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CONTRIBUTION OF LUNG ULTRASOUND IN THE EARLY DIAGNOSIS OF VENTILATOR-ASSOCIATED PNEUMONIA: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Ventilator-associated pneumonias(VAP) represent the most frequent nosocomial infection in the intensive care unit. Their diagnosis remains problematic and an early diagnosis could largely improve the prognostic outcomes. Several clinical, radiologic and biologic tools were developed to improve the speed and the diagnostic performance. Recently, lung ultrasound became a tool allowing to estimate the lung morphology at the bedside. The purpose of this study was to determine the sensibility, the specificity and the performance of diagnosis of lung ultrasound alone and associated to bronchoalveolar lavage. **Methods:** In a monocenter prospective study of 60 patients with suspected ventilator-associated pneumonia, conducted in the intensive care unit of the principal military hospital of instruction of Tunis over a period of 12 months, we investigated the diagnostic performance of lung ultrasound and the sensibility and specificity of the signs ultrasound of pneumonia which are: subpleural consolidation, lobar consolidation and arborescent/linear air bronchogram. We also evaluated the combination of lung ultrasound with direct examination of bronchoalveolar lavage. **Results:** The prevalence of VAP was 60%. The two groups (patients with and without VAP) were similar in terms of general characteristics. The only significant differences between the two groups occurred in purulent secretions: more common in patients with ventilator-associated pneumonia. Lobar/hemilobar consolidation had a specificity of 33% while subpleural consolidation and arborescent/linear air bronchogram had a specificity of 100% and a positive predictive value of 100%. The association between lung ultrasound and bronchoalveolar lavage had a specificity of 100% and a positive predictive value of 100%. **Conclusion:** The lung ultrasound is an available tool of practical bedhead among critical patients in intensive care unit. It is a valid alternative for the early and reliable diagnosis of VAP. She could also allow to follow their evolution under treatment.

KEYWORDS: Lung, ultrasonography, resuscitation, ventilator-associated pneumonia, diagnosis.

INTRODUCTION

Ventilator-associated pneumonia (VAP) is a pneumonia that occurs in a patient whose breathing is assisted either invasively through an endotracheal tube or tracheostomy or non-invasively through a face mask or other device within the 48 hours prior to the onset of infection.[1]

VAP is the most common nosocomial infection in patients admitted to the intensive care unit (ICU). It accounts for 30 to 50% of infections acquired in the ICU. It is associated with a high mortality and morbidity rate and a longer duration of mechanical ventilation (MV) and resuscitation stay. Actually, the mortality rate due to VAP is increased by 10 to 30% and the length of stay by 7 days.[2,3]

The treatment consists of quickly identifying the causal germs and initiating active antibiotic therapy. Any delay in starting antibiotics leads to a significant increase in the mortality rate in case of severe sepsis.[4,5] This is often a dilemma. Either antibiotic therapy can be started only on a positive culture from a broncho-alveolar lavage (BAL) or tracheal aspiration. The incurred risk is to start the treatment too late and thus increase mortality. Or, patients with suspected VAP are treated with empirical antibiotic therapy while waiting for the bacteriological samples. The risk in this case is to encourage the emergence of multi-resistant germs through the inappropriate and massive use of antibiotics.[6,7]

The definition of VAP is based on the combination of clinical, microbiological and radiological criteria. The diagnosis remains problematic because these criteria are partly subjective.

According to the American Thoracic Society (ATS) and the Infectious Disease Society Of America (IDSA) 2016.[1] VAP is defined as any nosocomial pneumonia (NP) occurring in a patient with MV for more than 48 hours with presence of:

