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Contribution of lung ultrasound in diagnosis of community-acquired pneumonia in the emergency department: a prospective multicentre study

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ABSTRACT

Lung ultrasound (LUS) can help clinicians make a timely diagnosis of community-acquired pneumonia (CAP).

Objectives To assess if LUS can improve diagnosis and antibiotic initiation in emergency department (ED) patients with suspected CAP.

Design A prospective observational study.

Settings Four EDs.

Participants The study included 150 patients older than 18 years with a clinical suspicion of CAP, of which 2 were subsequently excluded (incorrect identification), leaving 148 patients (70 women and 78 men, average age 72±18 years). Exclusion criteria included a life-threatening condition with do-not-resuscitate-order or patient requiring immediate intensive care.

Interventions After routine diagnostic procedure (clinical, radiological and laboratory tests), the attending emergency physician established a clinical CAP probability according to a four-level Likert scale (definite, probable, possible and excluded). An LUS was then performed, and another CAP probability was established based on the ultrasound result. An adjudication committee composed of three independent experts established the final CAP probability at hospital discharge.

Primary and secondary outcome measures Primary objective was to assess concordance rate of CAP diagnostic probabilities between routine diagnosis procedure or LUS and the final probability of the adjudication committee. Secondary objectives were to assess changes in CAP probability induced by LUS, and changes in antibiotic treatment initiation.

Results Overall, 27% (95% CI 20 to 35) of the routine procedure CAP classifications and 77% (95% CI 71 to 84) of the LUS CAP classifications were concordant with the adjudication committee classifications. Cohen's kappa coefficients between routine diagnosis procedure and LUS, according to adjudication committee, were 0.07 (95% CI 0.04 to 0.11) and 0.61 (95% CI 0.55 to 0.66), respectively. The modified probabilities for the diagnosis of CAP after LUS resulted in changes in antibiotic prescriptions in 32% (95% CI 25 to 40) of the cases.

Conclusion In our study, LUS was a powerful tool to improve CAP diagnosis in the ED, reducing diagnostic uncertainty from 73% to 14%.

Trial registration number NCT03411824.

Strengths and limitations of this study

- ► This is a multicentre pragmatic study, including adults with presumptive diagnosis of community-acquired pneumonia in emergency departments.
- ► Lung ultrasounds (LUSs) were performed according to a defined protocol by investigators with a wide range of experience, from beginners to experts.
- ► Investigation tools (chest X-ray and laboratory tests) were conducted at the physician's discretion; this fact increases the external validity of the study.
- ► The inclusion of a convenience sample of patients may have induced a selection bias.
- ► The adjudication committee had access to LUS raw data, which may have influenced their diagnosis.

INTRODUCTION

Community-acquired pneumonia (CAP) is a common cause of acute infection worldwide and is responsible for frequent hospital admissions.[1] CAP remains the leading infectious disease cause of death in the USA.[2] Early antibiotic treatment is crucial to reduce in-hospital mortality,[3] emphasising the need for a timely detection and diagnosis. However, antibiotic overuse, mainly in lower respiratory tract infections, is a critical public health concern leading to increased bacterial resistance.[4] Meanwhile, the diagnosis of CAP in the emergency department (ED) is difficult given the limitations of clinical examination, chest X-ray (CXR) and laboratory tests. Indeed, association of cough, fever, tachycardia and crackles provides a CAP probability between

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20% and 50%.[5] Thus, the aetiologic diagnosis of an acute shortness of breath in the ED remains challenging, especially in elderly patients or those with concomitant chronic cardiac or pulmonary diseases.[5 6] In this population, diagnostic accuracy is difficult to achieve and the need for hospitalisation or the risk of death are higher than in younger patients.[7] The usual diagnostic workup, that is, without LUS or CT scan, can overlook mild pneumonia, delaying appropriate treatment, which can lead to an increased mortality risk.[8 9]

