagnostic tools commonly applied at bedside in the ED evaluation of patients complaining of pleuritic pain and showing nondiagnostic CXR.

2. Materials and methods

The study took place in the ED of the San Luigi Gonzaga Hospital, Turin, Italy. The latter is a university hospital, whose ED performs approximately 45 000 visits per year. Consecutive patients who presented with acute pleuritic chest pain, normal respiratory function, hemodynamic stability, and low-risk profile for thromboembolism were enrolled. All patients were submitted to history recording, physical examination, electrocardiogram, blood sampling, CXR in 2 views, and LUS. Only patients whose CXR did not visualize any pleural or pulmonary conditions as the possible source of pain were included in the study. Patients 15 years or younger and those with clearly traumatic or cardiac origin of pain were excluded. This analysis was possible because in our ED, bedside thoracic ultrasound for lung and heart examination is routine in all patients with suspected pulmonary and cardiac diseases. The overall population of the study comprised 90 patients (44 women and 46 men; mean age, 45.3 ± 16.9 years; age range, 16-85 years) who were classified into 2 groups. Group 1 consisted of 49 patients enrolled from November 2005 to October 2006, who were simultaneously registered for a study evaluating the usefulness of lung sonographic signs in the differential diagnosis of radio-occult lesions. Data from this study have been previously published [3]. Patients of group 1 were retrospectively analyzed by chart review. Group 2 consisted of 41 consecutive patients studied in a prospective fashion from April 2009 to June 2010. The examiner performed LUS after CXR plain film was obtained and read by the attending radiologist. The study was performed after the approval by the scientific and ethics committee of our institution, and written informed consent was signed by all participants.

2.1. Chest radiography

Chest radiography was immediately performed in 2 views, posterior-anterior and lateral, with the patient in the upright position. The first reading by the attending radiologist concluded that the patient could be enrolled. The CXR was, then, submitted to confirmation by a second reading of a second radiologist specifically trained in chest imaging.

2.2. Lung ultrasound

Lung ultrasound was conducted using a 5- to 3.5-MHz convex scanner and 7.5-MHz linear scanner (portable unit; Siemens Sonoline G50, Malvern, PA). Sonographic examination was performed at bedside by 1 independent EP aware of CXR reading but blinded to other diagnostic results. Sonographers involved in the study (G.V., A.M., and F.B.) perform approximately 500 bedside emergency ultrasound examinations per year, and G.V. and A.M. are particularly trained on LUS. The patient was either seated (dorsal application) or in a supine position (ventral application). The scanner was first applied to the intercostal space where the

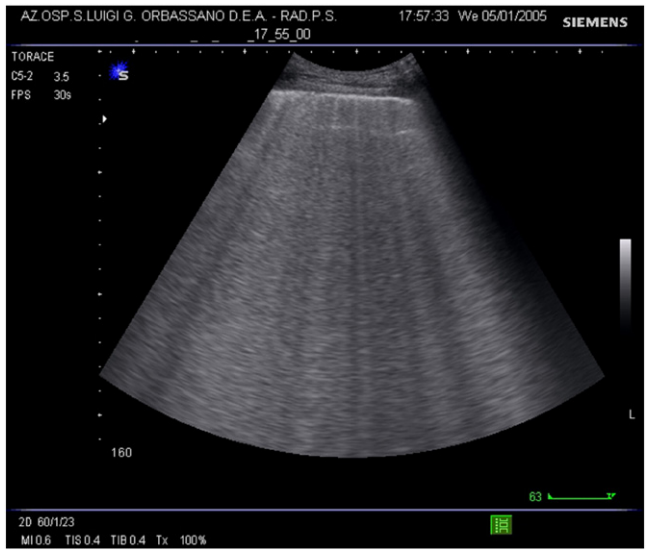

Fig. 1 The sonographic pattern with multiple echogenic vertical artifacts named B-lines. They generate from the pleural line, reach the edge of the screen without fading, and move synchronous with lung sliding. Visualization of this sign in the painful chest area was decisive for ruling in a pleural origin of the pain.