- **Radiological signs**
- at least two x-ray films with an image suggestive of pneumonia,
- A single x-ray or CT scan is enough if there is no history of underlying heart or lung disease.
- And at least one of the following criteria:
- Hyperthermia ≥ to 38.3°C or hypothermia (T< 36°C) with no other cause,
- Leukopenia (<4000GB/mm3) or hyperleukocytosis (>12000GSB/mm3),
- And at least one of the following signs:
- Appearance of purulent secretions or modification of their characteristics (color, odour, quantity, consistency),
- Suggestive auscultation,
- Aggravation of blood gases (desaturation) or increased need for oxygen or respiratory assistance,
- And depending on the diagnostic means used; bronchoalveolar lavage (BAL) or protected distal aspirate (PDA) or protected specimen brush (PSB):
- A BAL with a positivity threshold > 10^4 UFC/ml,
- A PDA with a positivity threshold > 10^3 UFC/ml,
- A PSB with a positivity threshold > 10^3 UFC/ml,

At the patient's bedside, in the intensive care unit (ICU), the diagnostic imaging and monitoring of NP relies primarily on chest x-rays (CXR). However, these are not reliable in daily practice.[8,9] Thoracic computed tomography (CT) scan is the gold standard, but it is a major source of radiation. It requires the mobilization of qualified personnel for the risky transport of often restless patients. Moreover, it is expensive.

Ultrasound is saving space in the ICU. Several studies have shown the effectiveness of ultrasound in the diagnosis of several pulmonary pathologies such as lung cancer, pleurisy, pneumonia, pneumothorax.[10,11]

It represents an additional tool for the diagnosis and follow-up of VAPs, which is simple, non-invasive, non-irradiating and inexpensive.[10,11]

The primary aim of this study was to evaluate the sensitivity, specificity and diagnostic performance of lung ultrasound alone and ultrasound associated with BAL.

The secondary aim was to assess the frequency of the characteristic ultrasound signs during VAP and to suggest a diagnostic approach for an early diagnosis combining the Clinical pulmonary infection score (CPIS), BAL and lung ultrasound.

METHODS

Type and duration of study

This is an observational, prospective, monocentric study, carried out in the Intensive Care Unit of the Military Hospital of Tunis over a period of 12 months from January 1st, 2020 to December 31st, 2020.

Patient selection

All patients admitted to resuscitation during the study period who were suspected of having VAP were selected.

Inclusion Criteria

This study included patients:

- Whose breathing had been assisted by mechanical ventilation for more than 48 hours.
- Having a new X-ray image or radiological extension (CXR and/or thoracic CT scan).
- With at least two of the following clinical criteria:
- Temperature ≥ 38.3°C or hypothermia (T< 36°C).
- Hyperleukocytosis > 11.10^3/ml or leukopenia (< 4.10^3/ml) or immature cells >10% (in the absence of other known causes)
- Hypoxemia with PaO2< 60mmHg or a PaO2/FiO2 ratio <300
- Purulent tracheal secretions

Non-inclusion criteria

- Patient with known pneumonia
- Age < 18 years
- Mechanical ventilation <48h
- Contraindication to pulmonary fibroscopy

Patients who were included received routine ultrasound monitoring. No additional treatment was administered as part of the protocol.

Biological (procalcitonin (PCT), leukocyte, neutrophil polymorphism (PNN)) and microbiological (BAL) specimens were part of the standard patient management. These tests were performed through already existing catheters. The timing of the sampling had already been scheduled as part of the patient's routine management. None of these samples required additional venipuncture.

Lung ultrasound was performed by the Trans-thoracic route using a VIVID 7 type ultrasound scanner with a 3 MHZ probe. The examination does not expose to radiation. It is perfectly painless and non-invasive.

CONDUCT OF THE STUDY

Data collection

Patients were included at the time VAP was suspected. Data collection was based on the patient's clinical record and did not require additional history taking.

The parameters that were collected were as follows:

- Patient characteristics: weight, Body mass index (BMI), SOFA and SAPS 2 scores, date of arrival in ICU, date of onset of VAP, previous treatments, history (Acute Renal Failure (ARF), Extra Renal Epuration (ERE)), aspect of tracheal secretions, fever, Clinical pulmonary infection score (CPIS).
- Ventilation parameters: ventilatory mode, tidal volume, inspiratory support, respiratory rate, FiO2, PEEP, peak pressure, plateau pressure.
- Infectious history: previous treated infections, previous isolated germs, number of days of antibiotics discontinuation, previous antibiotic therapy, and possible current antibiotic therapy.
- Biological data: leukocytes, PNN, blood gases (PaO2, PaCO2, pH, PaO2/FiO2, lactates)
- Radiological data: images suggestive of diffuse or localized lung infection.