While CXR is the most commonly used imaging modality to access CAP diagnosis, a significant inter observer variability has been demonstrated.[10] Furthermore, the intrinsic qualities of CXR for CAP diagnosis are limited, with a sensitivity and specificity of 43% and 93%, respectively.[11] A recent prospective multicentre study in patients with suspected CAP assessed the diagnosis changes induced by a CT scan of the chest.[12] The study found that CT scan improves diagnosis and management of ED patients with suspected CAP in terms of antibiotic initiation and hospitalisation. However, CT scan of the chest for CAP diagnosis is not routinely feasible in many ED and would expose to significant radiation.[13]

Lung ultrasound (LUS) is increasingly used in routine practice and can help the clinician make a rapid diagnosis in patients with acute respiratory failure.[14 15] A meta-analysis showed that LUS sensitivity ranged from 80% to 90% and specificity from 70% to 90%.[16] Similar results were found in ED focused meta-analysis with pooled sensitivity of 92% and pooled specificity of 93%.[17] Moreover, LUS sensitivity was found better than CXR in a prospective study.[18] As CT scan changed the diagnosis probability in patients with suspected pneumonia,[12] the rationale for our study was to assess the role of LUS, an easier accessible imaging modality, in suspected adults with CAP visiting the ED. As ED physicians play a major role in the initial work-up of CAP, we aim to investigate the diagnosis performance of LUS for suspected CAP and its impact on antibiotic treatment initiation in the ED.[19]

Patients and methods

Study design and setting

EchoPAC was a prospective study in four EDs between November 2016 and December 2018.

Selection of participants

The patients of the present study were a convenience sample of patients aged more than 18 years for whom the attending emergency physician made the presumptive diagnosis of CAP, based on signs and symptoms such as new onset of fever, pleural pain, shortness of breath, purulent expectoration and localised or bilateral auscultation abnormalities.[19] Patients were enrolled when a local investigator was available. Standard laboratory and radiographic testing were conducted at the discretion of the patient's treating clinician. The CXR was interpreted by the attending emergency physician. We excluded patients with a life-threatening condition with do-not-resuscitate-order, patient requiring immediate intensive care or with known pregnancy. Patients requiring immediate intensive care were excluded as (a) they could not consent to the study, (b) priority was given to placing the patient on mechanical ventilation and (c) these patients often had a CT scan before the LUS could be performed by investigators.

Study intervention

Informed consent approval was obtained and routine diagnosis procedure was performed by the treating emergency physician. This procedure included clinical, radiological and laboratory tests. X-ray was performed preferably with the patient in standing position with posteroanterior ray. When it was not possible for the patient to stand up, the chest X-ray was performed in a sitting position with anteroposterior ray. Once the routine diagnostic procedure was fulfilled, the patient's treating emergency physician established: (a) a CAP probability using a four-level Likert scale (definite, probable, possible and excluded) and (b) the need for antibiotic treatment. As in the Claessens *et al*'s study,[12] this classification was not a validated diagnosis classification but a global impression on CAP diagnosis. Once the standard procedure for CAP diagnosis was performed by the treating emergency physician, who established a CAP probability and proposed a treatment plan accordingly, an LUS was then performed by a local investigator blind to the antibiotic treatment. After the ultrasonography assessment, an LUS performer established another probability for CAP diagnosis and treatment (post LUS probability).

LUS was performed as soon as possible after the routine diagnosis procedure, using a 12-point method, and with a 3.5–5 MHz curved array probe. The operator was aware of the presumptive diagnosis of CAP. There were six scanning points on each hemithorax (figure 1): two anterior (up and down, between the sternum and the anterior

