

## Utility of chest ultrasound in the diagnosis of ventilator-associated pneumonia in the critical care unit of a tertiary care center: a prospective observational study

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### Abstract

Ventilator-associated pneumonia (VAP) is a type of nosocomial pneumonia developing in patients who are mechanically ventilated for  $\geq 48$  hours. Lung ultrasound (LUS) has been shown to be useful in evaluating various pathologic pulmonary conditions. We aimed to study the utility of chest ultrasound in the diagnosis of VAP in a critical care unit. This was a monocentric, prospective observational study carried out in the intensive care unit (ICU) of our institution. On clinical suspicion of VAP, patients were subjected to ultrasound chest (lung) examination, which was done in a supine position in six areas of each hemithorax on the same day, and endotracheal aspirate (ETA) for gram stain and aerobic culture was sent within 6 hours. The final diagnosis of VAP was made when the ETA culture was positive ( $>10^5$  CFU/mL). Days of mechanical ventilation, ICU stay, hospital stay, and mortality were separately recorded for monitoring outcomes. Diagnostic performance of risk factors for VAP was analyzed by parameters like sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratio (positive and negative). Concerning LUS signs, subpleural consolidations  $>2$  had a sensitivity of 96% and specificity of 63% with an odds ratio of 51.43 in predicting VAP. A dynamic air bronchogram within consolidation was seen in 45% of patients with a sensitivity and specificity of 29% and 73%, respectively. A clinical LUS score  $>2$  had a sensitivity of 100% in predicting VAP. LUS is a robust diagnostic tool with high sensitivity for diagnosing VAP. Clinical trials are needed to study whether LUS can be used as a tool for early diagnosis of VAP, which will help in the timely introduction of antibiotics.

**Key words:** VAP, VPLUS, lung USG.

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### Introduction

Ventilator-associated pneumonia (VAP) is a type of nosocomial pneumonia developing in patients who are mechanically ventilated for at least 48 hours [1]. VAP prolongs intensive care unit (ICU) stay and results in increased costs of hospitalization. In one study, the total cost for VAP patients was about 3 times higher compared to non-VAP patients [2]. Hence, VAP causes statistically significant resource utilization, and there is an urgent need for cost-effective interventions for prevention, early diagnosis, and treatment of VAP. It is a well-recognized fact that the diagnosis of VAP is difficult only on the basis of clinical grounds. There is a lack of universal agreement in terms of diagnostic criteria and optimal methods for obtaining specimens for microbiological culture [3]. This intricateness is primarily due to the huge diversity of pathologies that can cause radiological infiltrates. The high frequency of bacterial colonization in the proximal respiratory tract of ventilated patients also adds to this complexity [4]. Early accurate diagnosis is important in achieving a favorable outcome without compromising the risk of antibiotic resistance. Investigators

have proposed several criteria for diagnosing VAP in clinical settings, which include clinical features, radiological features, methods of obtaining and interpreting microbiological samples, and biomarkers [3]. Lung ultrasound (LUS) gives a real-time evaluation of lung parenchymal changes during the development of VAP with increasing degrees of loss of aeration. In a multicenter prospective study including 99 patients of suspected VAP, LUS findings of subpleural consolidations and air bronchogram when combined showed a positive predictive value of 86% [5]. However, the diagnosis of VAP should not be based on LUS findings alone, but on the combination of clinical findings, microbiological results, and LUS findings, which increases the diagnostic accuracy [5]. Our study involves the utility of chest ultrasound in diagnosing VAP and its correlation with clinical criteria.

### Materials and Methods

#### Objectives

The objective of this article was to study the utility of chest ultrasound in the diagnosis VAP in the critical care unit.



## Study design

This is a prospective time-bound observational study.

## Study participants

All consecutive patients mechanically ventilated in the adult ICU of All India Institute of Medical Sciences, Jodhpur, Rajasthan, from February 2021 to May 2022 were enrolled after satisfying the inclusion and exclusion criteria.