Study protocol

At inclusion, we calculated the CPIS, performed and recorded the result of the PCT test, collected BAL samples for direct examination and culture. Lung ultrasound, BAL, and direct examination were all performed within 8 hours after inclusion.

The CPIS score

A score includes the main clinical, biological, radiological and microbiological parameters used in the diagnosis of VAP. A CPIS equal to or greater than 5 allows affirming the diagnosis of ventilator-associated pneumonia with a sensitivity of 93% and a specificity of 100%.[12]

Tracheal secretions were aspirated and evaluated by nurses (quality and quantity)

Oxygenation parameters were calculated on blood gases. Chest X-ray was interpreted by doctors.

Bronchoalveolar lavage (BAL)

Bronchoalveolar lavage was performed in the affected lung lobe on the chest X-ray. The patients were on 100% FiO2 throughout the procedure. The fiberscope was inserted without suction after putting a bite block on the patient. Once blocked at a segmental orifice, repetitive injections of physiological saline (max 5 times) using 20 ml syringes were performed. Then we proceeded to gentle aspirations (50 to 80mmHg) of the injected fractions.

The sample collected in the collection trap was approximately 40 to 70% recovery of the total instillate. The sample was immediately sent to the laboratory.

The sample was considered positive if the number of microorganism was ≥ 1 with a concentration ≥ 10^4 CFU/ml.

Lung ultrasound

A complete scan was carried out by trans-thoracic route using a VIVID 7 type ultrasound scanner and a 3 MHZ probe. The ultrasound examination involved exploration of the six lung regions for each lung (upper and lower areas of the anterior-lateral and posterior fields using the anterior and posterior axillary lines as landmarks). **Fig. 1**

We looked for the presence of:

- Lobar or hemi-lobar consolidation
- Broncho linear aerial gram in consolidations
- Sub pleural consolidation

Study population

In our study, patients were divided into two groups:

VAP positive group (VAP+)

This group represented all patients in whom VAP was initially suspected and then confirmed. It consisted of two subgroups:

Positive VAP group with positive sampling (VAP+BAL+)

The diagnosis of sample-positive VAP (VAP+ BAL+) was maintained when associating:

A positive direct BAL test (≥1 microorganism with a concentration ≥ 10^4 colonies per unit in bronchoalveolar secretions)

With at least two of the following signs:

- Temperature ≥ 38.3° C or hypothermia (T < 36 C°)
- Leukocytes >10 103/ml or leucopenia (< 4 10^3/ml) or immature cells >10% (in the absence of other known causes)
- Hypoxemia (PaO2 <60 mm Hg) or a PaO2/FiO2 ratio < 300
- Purulent secretions

Positive VAP group with negative sampling (VAP+BAL-)

The diagnosis of VAP with negative specimen (VAP+ BAL -) is retained if:

- All of the above clinical criteria were present
- In a patient who has been receiving antibiotic therapy for at least 48 hours prior to sampling.

Negative VAP group (VAP-)

This group represented all patients in whom VAP was initially suspected but not confirmed by either BAL or clinical signs.

Statistical analysis

Qualitative variables were expressed in numbers (percentage) and were compared using the Pearson Chi-2 test. Quantitative values were expressed as mean ± SD or median (interquartile range) depending on the distribution of the data. Two groups were compared (patients with (VAP+) and without (VAP-)) using the Mann-Whitney test for numerical data and Fisher's exact

test for categorical data. All p-values were two-sided and p <0.05 was considered significant.

Test performances (the different signs of lung ultrasound, CPIS, BAL (direct examination and culture)) were expressed in terms of sensitivity, specificity, positive and negative predictive value, and positive and negative likelihood ratio.