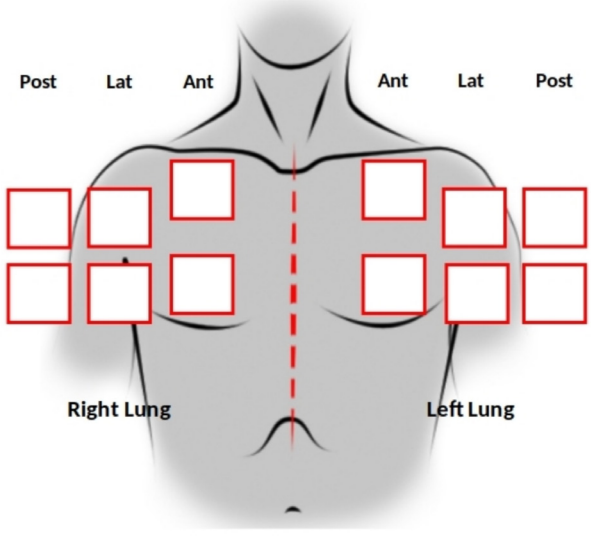


Figure 1 Lung ultrasound procedure applied in the echoPAC study.

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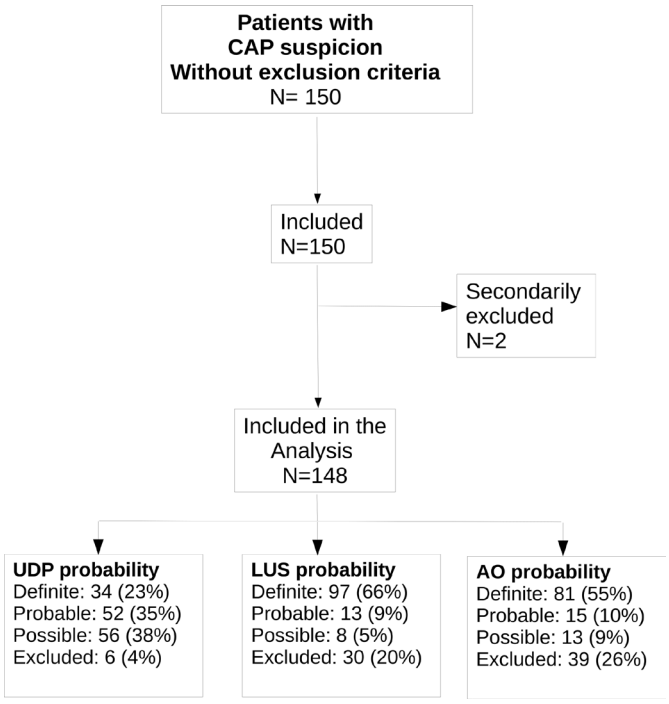


Figure 2 Flow chart of patients included in the echoPAC study. AO, adjudication committee; LUS, lung ultrasound; UDP, usual diagnosis procedure.

axillary line), two lateral (up and down, between the anterior and posterior axillary lines) and two posterior (up and down, at the back of the hemithorax). For each point, the investigator reported the presence/absence of lung sliding, B lines >3, condensation and pleural effusion or impossibility to conclude. In the context of presumptive diagnosis of CAP, the LUS findings confirming the diagnosis were a localised consolidation with or without surrounding effusion or a unilateral presence of more than three B lines.[14 15 20] To comply with protocol, investigators were not allowed to use high frequency linear array probe. The operator reported his experience (beginner, experienced and expert), the LUS difficulty (from 1 impossible to 10 very easy) and the duration. All operators attended various training courses and were classified as follows: beginners for less than 30 exams performed, experienced for 30–100 exams performed and expert for at least 100 exams performed.

Adjudication committee

An adjudication committee was established, involving three independent experts in emergency medicine, internal medicine and infectious diseases. They independently reviewed all data collected from case report forms, including routine diagnosis procedure (clinical, radiological and laboratory tests), LUS raw data, patient follow-up during hospital stay and the discharge diagnosis. They were blinded to each other's review and were not aware of both clinical and LUS CAP probabilities. When the experts were not unanimous, the final result was determined after discussion. For each patient, the adjudication committee established a probability (based on their expert analysis of the data described above) using the same four-level Likert scale, which was used for the standard diagnosis.