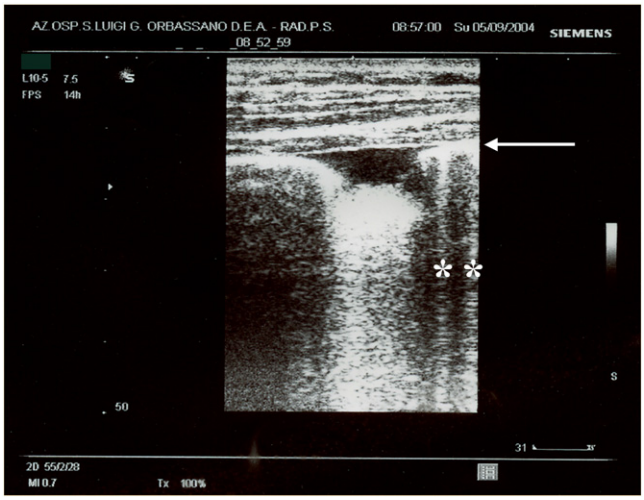

Fig. 2 Disruption of the pleural line (*white arrow*) with a wedge-shaped, pleural-based hypoechoic image with sharp margins and some B-lines in the surrounding area (*asterisks*). This image is typical of a small lung consolidation due to a peripheral infarction. Final diagnosis was pulmonary embolism.

patient localized the pain. Maximal inspiration and exhalation were used to gain access to areas covered by solid structures of the thoracic cage. Breath holding by the patient was useful to exclude breath motion–related artifacts. Further details on the technique and pathologic signs of LUS are described in a previously published article [3].

An examination of the painful thoracic area was considered normal in presence of both the respiratory pleural sliding and the scattered aerated image under the pleural line, without visualization of multiple vertical linear echogenic artifacts named B lines (B+ pattern) [3,5,6]. Lung ultrasound was considered positive when direct scanning of the painful chest area allowed visualization of at least one of the following: absence of sliding, B+ pattern on more than 1 intercostal scan (focal interstitial syndrome), peripheral alveolar consolidation, or disruption with irregularity of the pleural line with or without effusion (Figs. 1 and 2).

2.3. Blood sample

A sample of whole blood was collected at admission and sent to the laboratory. D-dimer plasma level was assessed by latex-enhanced turbidimetric quantitative test (Dade-Behring, Milan, Italy; normal value [NV] <283 ng/mL). C-reactive protein (CRP) plasma level was assessed by immunoturbidimetric method (Sentinel Diagnostics, Milano, Italy; NV <0.71 mg/dL). White blood cell (WBC) count was determined as part of the Multi-Angle-Polarised-Scatter-Separation (Abbott, IL; NV 4.5-11.6 × 10^9/L).

2.4. Symptoms

Physical examination and history were recorded at presentation by the attending EP. Particular attention was reserved to specific symptoms, such as history of cough, hemoptysis, and fever along with pleuritic pain.

2.5. Diagnostic criteria

All final diagnoses were determined from independent reviewers after a combination of the following procedures: spiral computer tomography (sCT), perfusional scintigraphy, positron emission tomography (PET), compression ultrasonography of the legs, follow-up at few days and 1 to 3 months, and response to treatment. The risk profile for pulmonary thromboembolism was recorded after the Wells criteria [7].

All patients diagnosed with parietal chest pain of an unknown origin were discharged without therapy and submitted to a 2-step clinical examination and blood