The sensitivity of a test is the probability that the test would be positive in a patient with the disease. It is the number of true positive (TP) tests divided by the total number of patients with the disease.

The specificity of a test is the probability that the test would be negative in a patient without the disease. It is the number of true negatives (TN) divided by the total number of patients with the disease.

The positive predictive value (PPV) is defined as the ratio of TP to the sum of TP and false positives (FP). (PPV= TP/ (TP+FP)).

Negative Predictive Value (NPV) is defined as the ratio of TN to the sum of TN and false negatives (FN). (NPV= TN/(TN+ FN))

The Negative likelihood ratio (LR-) is defined by the ratio (1-sensitivity) by specificity. (LR- = (1-sensitivity) / specificity)

The positive likelihood ratio (LR+) is defined by the ratio of sensitivity to (1- specificity). (LR+ = sensitivity / (1- specificity)).

RESULTS

General characteristics of the population

Sixty patients were initially included. A VAP was confirmed in 45 (i.e. 60% of the included patients)

The clinical characteristics of the patients are shown in **Table I**.

The two groups VAP+ and VAP- were comparable in terms of age, gender and severity at admission as assessed by SOFA and SAPS2 scores. The reason for admission to resuscitation was medical in 71% of patients and surgical in only 28% of the included patients. There was no significant difference between the two groups VAP+ and VAP- in terms of: The duration of mechanical ventilation on inclusion, the total duration of MV, the PaO2/FiO2, the BMI, markers of infection: temperature, white blood cells, procalcitonin, length of stay in intensive care, mortality, radiological data (diffuse or localized image). The only significant difference was found in the aspect of secretions. The purulent aspect was more frequent in the VAP+ group.

Distribution of microorganisms responsible for VAP

Gram-negative bacilli were found in all VAP+ BAL+. The most frequently isolated germ was *Acinetobacter Baumanii* (47.7%), followed by *Pseudomoans Aeruginosa* (15.9%), *Klebsiella Pneumonia* (12.3%), Proteus Mirabilis (9.0%), *Entérobacter Cloacae* (8.7%), and *Providencia stuwarti* (6.4%).

Characteristics of diagnostic markers for VAP

The diagnostic performances of clinical biological and microbiological markers are shown in **Table II.**

The CPIS score

The sensitivity of the CPIS score was better for a score value ≥ 6 compared to a score ≥7, whereas the specificity was better for a CPIS score ≥7. The CPIS score ≥6 and ≥7 were associated with almost similar LR+ (1.29 and 2).

Lung ultrasound

Lung ultrasound alone was associated with a sensitivity of 91% and specificity of 33%.

When all ultrasound signs of infection were present (lobar/hemi-lobar consolidation with air bronchogram and sub pleural consolidation), ultrasound confirmed the diagnosis of VAP with 100% specificity.

Lobar or hemi-lobar consolidation was found in almost all included patients and was not therefore specific for VAP. Sub pleural consolidation and the bronchogram were only found in patients who developed VAP.

Bronchoalveolar lavage

The sensitivity and specificity of the BAL with a positive direct examination were 88% and 73% respectively, with a high LR+ at 3.25 and a LR- at 0.16. When the culture was positive, specificity and sensitivity were reported to have been nearly similar to those reported with a positive direct examination.

Diagnostic value of the combination of the different markers

The combination of lung ultrasound with direct examination of positive BAL improved sensitivity from 33% to 90% and specificity from 33% to 75%.

The presence of subpleural consolidation and bronchogram on ultrasound alone or in combination with positive direct examination had a specificity that was equal to 100%. High PPV was also found at 97% and 100%. Positive likelihood ratios were high at 3.6 and 3.7 respectively. The combination of lung ultrasound with a positive BAL culture resulted in 100% specificity and 100% PPV and a very high LR+ (**Table III**).

Table I: General characteristics of the population.