Objectives

The primary objective was to assess the impact of LUS on diagnostic accuracy of CAP, by measuring the concordance rate of CAP diagnostic probabilities between routine diagnosis procedure or LUS and the final probability of the adjudication committee. The secondary objectives were to assess the changes in CAP probability induced by LUS, the changes in antibiotic treatment initiation, the self-reported experience (beginner, experienced and expert) and the duration and difficulty (from 1 impossible to 10 very easy) of LUS.

Statistical analyses and sample size calculation

Statistical analyses were performed using PASW Statistics (SPSS, released 2009, PASW Statistics for Windows, V.18.0). Continuous data were expressed as mean and SD if normally distributed, or median and IQR. Categorical data were reported as percentages and 95% CI. Continuous data were compared using Wilcoxon test, categorical data with χ^2 test or the McNemar's test. Diagnosis concordances were explored using the Cohen's kappa coefficient. A p value <0.05 was considered significant. Based on a previous monocentric study (unpublished data), we anticipated a concordance rate with the adjudication committee probability of 55% for the clinical probability and 80% for the post LUS probability. With a type I error of 0.05 and a 90% power to detect this difference, the required number of patients would be 144.

RESULTS

Characteristics of study subjects and routine diagnosis procedure

During the study period, 150 patients were included and 2 were excluded due to incorrect identification, leaving 148 analysed patients (figure 2). The main characteristics are indicated in table 1. The mean age was 72±18 years (range: 19–100 years), 71 patients (48%) were aged more than 75 years and 52% were men. Routine diagnosis procedure involved laboratory tests in 135 patients, and CXR in 138 patients. Following routine diagnosis procedure, CAP probabilities were assessed as follows: definite: 34 (23%), probable: 52 (35%), possible: 56 (38%) and excluded: 6 (4%). Initiation of antibiotic treatment was decided for 106 patients (72%).

Impact of LUS on CAP management in the ED

LUS examination results modified CAP probability classification in 106 patients, 72% (95% CI 61 to 80), as detailed in table 2, and 82 modifications. After LUS, CAP was classified as definite in 97 patients (66%), probable in 13 (9%), possible in 8 (5%) and excluded in 30 (20%) (table 3). The most frequent changes affected probable or possible categories: 108 patients from these categories

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Table 1 Baseline characteristics of study patients

Characteristics	No. (%) or mean±SD
Age (years)	72±18
Sex (male)	78 (53)
Temperature (°C)	37.6±1.1
Heart rate (beats/min)	96±20
Respiratory rate (movements/min)	26±6
Systolic arterial pressure (mm Hg)	124±27
Diastolic arterial pressure (mm Hg)	68±20
Oxygen saturation (%)	95±4
Crackles	66 (45)
Chest X-ray	
Parenchymal infiltrate	131 (88)
Including unilateral finding	69 (53)
Including bilateral finding	62 (47)
Pleural effusion	28 (19)

after routine diagnosis procedure were reclassified as definitive (n=64, 59%) and excluded (n=27, 25%), leaving 21 patients (14%) in probable or possible categories following LUS (figure 3). After LUS, other diagnoses were chronic obstructive pulmonary disease exacerbation (n=11, 7%), acute heart failure (n=11, 7%), other or no diagnosis (n=14, 9%).

Following LUS, 47 changes (32%; 95% CI 25 to 40), in antibiotic prescriptions, were proposed: 21 antibiotic treatments (45%; 95% CI 31 to 59) were started, while 26 (55%; 95% CI 41 to 69) were discontinued. Adequacy between antibiotics prescription and final diagnosis in these 47 patients is displayed in table 3.

Adjudication committee CAP probability

The adjudication committee was initially unanimous in 137 patients and an agreement was reached after discussion in the remaining 11 patients. Adjudication committee CAP probability was definite in 81 patients (55%), probable in 16 (11%), possible in 12 (8%) and excluded in 39 (26%) (table 2). Overall, compared with the adjudication committee CAP probability, 39 out of 148 routine diagnosis procedure CAP probability were correct, while 109 LUS CAP probability were correct, 27% (95% CI 20 to 35) versus 77% (95% CI 71 to 84), respectively; p<0.001 (figure 3). Cohen's kappa coefficients between routine diagnosis procedure and LUS, according to the adjudication committee, were 0.07 (95% CI 0.04 to 0.11) and 0.61 (95% CI 0.55 to 0.66), respectively.