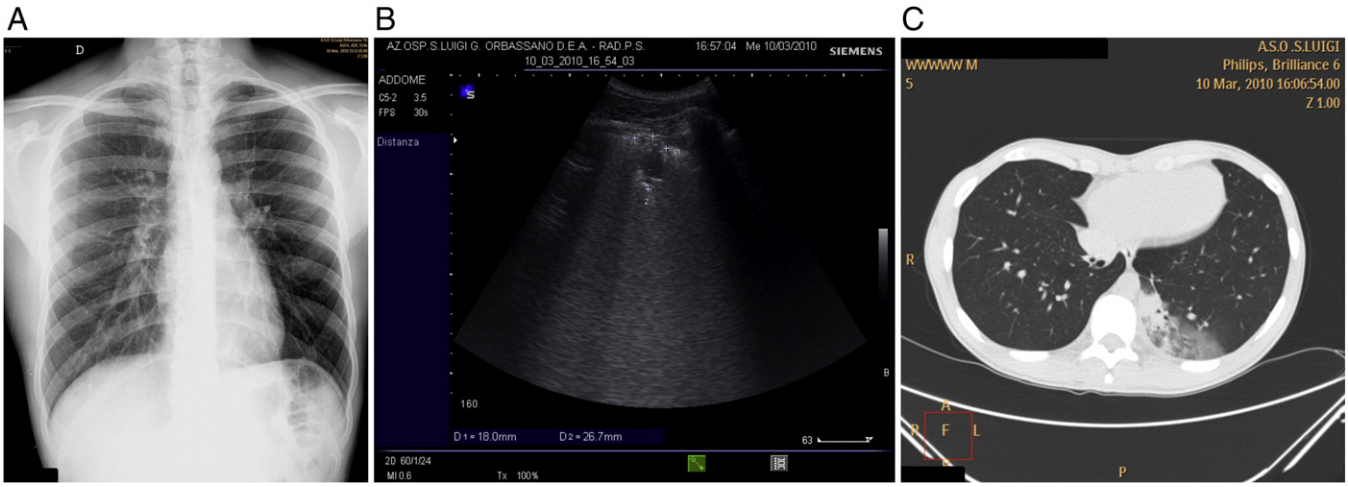

Fig. 3 A, Upright CXR study of a 28-year-old man admitted to the hospital because of severe left dorsal pleuritic pain and cough. B, Corresponding sonogram of the painful dorsal chest area showing irregular pleural line, coalescent B-lines (B+ pattern), and subpleural irregular shape consolidation. C, Corresponding sCT scan. One basal dorsal soft consolidated area of the lung is visible. The final diagnosis was radio-occult pneumonia.

Table 1 Comparison between diagnostic accuracy of LUS, routine blood tests, and symptoms in predicting any pleural and/or pulmonary radio-occult condition in 90 patients who presented to the ED complaining of pleuritic pain and no symptoms of respiratory distress

Diagnostic test	Sensitivity	Specificity	Positive PV	Negative PV
LUS	96.97	96.49	94.12	98.21
	84.68-99.46	88.08-99.03	80.91-98.37	90.55-99.68
Blood tests				
d-dimer	75.76	84.21	75.53	85.71
	58.98-87.17	72.64-91.46	56.88-85.14	74.26-92.58
CRP	90.91	80.7	73.17	93.88
	76.43-96.86	68.66-88.87	58.07-84.31	83.48-97.9
WBC	51.52	96.49	89.47	77.46
	35.22-67.5	88.08-99.03	68.61-97.06	66.48-85.63
Symptom-based tests				
Fever	42.42	87.72	66.67	72.46
	27.24-59.19	76.8-93.9	45.37-82.81	60.95-81.61
Cough	36.36	64.91	37.5	63.79
	22.19-53.38	54.94-76	22.93-54.75	50.93-74.95
Hemoptysis	3.03	96.49	33.33	63.22
	0.54-15.32	88.08-99.03	6.15-79.23	52.73-72.59
Sequential tests				
Laboratory+ [a]	100	70.18	66	100
	89.57-100	57.34-80.47	52.15-77.56	91.04-100
Symptom+ [b]	57.58	53.3	46.34	71.43
	40.81-72.76	48.43-72.94	32.06-62.25	57.59-82.15

Data are expressed as percentage (95% CI). PV indicates predictive value.

[a] At least 1 positive blood test, among WBC, CRP, and D-dimer.

[b] At least 1 symptom in the history recording, among fever, cough, and hemoptysis.

sampling, at few days and 1 month. On occasion, a new CXR was performed.

All patients with high D-dimer were submitted to one of the following paths to rule out pulmonary embolism: (1) sCT of the thorax and compression ultrasonography; (2) perfusional lung scintigraphy and compression ultrasonography; (3) compression ultrasonography and follow-up at few days, 1 month, and 3 months [8]. Only patients with confirmed diagnosis of pulmonary embolism were treated with anticoagulants.