## Inclusion criteria

All patients on invasive mechanical ventilation for more than 48 hours and having clinical suspicion of VAP were included. Clinical suspicion of VAP was based on the Johanson criteria [6], *i.e.*, invasive mechanical ventilation for more than or equal to 48 hours, with newly appeared/evolving chest X-ray infiltrate, and two or more of the following clinical criteria: i) temperature more than or equal to 38.5°C or hypothermia (<36.5°C); ii) leucocytosis >10<sup>4</sup>/mL, or leukopenia <4×10<sup>3</sup>/mL; iii) purulent tracheal secretions; iv) partial pressure of arterial oxygen (PaO<sub>2</sub>)/fraction of inspired oxygen (FiO<sub>2</sub>) <300 mm Hg. The final diagnosis of VAP was made when endotracheal aspirate (ETA) or bronchoalveolar lavage culture was positive with a threshold of >10<sup>5</sup> CFU/ml.

## Exclusion criteria

1. Age less than 18 years old.
2. Those with pneumonia as the primary reason for invasive mechanically ventilation.
3. Chest trauma and thoracic surgeries which will lead to distorted anatomy of thorax.

## Sample size

This was a time-bound study, and all patients fitting the inclusion criteria within the study period were planned to be included. Because of the restrictions due to the COVID-19 pandemic, only 50 patients could be enrolled in the study. The study was approved by the institutional ethics committee (AIIMS/IEC/2021/3435).

## Methodology

All patients satisfying the inclusion and exclusion criteria during the study period were assessed for eligibility. Those fulfilling the inclusion criteria were enrolled after obtaining informed written consent from next of kin. Data was collected using a pre-designed, structured proforma. Demographic and clinical details of all patients were noted. Patients on invasive mechanical ventilation for more than 48 hours and having clinical signs of VAP (satisfying exclusion criteria) were included in the study.

On clinical suspicion of VAP, patients were subjected to an ultrasound of the chest (lung), and ETA for gram stain and aerobic culture were sent within 6 hours. Ultrasonography of the chest was performed by Sonosite M turbo ultrasound systems (FUJIFILM SonoSite Inc., Washington, USA). A curvilinear low-frequency probe (2-5 MHz) was used for LUS.

Examination was done in the supine position in six areas of each hemithorax (superior and inferior areas in the anterior, lateral, and posterior fields using anterior and posterior axillary lines as landmarks, with a transverse line between parasternal and paravertebral line through the nipple). For examining the posterior lung surface, the lateral position was used.

The following ultrasound findings were noted in each area: i) small subpleural consolidations (echo-poor regions >0.5 cm in

diameter); ii) dynamic linear or arborescent air bronchogram within lobar/ hemilobar consolidations (air entrapped within bronchi with simultaneous movement with inspiration).

The examination was carried out by a pulmonary medicine resident whose dissertation topic was this study. As is the curriculum in the 3-year super specialty training in our institute, the resident underwent a 2-week training in the radiology department. He was trained in performing LUS and reading computed tomography (CT) thorax scans.

We calculated the clinical-LUS score (VAPLUS score) as per the LUS findings, which is a combination of ultrasound signs and purulent ETA: 2 areas with subpleural consolidations - 1 point; 1 area with dynamic arborescent/linear air bronchogram - 2 points; purulent ETA - 1 point.

ETA was collected through a single-lumen sterile catheter passed through an endotracheal/tracheostomy tube. Bronchoscopy was done if clinically indicated, and lavage was taken. Samples were sent for gram stain and aerobic culture. Patients were subjected to antibiotic modification as per the clinician's decision, local distribution of pathogens associated with VAP, and their antimicrobial susceptibilities. Patients were continued on other supportive treatment as per the primary disease.

## Statistical analysis

Data was entered into Microsoft Excel and analyzed using R software version 4.2.0. Quantitative data were expressed in means and standard deviation, median, and interquartile range. Statistical tests, including the chi-square test, *t*-test for means, and *t*-test for proportions for quantitative data. For non-parametric data, the Mann-Whitney test was used. Diagnostic performance of risk factors for VAP was analyzed by parameters like sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratio (positive and negative). Receiver operating characteristic (ROC) curve analysis was also done, and the area under the curve (AUC) values for each parameter were calculated. A *p*-value <0.05 was taken to be significant.