Feasibility of LUS in the ED

There were 13 operators with self-reported experiences as follows: beginner for 4, experienced for 4 and expert for 5. Impossibility to acquire the images was reported for 55 scanning points (6%) in 20 patients. Self-reported difficulty of LUS was 8.1±2.2 (ie, easy) and mean duration of LUS was 6±2.4 min.

DISCUSSION

In our prospective study, including ED patients with presumptive diagnosis of CAP, we found that LUS modified the probability of CAP diagnosis in 72% of the cases, mostly (77%) in agreement with the probability of the adjudication committee. The major finding was that LUS reduced diagnostic uncertainty from 73% to 14%. We also observed that LUS findings resulted in changes in antibiotic prescriptions in 30% of the patients. Using a different primary endpoint (change of CAP probability), a prospective study reported high-accuracy diagnosis of LUS in patients with suspected CAP.[19] Indeed, LUS has been recognised for several years to have a very good diagnostic performance in CAP with a positive likelihood ratio (LR) of 16.8 and a negative LR of 0.07 (meta-analysis, including 10 studies dating from 1996 to 2013).[21] Our results are in line with these previous studies, which show

Table 2 Distribution of changes in CAP probability classification before and after LUS in 148 patients

	LUS CAP probability					Changes in classifications	
	Definite	Probable	Possible	Excluded	Total	Number	Rates (95% CI)
Routine diagnosis procedure CAP probability							
Definite	31	1	0	2	34 (23%)	3	9% (3 to 24)
Probable	30	5	3	14	52 (35%)	47	90% (79 to 96)
Possible	34	4	5	13	56 (38%)	51	91% (80 to 96)
Excluded	2	3	0	1	6 (4%)	5	83% (42 to 99)
Total	97 (66%)	13 (9%)	8 (5%)	30 (20%)	148	106	72% (61 to 80)
Adjudication committee probability							
	81 (55%)	15 (10%)	13 (9%)	39 (26%)			

CAP, community-acquired pneumonia; LUS, lung ultrasound.

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Table 3 Antibiotic prescription according to final diagnosis in the 47 patients with treatment changes after LUS

	Post LUS CAP probabilities			
	Definite	Probable	Possible	Excluded
Antibiotic treatment withdrawn	0	3	3	20
Antibiotic treatment prescribed	11	7	3	0

CAP, community-acquired pneumonia; LUS, lung ultrasound.

very good LRs with a much higher diagnostic certainty of CAP with LUS. Nevertheless, Reissig *et al*[22] estimated that 8% of CAP was not detectable with LUS. Another point-of-care ultrasound approach involving lung, heart and deep veins also showed promising results.[23]

In our study, we applied LUS criteria for pneumonia described in a seminal study and confirmed in a consensus conference.[14 15] They included direct visualisation of a condensation or signs of a localised pulmonary oedema (B lines >3 by spot). We chose a modified eight-point method by adding up and down posterior points.[15] A recent study demonstrated that the 8-point method had similar performances for acute heart failure diagnosis that the 28-point one,[24] and was less time consuming.[19] When LUS was performed by experienced physicians, the procedure time can vary from less than 5 min in Cortellaro *et al*'s study[19] to 7–13 min in Testa *et al*'s study.[25] In our study, the mean time to perform LUS was 6 min, whereas this procedure was not only performed by experts but also by beginners. We added posterior points since pneumonia regularly occurred in posterior parts of the lung. Furthermore, CXR anteroposterior view performed in bedridden patient can increase the risk of falsely negative CXR.[26]