	Patients (n=60)	VAP + (n= 45)	VAP – (n= 15)	p
Age (year, mean ± SD)	61 ± 18	62 ± 18	55 ± 17	0,184
Male sex (%)	78	77	78	
SAPS2 (mean ± SD)	42 ± 16	43 ± 16	39 ± 16	0,445
SOFA (mean ± SD)	7 ± 3	7 ± 3	7 ± 2	0,793
Reason for admission at ICU [n %] Medical : Surgical :	 71,7 28,3	 80 20	 46,7 53,3	0.018
Duration of MV start VAP [days, median(IQR)]	10 (5—11)	10 (4—10)	10 (5—11)	0,966
Duration of MV in ICU [days, median(IQR)]	24 (12—49)	30 (12—46)	35 (12—66)	0,585
Duration of stay in ICU [days, median(IQR)]	46 (15—63)	45 (15—60)	52 (18—90)	0,572
Temperature (°C, mean ± SD)	38,6 ± 0,5	38,6 ± 0,5	38,4 ± 0,4	0,194
Purulent aspects of secretions (%)	81.7	88.9	60	**0.021**
Leucocytes (giga/L, mean ± SD)	15,3 ± 5,9	15,9 ± 6,1	13,6 ± 5,1	0,205
PaO2/FiO2 (mean ±SD)	186 ± 63	188 ± 64	179 ± 62	0,626
CPIS [median (IQR)]	6 (5-7)	6 (6-7)	6 (5-6)	0,108
Procalcitonin [ng/ml, median (IQR)]	8,4 (0,4-8,1)	10 (0,4-16)	3,7 (0,5-4,2)	0,133
Mortality in ICU (%)	32	30,5	44,1	0,124
BMI (kg/m2, mean ± SD)	29.3 ±1.2	27.8 ±0.9	28.9±0.8	0.332
Chest X-ray (%) Localized image: Diffuse image:	 66 34	 68.5 31.5	 57 43	 0,146 0,124

Table II: Characteristics of diagnostic markers of VAP (CPIS, BAL, lung ultrasound) in patients suspected of having VAP.

	Sensitivity	Specificity	PPV	NPV	LR+	LR-
CPIS ≥ 6	77%	40%	79%	37%	1.29	0.57
CPIS ≥ 7	40%	80%	85%	30%	2	0.75
Direct exam + BAL	88%	73%	90%	68%	3.25	0.16
Positive culture of BAL	76%	80%	93%	48%	3.8	0.3
ultrasound with lobar/hemi-lobar consolidation	91%	33%	80%	55%	1.36	0.27
ultrasound with lobar/hemi-lobar consolidation OR sub pleural consolidation	100%	33%	81%	100%	1.49	0
ultrasound with lobar/hemi-lobar consolidation AND sub pleural consolidation or bronchogram	17%	100%	100%	28%	-	0.83

Table III: Diagnostic Value of Combined Ultrasound and BAL in patients with suspected lung disease.

	Sensitivity	Specificity	PPV	NPV	LR+	LR-
Direct examination + with lobar/hemi-lobar consolidation on ultrasound.	90%	75%	97%	42%	3.6	0.13
Direct examination + with lobar/hemi lobar consolidation or sub pleural consolidation on ultrasound.	92%	75%	97%	50%	3.7	0.1
Direct examination + with lobar/hemi lobar consolidation and sub-pleural consolidation	17%	100%	100%	28%	-	0.82

or bronchogram on ultrasound.						
Culture + with lobar/hemi-lobar consolidation or sub-pleural consolidation or bronchogram on ultrasound.	25%	100%	100%	11%	-	0.75