All patients discharged with a diagnosis of pneumonia were submitted to oral antibiotic regimen (claritromicine and amoxicillin) and repeated clinical examination, blood sample, LUS, and CXR after a few days and 1 month. Confirmation of diagnosis was obtained by one of the following: (1) visualization by sCT of the consolidated lung by showing the typical radiologic pattern; (2) recovery from symptoms together with clearing of LUS images and normalization of blood tests after antibiotic treatment; (3) appearance of a radiologic opacity at CXR control after a few days, corresponding to the painful thoracic area, with complete clearing at follow-up.

2.6. Computer tomography

Spiral computer tomographic scanning (64-row CT, Philips Brilliance, MX80001DT; Philips Medical Systems, Eindhoven, The Netherlands) was performed in the radiology unit using the same technique (3-mm section thickness, 3- to 4-mm increments, and pitch 2). Contrast medium was administered for visualization of the pulmonary arteries when needed. Spiral computer tomographic scans were analyzed for intraluminal filling defects. The sCT images were read by an expert in chest imaging and emergency radiology.

2.7. Statistical analysis

The results of LUS and blood tests (D-dimer, CRP, and WBC count) and presence of symptoms (cough, hemoptysis, and fever) were compared with the final diagnoses. Estimates of sensitivity, specificity, and positive and negative predictive values were calculated for each test, considering either dichotomous or continuous variables. The optimal threshold for continuous variables was chosen to maximize the sum of sensitivity and specificity. The combination of blood tests and tests based on the presence of symptoms was also considered; test characteristics were calculated by applying the parallel method (ie, an individual is considered positive if positive with any test). Receiver operating characteristic (ROC) analysis was performed to calculate the area under the ROC curve (AUC) with 95% confidence interval (CI) of each test. Comparison between AUC of LUS with all the other tests was carried out using DeLong's test. Differences were considered to be statistically significant at $P < .05$. The data were analyzed by using R version 2.10.1 [9].

3. Results

Fifty-seven patients (63%) had a final diagnosis of parietal chest pain. In this group, pulmonary disease was finally ruled out at follow-up in 42 patients, by a combination of sCT (n = 2), venous compression ultrasonography (n = 15), and lung scintigraphy (n = 1) in the remaining 15 patients. Thirty-three (37%) patients had a final diagnosis of radio-occult pleural-pulmonary disease with the lesion topographically corresponding to the painful thoracic area. Twenty-four patients (27%) had a final diagnosis of pneumonia or pleuritis; 8 confirmed at sCT; 4, at CXR control performed after few days; and 12, at follow-up after antibiotic treatment. Other 7 patients (8%) had a final diagnosis of pulmonary embolism, all confirmed by sCT and venous compression ultrasonography of the legs. One patient had a final diagnosis of lung cancer, confirmed at sCT and PET, and 1 patient had a final diagnosis of spontaneous pneumothorax, confirmed at sCT.

Lung ultrasound detected a radio-occult pleural-pulmonary lesion in 32 of the 33 patients with a confirmed pulmonary condition. In 1 case, LUS was not able to detect a consolidation due to pneumonia, which was subsequently visualized 3 days later both at CXR and LUS control. Our LUS examinations also included 2 false positives, consisting of little peripheral consolidations without focal interstitial syndrome. These lesions were not confirmed at sCT (in 1 case) and were constantly detected at LUS during follow-up at 3 days and 1 month, despite recovery from symptoms (in both cases). A constant topographic correlation with LUS findings was observed when confirmation was achieved radiologically by sCT (Fig. 3A-C), PET, or CXR performed at follow-up. Lung ultrasound showed sensitivity of 96.97% (95% CI, 84.68%-99.46%) and specificity of 96.49% (95% CI, 88.08%-99.03%) in detecting any pleural or pulmonary radio-occult condition manifesting as pleuritic pain. The AUC was 0.967 (95% CI, 0.929-1.00).

C-reactive protein was higher than NV in 41 patients (21/24 with pneumonia or pleuritis, mean value ± SD, 8.21 ± 8.18 mg/dL; 7/7 with pulmonary embolism, 7.15 ± 5.19 mg/dL; 1/1 with lung metastasis, 4.67 mg/dL; 1/1 with peumothorax, 1.49 mg/dL; 11/57 with parietal chest pain, 1.76 ± 0.53 mg/dL).