LUS versus CXR performances were compared in several studies,[18 19] and in two meta-analysis.[16 26] Overall, LUS sensitivity was higher than CXR, 0.95 (95% CI 0.93 to 0.97) versus 0.77 (95% CI 0.73 to 0.80), respectively, while specificity was not significantly different.[26] Furthermore, in a geriatric population, almost half of our population, LUS exhibited higher diagnostic accuracy for pneumonia than CXR, 0.90 (95% CI 0.83 to 0.96) versus 0.67 (95% CI 0.60 to 0.74), respectively.[23] In a study using

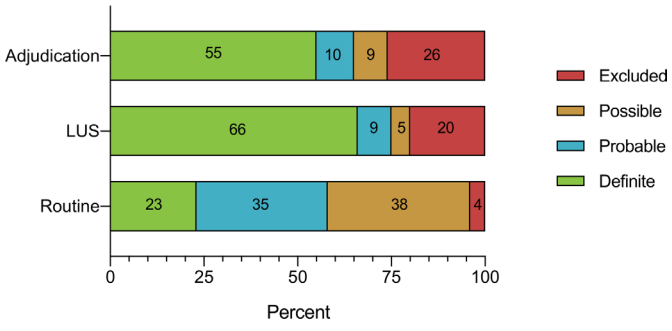


Figure 3 CAP diagnosis concordance between routine diagnostic procedure, LUS examination and adjudication committee. CAP, community-acquired pneumonia; LUS, lung ultrasound.

CT scan as gold standard, LUS sensitivity and specificity to diagnose CAP were about 90% and 97%, respectively.[27] Overall, LUS has showed good diagnostic performances even when compared with CT scan in the literature.

Our study was a preliminary investigation, which aimed to assess diagnostic and therapeutic changes in CAP following LUS, as it was previously reported for CT scan.[12] Unlike CT, ultrasound devices are widely available in ED, thus LUS could be increasingly used for the CAP diagnosis. LUS is performed at the bedside in few minutes without any irradiation. Importantly, our findings were not different from the Claessens *et al*'s study,[12] with CAP diagnosis probability changes following LUS and CT scan in 72% versus 59%, respectively. Moreover, in our study, 77% of the CAP diagnosis probabilities following LUS were in accordance with the adjudication committee compared with 80% following CT scan in the Claessens *et al*'s study.[12] Likewise, antibiotics prescription changes following LUS and CT scan were not different, antibiotic treatment was started after LUS in 54% and 45% after CT scan, and discontinued in 22% versus 14%, respectively.

Limitations

Our study has several limitations. First, the CXR was interpreted by the patient's treating emergency physician and not by a radiologist, which may have led to lower diagnostic performance. However, this is the routine procedure in many EDs. Second, as this was a pragmatic study, diagnostic testing was at the discretion of the treating physician, and CT scan was not required for CAP diagnosis, which may have led to missing CAP diagnosis in the ED. However, to date, a CT scan is not recommended as a routine radiological test for the diagnosis of CAP in the ED. Moreover, the independent experts involved in the adjudication committee had access to the detailed medical records of the included patients. Third, some potentially eligible patients were missed when a local investigator was not present and during ED's busy periods, which may have led to selection bias. Fourth, the study required the performing of LUS after the routine diagnosis procedure, which may have led to a selection of patients with less severe disease. Fifth, the adjudication committee experts had access to the LUS examination results and may have been influenced by LUS findings. Sixth, the prevalence of CAP in our study was high (about 80%), and our results should be interpreted with caution in other sites with lower prevalence of the disease. Finally, some variables were not collected in our study, such as

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information on residence in nursing homes or nursing facilities, which limits the description of our population and, therefore, the extrapolation of our results, as well as the information of overlapping diagnoses in subjects with CAP (eg, CAP and heart failure).

CONCLUSION

In conclusion, our study suggests that adding LUS to the routine diagnosis procedure could improve CAP diagnosis accuracy and could help to reduce diagnosis uncertainty and unnecessary antibiotic prescriptions. Other studies are warranted to compare LUS to CT scan in CAP diagnosis in the ED.

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Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

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Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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