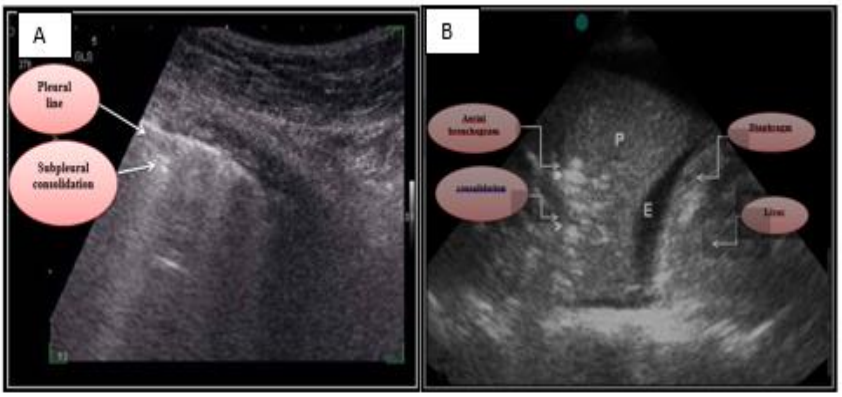

Fig. 1: Lung ultrasound
A- Longitudinal ultrasound view of a lung; irregularly spaced B-lines arising from a small juxta-pleural infectious site.
B- Massive alveolar consolidation, transverse view of lung ultrasound; P=lung; E= pleural effusion

DISCUSSION

In our study, the incidence of VAP was 60%. The two groups VAP+ and VAP- were comparable in terms of age, gender and severity at admission. No significant differences were found between the two groups VAP+ and VAP- regarding the duration of mechanical ventilation at baseline, the total duration of MV, the PaO2/FiO2 ratio, the markers of infection (temperature, leucocytes and procalcitonin), the length of stay in the intensive care unit and mortality.

The only significant difference was found in the aspect of purulent secretions. The purulent aspect was more frequent in the VAP+ group.

Gram-negative bacilli were responsible for all VAP+ BAL+ with *Acinetobacter Baumanii* at the top of the list. On lung ultrasound, the presence of lobar or hemi-lobar consolidation as the only sonographic sign of VAP was not specific for VAP. However, when all the characteristic sonographic signs of VAP (including lobar or hemi-lobar consolidation, sub-pleural consolidation and air bronchogram) were present, the specificity of lung ultrasound reached 100%, PPV was 100% with a very high LR+. Direct examination of the BAL and the BAL culture had similar sensitivity (88% and 76% respectively) and specificity (73% and 80% respectively). Similarly, the PPVs were similar (90% for direct examination and 93% for culture) as well as the LR+ (3.25 and 3.8 respectively). The combination of pulmonary ultrasound and direct examination of BAL had a specificity of 75% and could reach 100% (if all ultrasound signs were present) as well as a very high PPV 97%. The combination of lung ultrasound and positive BAL culture had almost the same results. Indeed, the specificity is 100%, the PPV is 100% and the LV+ is very high.

The fundamental obstacle to the diagnosis of VAP is the lack of formal criteria for a definitive diagnosis. The diagnosis and treatment of VAP remain problematic. There are no specific clinical signs that can be used solely for the diagnosis of VAP.[13] Traditionally, the clinical diagnosis of VAP is made on the occasion of new or progressive radiological consolidation in a patient with fever or hypothermia, leucocytosis or leucopenia, and purulent tracheal secretions. These criteria were suggested by Johnson in 1972.[14] Their sensitivity was only of 69% and specificity was no better than 75%. Despite this relatively low accuracy, these criteria have been recommended by the ATS for the diagnosis of VAP.[15] Combinations of different criteria for making a diagnosis in patients with VAP have been suggested and validated. The Clinical Pulmonary Infection Score (CPIS) has been advanced by Pugin. It is a score comprising six variables (fever, leucocytosis, tracheal aspirations, oxygenation, radiographic infiltrates and semi-quantitative tracheal aspiration cultures with Gram stain) with a sensitivity of 93% and a specificity of 100%. The study that proposed this score as a diagnostic tool included only 28 patients. Since this original survey, several studies have attempted to evaluate the usefulness of the score as a diagnostic tool. Several prospective and retrospective methods were used, and analyses were focused on larger cohorts and patient types. The authors' conclusions indicate that at the 6-point threshold, the