D-dimer was positive in 34 patients (17/24 with pneumonia or pleuritis, 565.8 ± 306.8 ng/mL; 7/7 with pulmonary embolism, 1391 ± 957.7 ng/mL; 1/1 with metastasis, 965 ng/mL; 9/57 with parietal chest pain, 774 ± 812 ng/mL).

White blood cell was elevated above NVs in 19 patients (12/24 with pneumonia or pleuritis, 16.11 ± 5.20 × 10^9/L; 4/7 with pulmonary embolism, 14.77 ± 1.74 × 10^9/L; 1 with metastasis, 13.7 × 10^9/L; 2/57 with parietal chest pain, 12 ± 1.41 × 10^9/L). No patients had WBC below NVs.

The main accompanying symptoms recorded during the first examination were cough (n = 32) and fever (n = 21). Hemoptysis was reported only in 3 cases, 1 pulmonary embolism and 2 parietal chest pain in acute bronchitis, too few to be considered in statistical analysis. In 49 patients, pleuritic pain was the only symptom reported. Table 1 shows values of sensitivity; specificity; and positive and negative predictive values of LUS, blood tests, and symptoms in predicting pleural-pulmonary disease. Table 2 shows AUC of all the tests and symptoms and comparison with AUC of LUS.

In Fig. 4, tests are compared through their likelihood ratio, which measures their predictive ability [10].

Table 2 Areas under the ROC curves of routine blood tests and symptoms in predicting any radio-occult pleural and/or pulmonary condition in 90 patients who presented to the ED complaining of pleuritic pain and pairwise comparison with LUS ROC curve

Diagnostic test	AUC	Difference between areas (LUS)	*P*
LUS	0.967 0.929-1.00	–	–
Blood tests			
D-dimer	0.815 0.720-0.911	0.152	.001
CRP	0.926 0.869-0.983	0.041	.22
WBC	0.778 0.671-0.884	0.19	.001
Symptom-based tests			
Fever	0.651 0.555-0.747	0.317	<.001
Cough	0.506 0.402-0.611	0.461	<.001
Hemoptysis	0.498 0.459-0.536	0.469	<.001
Sequential tests			
Laboratory+ [a]	0.851 0.791-0.911	0.116	.001
Symptom+ [b]	0.595 0.488-0.702	0.372	<.001

Data are expressed as percentage (95% CI).

[a] At least 1 positive blood test, among WBC, CRP, and D-dimer.

[b] At least 1 symptom in the history recording, among fever, cough, and hemoptysis.

4. Discussion

Lung ultrasound has been successfully applied in the diagnosis of pneumonia and pleural effusion [11-14], pulmonary embolism [14,15], and pneumothorax [5,16,17]. Many articles have shown that LUS is at least equal if not superior to CXR. In a previous study, we showed the usefulness of LUS in visualizing radio-occult pulmonary conditions on a series of patients with pleuritic pain and no symptoms of respiratory distress [3]. These

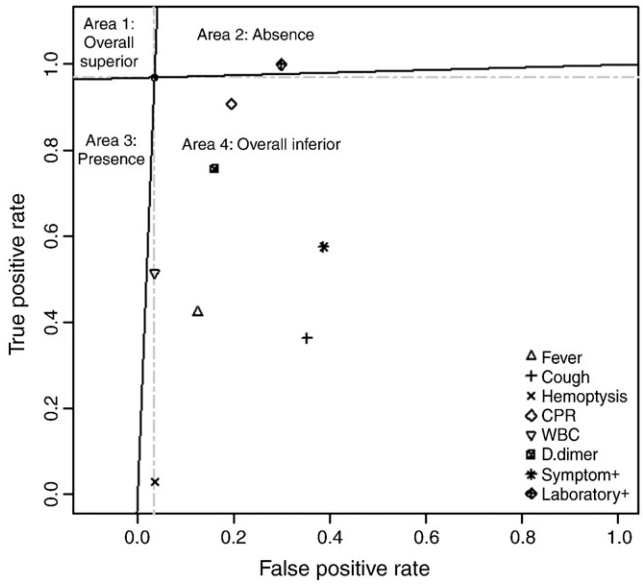

Fig. 4 Negative and positive likelihood ratio is numerically equivalent to the slopes of the solid lines. The solid line passing through (0.0) is the likelihood ratio positive line, and the solid line passing through (1.1) is the likelihood ratio negative line. The solid lines split the graph in 4 areas. Tests falling in area 1 are overall superior to LUS, those falling in area 2 are superior for confirming absence of disease, tests in area 3 are superior for confirming presence of disease, and, finally, tests in area 4 are overall inferior. The dashed lines represent the sensitivity and specificity of LUS.