## Results

A total of 50 patients were enrolled in the study after satisfying the inclusion and exclusion criteria during the study period. The mean age ± standard deviation of patients in our study was 56.76±17.57 years. Out of 50 patients, there were 35 males (70%) and 15 (30%) females. The clinical and demographic features of the study population are given in Table 1. With respect to the components of the VAP suspicion criteria, the commonest parameters found both in VAP and non-VAP patients were those of PaO<sub>2</sub>/FiO<sub>2</sub> <300 and purulent tracheal secretions. This data is shown in Table 2. The microbiological yield in patients with VAP is shown in Table 3. *Acinetobacter* spp., *Klebsiella*, and *Pseudomonas* spp. were the commonest organisms in VAP patients.

The diagnostic performance of laboratory parameters and LUS score was studied in the diagnosis of VAP, as shown in Table 4. Positive gram stain in endotracheal secretions was the most significant predictor of VAP with an odds ratio of 18.9. Interestingly, procalcitonin levels in blood predicted VAP with only an odds ratio of 1.2. In the LUS score, subpleural consolidations >2 and CLUS >2 were most significantly associated with VAP, with odds ratios of 51.43 and 69.3, respectively. ROC curves of subpleural consolidation and LUS score with respect to diagnosis of VAP are given in Figures 1 and 2, with AUC of 0.84 and 0.83, respectively.



**Table 1.** Clinical characteristics in study population.

Characteristic	VAP (n=31)	Non-VAP (n=19)	p	Statistical test used
Age (years), mean ± standard deviation	56.9±17.6	56.5±18.1	0.93	t-test for means
Male, n (%)	24 (77)	11 (57)	0.14	Chi-square test
Female, n (%)	7 (22)	8 (42)		
Comorbidities, n (%)				
Systemic hypertension	10 (32)	6 (31)	0.48	Chi-square test
Diabetes mellitus	7 (22)	5 (26)	0.38	Fisher exact test
COPD	5 (16)	2 (10)	0.3	Fisher exact test
Ischemic heart disease	3 (9)	1 (5)	0.29	Fisher exact test
Chronic kidney disease	2 (6)	1 (5)	0.29	Fisher exact test
Chronic lung diseases (ILD, COPD, post tubercular sequelae)	6 (19.4)	5 (26.3)	0.7	Chi-square test
Clinical profile, n (%)				
Medical	22 (70)	15 (79)	0.53	Chi-square test
Post-surgical	9 (30)	4 (21)		

VAP, ventilator-associated pneumonia; COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease.

**Table 2.** Ventilator-associated pneumonia suspicion criteria in the study population.

VAP suspicion criteria	VAP (n=31) n (%)	Non-VAP (n=19) n (%)	p	Test used
Temperature (degree Celsius) ≥38.5 or <36.5	6 (19)	2 (10)	0.41	Fishers exact test
WBC count >10 <sup>4</sup> /mL or <4×10 <sup>3</sup> /mL	26 (84)	12 (63)	0.1	Chi square test
Purulent tracheal secretions	28 (90)	16 (84)	0.84	Chi square test
PaO <sub>2</sub> /FiO <sub>2</sub> <300	30 (97)	16 (84)	0.11	Chi square test

VAP, ventilator-associated pneumonia; WBC, white blood cells; PaO<sub>2</sub>, partial pressure of arterial oxygen; FiO<sub>2</sub>, fraction of inspired oxygen.

**Table 3.** Microbiological data from positive endotracheal aspirate specimens.

Pathogens positive of ET aspirate (n=31)	Number (%)
Gram-negative bacteria	30 (96)
<i>Acinetobacter baumannii</i>	19 (61)
<i>Klebsiella pneumoniae</i>	5 (16)
<i>Pseudomonas aeruginosa</i>	5 (16)
<i>Escherichia coli</i>	1 (3)
Gram-positive bacteria	1 (3)
MRSA	1 (3)

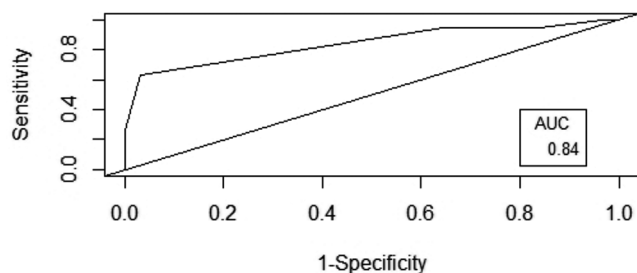
ET, endotracheal aspirate; MRSA, methicillin resistant *Staphylococcus Aureus*.