CPIS achieves a sensitivity of 72% and a specificity of 85%. In our study, our results indicate a limited value of the CPIS in the two groups VAP+ and VAP-. Actually, a CPIS score greater than or equal to 6 reaches a sensitivity of 77% whereas the specificity is poor and is only 40%. It is only from a score of 7 that specificity rises to 85% but at the expense of sensitivity reduced to 40%. Our results are in line with those of Fàbregas who attempted to validate the CPIS by performing sputum samples immediately after the death of 25 patients on MV followed by an immediate post-mortem lung biopsy. The sensitivity of a CPIS score ≥6 was 77% while the specificity was only 42%.[16] Our results are also very similar to those of Mongodi, which showed a sensitivity of 68% and a specificity of 50%.[17]

A major limitation in the literature regarding the validation of the CPIS for the diagnosis of VAP is that BAL culture is not a true gold standard.[16] In addition, the calculation of the CPIS has been modified by some authors, and different cut-off points have been used for the diagnosis of VAP.[18] Similarly, it is important to note that the inter-observer agreement in the calculation of the CPIS turned out to be low.[18]

The clinical approach suggests the administration of broad-spectrum antibiotics in patients suspected of having VAP. Such overuse and sometimes unnecessary use of antibiotics promotes the selection of multi-resistant bacteria and exposes the patient to subsequent treatment complications.[15]

The use of bronchoscopic techniques to obtain BAL samples from the affected area in the lung makes it possible to develop a strategy (strategy or bacteriological approach) superior to that based exclusively on clinical evaluation. Several studies have described a variety of nonbronchoscopic techniques for sampling lower respiratory tract secretions. The results have been similar to those obtained using bronchial fibroscopy.[19] However, fibroscopic sampling with quantitative cultures may lead to a decrease in antibiotic exposure (less initial antibiotic therapy, and less selection of multi-resistant bacteria).[20]

Although some researchers have concluded that BAL provides the best reflection of lung bacterial load, quantitatively and qualitatively, others have reported mixed results with low specificity of BAL fluid cultures in patients with high tracheobronchial colonization.[21-23]

In our study the sensitivity of the culture of the BAL samples was 76% and the specificity was 80%. These results are similar to those found in the literature, which are 73 ± 18% and 82 ± 19% respectively.[22]

A positive quantitative culture (>10^4 CFU/ml) of a BAL sample allows the diagnosis of VAP. However, bacteriological samples can be falsely negative and it takes 24 to 48 hours to obtain definitive results. Such a microbiological approach is very specific but can lead to a delay in treatment, resulting in increased mortality.[4,5]

Reliable diagnostic tools for the early diagnosis of VAP are therefore essential so that antibiotic treatment can be started as soon as possible, avoiding the negative effects of these two extreme approaches.

In terms of imaging, the most commonly used examination is a chest X-ray. However, its quality and reliability in intensive care unit patients is very poor, as demonstrated by several previous studies. The reference radiological examination for the diagnosis of VAP remains the chest CT scan. However, it is less readily available and requires the involvement of qualified personnel. It is radiant and expensive. It would therefore be easier to use a chest ultrasound.

Ultrasound is drawing more and more attention in intensive care and emergency medicine. A number of studies have shown that ultrasound is highly effective in the evaluation of multiple lung diseases.[24]

Several studies have stated that community-acquired pneumonia can be diagnosed by the presence of consolidation on lung ultrasound and controlled by the number and size of ultrasound images.[25] In ventilated patients, pulmonary ultrasound has good sensitivity in detecting the consolidations frequently found in the lower lobes.[25] In our study the sensitivity of lung ultrasound was 91%. However, many causes other than pneumonia may explain the asymmetric consolidations. As our results clearly demonstrate, lobar or hemi-lobar consolidation was not specific for VAP. The specificity of the lung ultrasound was only 33%. Our results are therefore similar to those of Mongodi.[17]