patients are at high risk of misdiagnosis, and the decision to ask for an additional second-level imaging test is not always easy for the attending EP, especially in the case of overcrowded or poorly equipped institutions and when referral takes place at night or during the weekend. Lung ultrasound can reduce both the amount of negative diagnostic image testing in the ED and the number of patients symptomatic for a lung disease who are discharged without the proper diagnosis [18].

Our data show that LUS is highly accurate in visualizing radio-occult pleural and pulmonary lesions in patients with pleuritic pain, successfully screening cases with pulmonary conditions from those with parietal chest pain. No other routine tests performed at bedside nor symptoms recorded during the visit in the ED were better indicators of pulmonary disease. Sensitivity and specificity of LUS were higher than all the other tests considered, even if only the difference with the AUC of CRP did not reach any statistical significance.

We also tried to explore the positivity of at least 1 laboratory test or symptom as diagnostic criteria to identify patients with a pulmonary disease. The blood tests combined showed a very high sensitivity but a lower specificity rate than the specificity rate of each test independently. Thus, in the case of normal plasma D-dimer, CRP, and WBC levels, patients with pleuritic pain, normal CXR, normal respiratory function, and physical examination can be untimely discharged without further diagnostic testing (including LUS). At the same time, positivity of at least one of the blood test considered does not necessarily predict pleural or pulmonary diseases and could induce the attending physician to useless further investigations.

Lung ultrasound has the great advantage of being a noninvasive bedside approach easily performed in a few minutes by the EP with a minimum amount of training. In our patients, it showed high sensitivity and specificity in detecting relevant pulmonary diseases. For the first time, we showed a clear diagnostic superiority of LUS over CXR and all the other routine diagnostic procedures commonly applied in the ED. Sonographic examination can be limited to the painful thoracic area, thus requiring no more than 1 to 2 minutes (not to say seconds in most cases). Moreover, LUS has another advantage over other routine tests, as it can be useful to differentiate between different types of lesions [3,18,19]. Data from this study have been evaluated without considering the potential of LUS in differentiating the etiology of the sonographic lesion. Indeed, our objective was to test the ability of LUS in its simplest application that is the easy differentiation between normal and pathologic pattern by directly scanning the painful chest area (first-level sonographic examination or basic LUS). Differential diagnosis of pleural and pulmonary sonographic lesions requires a higher level of skill and training (second-level sonographic examination or advanced LUS). We propose an ultrasound evaluation of patients with pleuritic pain in 2 steps, depending on the expertise of the sonographer. This article analyzed the first step that is based on exclusion of any of the sonographic signs described in our study, whose visualization should rule out a diagnosis of parietal chest pain and should induce the attending EP to perform further examinations. On the contrary, absence of any sonographic lung and pleural sign allows safe discharge of the patient with a diagnosis of parietal chest pain of unknown origin or further

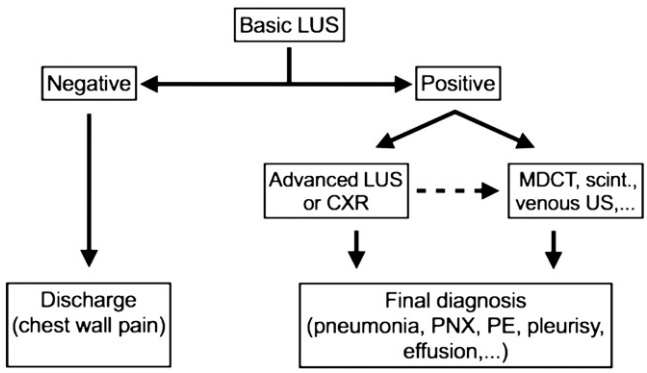

Fig. 5 Flowchart that explains our proposal of evaluation of pleuritic pain in the ED in patients without signs of respiratory distress or hemodynamic instability, when LUS is available. Basic LUS is based on the assessment of 4 simple signs: (1) absence of sliding, (2) B+ pattern on more than 1 intercostal scan, (3) peripheral alveolar consolidation, and (4) disruption with irregularity of the pleural line with or without effusion. MDCT indicates multidetector computer tomography; US, ultrasound; PNX, pneumothorax; PE, pulmonary embolism.