**Table 4.** Diagnostic performance of laboratory parameters and lung ultrasound in the diagnosis of ventilator-associated pneumonia.

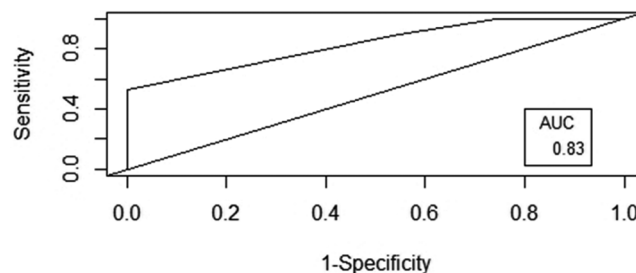
Variable	No. of patients	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV (95% CI)	NPV (95% CI)	LR (+) (95% CI)	LR (-) (95% CI)	Odds ratio (95% CI)
<b>Diagnostic performance of tracheal aspiration, laboratory and procalcitonin in diagnosis of ventilator-associated pneumonia</b>								
Purulent secretions	44	90.32 (74.3-97.9)	15.8 (3.4-39.6)	63.64 (58.3-68.7)	50 (18.32-81.7)	1.1 (0.86-1.34)	0.61 (0.14-2.73)	1.8 (0.3-9.7)
Positive endotracheal aspirate gram stain	32	87.1 (70.2-96.4)	73.7 (48.8-90.1)	84.4 (71.5-92.1)	77.8 (57.4-90.1)	3.3 (1.54-7.1)	0.18 (0.07-0.45)	18.9 (4.4-81.8)
PCT≥0.5 ng/ml	45	87.1 (70.2-96.4)	5.3 (0.13-26.03)	60 (55.8-64.1)	20 (2.9-67.5)	0.92 (0.8-1.1)	2.5 (0.3-20.34)	1.3 (0.04-3.6)
<b>Diagnostic performance of lung ultrasound signs in diagnosis of ventilator-associated pneumonia</b>								
Lobar/hemilobar consolidations	16	25.8 (11.9-44.6)	57.9 (32.5-79.8)	50 (31.1-68.9)	32.4 (23.6-42.5)	0.61 (0.28-1.36)	1.28 (0.83-1.98)	0.47 (0.14-1.61)
Subpleural consolidations ≥1	45	100 (88.78-100)	26.32 (9.2-51.2)	68.9 (62.9-74.3)	100	1.36 (1.04-1.78)	0	23.9 (1.24-26.2)
Subpleural consolidations ≥2	37	96.8 (88.3-99.9)	63.2 (38.4-83.7)	81.1 (70.3-88.6)	92.3 (62.9-98.8)	2.63 (1.5-4.8)	0.05 (0.01-0.36)	51.43 (5.7-464)
Dynamic linear air bronchograms ≥1	14	29.3 (14.2-48)	73.7 (48.8-90.9)	64.3 (41.5-82)	38.9 (30.9-47.5)	1.1 (0.43-2.8)	0.96 (0.7-1.4)	1.14 (0.32-4.2)
Clinical lung ultrasound score (lung ultrasound) ≥2	40	100 (88.8-100)	52.6 (28.9-75.6)	77.5 (68.2-84.9)	100	2.11 (1.3-3.4)	0	69.3 (3.7-1301.9)

CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value; L, likelihood ratio; PCT, procalcitonin.





**Figure 1.** Receiver operating characteristic (ROC) curve of subpleural consolidation with ventilator-associated pneumonia (VAP). AUC, area under the curve.



**Figure 2.** Receiver operating characteristic (ROC) curve of clinical lung ultrasound (LUS) score with ventilator-associated pneumonia (VAP). AUC, area under the curve.