VAP is marked by several histopathological features. First, it is a multifocal process involving both lungs, particularly the lower lobes. It is probably due to the spread of germs colonizing the tracheo-bronchial tree by positive pressure mechanical ventilation. Secondly, VAP involves the simultaneous presence of different histological grades of bronchopneumonia. As the foci of bronchopneumonia spread to the periphery, the different grades can be detected by lung ultrasound: irregularly spaced B-lines foci correspond to the early stages of infection by interstitial inflammation while focal and confluent bronchopneumonia is detected as small, lobar or hemi-lobar and subpleural consolidations.[26] Bronchi filled with air and secretions appear as hyperechoic linear or tree-like bronchograms in the consolidations, moving synchronously with respiratory movements.[26]

Our results confirm these pathophysiological data. Indeed, the presence alone of lobar or hemi-lobar consolidation or sub-pleural consolidation had a sensitivity of 91% while specificity was only 33%. The simultaneous presence of the different ultrasound signs corresponding to the different histopathological grades

(lobar or hemi-lobar consolidation, subpleural consolidation and aerial bronchogram) varied specificity by up to 100%. Our results are consistent with those of Mongodi.[17] On the basis of these results, ultrasound could be useful in the diagnosis of VAP. The use of antibiotics in patients with lobar or hemi-lobar consolidation may lead to the erroneous treatment of subjects without pulmonary infection. The combination of lobar consolidations with aerial bronchogram and/or subpleural consolidations is less frequent but more useful for diagnosis.[27]

Currently, only the classical microbiological techniques of direct examination and culture are available and validated. In our study, endotracheal samples are sampled from the bronchoalveolar lavage for direct examination of Gram staining and for culture.

Microscopic examination and culture results are often inconclusive in patients suspected of having VAP. The upper pulmonary airways of most intensive care patients are colonized with potential pathogens regardless of the presence of pneumonia.[28]

Our observational study evaluated the value of combining lung ultrasound with microbiological samples. Sensitivity increased from 73% for direct examination alone to 75% with only the presence of consolidations and to 100% if all ultrasound signs were present. With regard to culture, the sensitivity increases from 80% to 100% if combined with lung ultrasound with a very high positive likelihood ratio indicating a conclusive increase in the occurrence of the disease. Our results are similar to those of Mongodi.[17]

The combination of direct examination of the Gram stain and lung ultrasound allows a reliable and rapid diagnosis of VAP. It therefore allows the early introduction of effective antibiotic therapy. It spares us from wrongly treating patients without VAP (100% PPV). The treatment will be adjusted later on according to the results of the microbial cultures. This study has several strengths, outcome data does not require an additional treatment or biological and microbiological specimens: the protocol is a part of the patient's routine management. Lung ultrasound is simple, non-invasive, non-irradiating and inexpensive compared to the chest CT. The use of lung ultrasound ovoid a risky transport of restless patients and allows an early diagnosis so no therapeutic delay.

There are certain limitations to our study. We only included 60 patients. This study needs to be confirmed with a larger enrollment. VAP was only diagnosed when clinical signs were present. The incidence of VAP was high in the study population, approximately 60%. This may explain the good positive predictive value and the low negative predictive value. Pulmonary ultrasound is operator-dependent and requires a qualified physician. Some patients may be difficult to examine (obese subjects with chest dressings, presenting subcutneous emphysema, hemodynamically unstable) and the value of pulmonary ultrasound in monitoring the development of lung infection was not investigated.

We propose a strategy for the early and reliable diagnosis of VAP including lung ultrasound. For patients with suspected VAP on clinical criteria with a CPIS score ≥6, bacteriological samples are taken from BAL and a non-invasive radiological examination using pulmonary ultrasound is performed. If the direct examination is positive and if the pulmonary ultrasound shows signs in favor of VAP, i.e. lobar or hemilobar consolidation and/or subpleural consolidation and aerial bronchogram, antibiotic therapy will be started immediately. This antibiotic therapy will be adapted secondarily to the results of the microbial cultures. If the ultrasound is inconclusive and the direct examination is negative, other etiologies will be investigated. We will then wait for the culture results before starting antibiotic therapy. If the cultures come back positive, appropriate antibiotic therapy will be initiated.

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Conflicts of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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