searching for a muscoloskeletal cause (Fig. 5). The second step, often decisive in differentiating the etiology of the lesion visualized at LUS, should be reserved to experienced sonographers and have been explored in a previous article [3]. When LUS is not available, CXR and blood tests are always needed (Fig. 6).

5. Limitations

A major limitation of our study is the lack of a systematic comparison between ultrasound and sCT. Most diagnoses were confirmed by CXR control within a few days and/or follow-up by repeated clinical examination, blood assay, and LUS up to 1 month. Our intention was to avoid useless irradiation of the patients. Moreover, this is a clinical study, which evaluates the accuracy of diagnostic methods to be used in the ED to predict pulmonary conditions. For these reasons, we chose to use the confirmed final diagnosis as the criterion standard instead of systematically confirm sonographic morphology of lesions by sCT. Indeed, follow-up at preset timing is a method widely used in the literature to confirm diagnosis. Although morphologic evaluation of the lesions was not systematically compared with radiology, we found a close match in size and location of lesions when sCT was applied.

Finally, the benefit of finding radio-occult pulmonary conditions using LUS is debatable. In general, pneumonias not detected on CXR in patients in good health do well without antibiotic treatment, and we do not know if LUS can make any difference in the general outcome of the patients. Anyway, there are some points that need to be addressed: (1) nobody can state that radio-occult lesions never evolve into clinically severe forms, (2) "radio-occult" does not mean "small" because lack of visualization at CXR also depends on the pathophysiology of the consolidation and its location, (3) the best therapy to recover faster and safer from symptoms is etiological, (4) there are many legal dispute that can be prevented even when misdiagnosis would not make any change in the clinical outcome, and (5) diagnosing even the most peripheral pulmonary infarction due to the smallest embolus could be crucial to promote investigation for predisposing factors or recommend discontinuation of contraceptives and stop smoking.

6. Conclusions

This study provides further evidence that bedside LUS is superior to conventional CXR in many situations. Bedside sonographic evaluation of the lung by the attending EP in the ED is a reliable easy-to-use method and accurate enough to be routinely used in patients presenting with pleuritic pain. Lung ultrasound has shown to be of value to rule out radio-occult pulmonary conditions and to identify patients who need a second-level image testing. No other routine laboratory test or accompanying symptom can replace the use of LUS as an indicator of radio-occult pulmonary lesions causing chest pain.

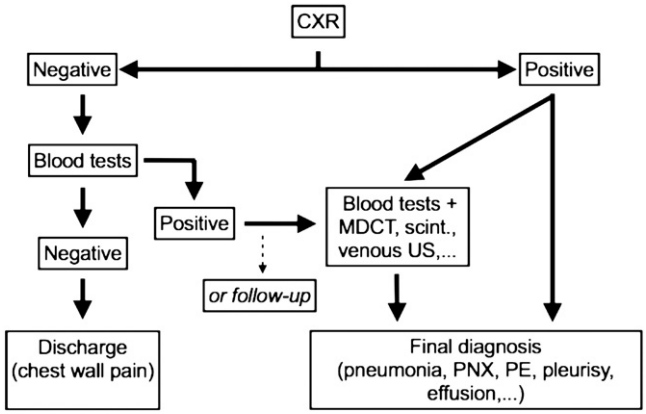

Fig. 6 Evaluation of pleuritic pain in the ED when LUS is not available. We start from the CXR study and discharge the patient with diagnosis of chest wall pain only when both radiography and blood tests are negative. In case of visualization of radiographic lesions, we can make the diagnosis or require blood tests and second-level imaging. MDCT, multidetector computer tomography; US, ultrasound; PNX, pneumothorax; PE, pulmonary embolism.

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