## Discussion

The overall incidence of VAP in our study population was 62%. Another prospective study by Ranjan *et al.* from the Indian subcontinent also showed a higher incidence of VAP (57%) [7]. Gram-negative organisms were the predominant microbiological flora from ETA culture (96%), with *Acinetobacter baumannii* being the commonest organism isolated. Similar bacteriological yield was seen in other Indian studies [7,8]. Higher incidence of gram-negative bacterial flora can be attributed to late onset VAP in our study population (mean duration 7.58 days).

Lung consolidations are characterized by a tissue-like echotexture similar to liver parenchyma on LUS. The fact that LUS is highly sensitive and specific in diagnosing consolidation is supported by various studies [9,10]. Equal diagnostic efficacy is seen in ventilated ICU patients. However, there are numerous other causes of consolidation pattern in LUS, like atelectasis, contusion, and ARDS, *etc.* [9,10]. Hence, lung consolidation is not specific for VAP. This can be clearly seen in our results with low sensitivity and specificity of lobar consolidations.

Hyperechoic punctiform linear streaks within consolidation during inspiration, known as dynamic air bronchograms representing air-filled bronchi, are considered more specific for VAP. Our study showed a specificity of 74%, which was almost similar to the pioneer study by Mongodi *et al.* (81%) [5]. Lichtenstein *et al.* assessed dynamic air bronchogram in mechanically ventilated patients with pneumonia or atelectasis and reported a sensitivity of 61% and a specificity of 95% in diagnosing pneumonia [11]. In our study, in contrast to the study by Lichtenstein *et al.*, the positive predictive value of the ultrasound sign of dynamic air bronchogram was lower with respect to >2 subpleural consolidations (64% vs. 81%, respectively). This can be explained by the fact that the prevalence of dynamic air bronchogram in our study was quite lower than that of subpleural consolidation. Lower prevalence might have decreased the positive predictive value of the dynamic air bronchogram sign. In a study where around a quarter of patients are post-surgical, mucous plugging and parenchymal contusions are quite common, which can lead to a lower prevalence of dynamic air bronchogram. About 20% of the lung surface is not visualized by LUS due to anatomical structures like the clavicle and scapula [12]. The efficiency of LUS in VAP is also influenced by the lesion and the lung surface. LUS is not efficient in detecting small consolidations <20mm and away from the pleura [13]. These

factors might have also contributed to the lower prevalence of dynamic bronchogram in our study.

In the formulation of the recently minted Clinical Pulmonary Infection Score (CPIS), along with clinical parameters like fever, leucocytosis, and microbiological parameters like ETA culture and gram stain, chest X-ray identification of new infiltrates forms an important component. A recent meta-analysis has shown that any new infiltrate on the chest radiography as a predictor of VAP has a specificity of only 26% [14]. Pulmonary embolism, pulmonary edema, atelectasis, and pleural effusion are some of the many differentials that a clinician is faced with while decoding an opacity on the chest X-ray. CPIS>6 is supposed to predict VAP but was found to have a low specificity of 66% in the same meta-analysis [14]. In another meta-analysis looking at the role of LUS in the diagnosis of VAP, a pooled specificity of 85% and a negative likelihood ratio of 0.05 were found [15]. We believe that incorporating LUS in place of chest X-rays in VAP prediction scores will increase the diagnostic accuracy.

Apart from chest X-ray, CT thorax is a very sensitive technique to assess VAP, but it also has drawbacks. CT is not a daily repeatable test and hence cannot be used as a daily screening method in the ICU. LUS becomes an important alternative by virtue of being carried out bedside, with no radiation exposure, cheap and accurate in diagnosing VAP and its complications, like parapneumonic effusion, loculations, or empyema.

Local architectural destruction like fibrosis, honeycombing, or associated lung malignancy can sometimes alter the ultrasound imaging, leading to false positive detection of air bronchograms or consolidations. To remove this, confounding, purulent endotracheal secretions were added to increase the specificity of the score in predicting VAP. This is a trade-off because, in certain clinical conditions like tracheobronchitis, patients can have purulent secretions without VAP. Clinical-LUS score (VPLUS), which is a combination of LUS findings with a simple clinical criterion (purulent secretions), requires less expertise and produced specificity and sensitivity (around 70%) in the study by Mongodi *et al.* [5]. Our study showed a much higher sensitivity (100%) with a specificity of 53%. Low specificity in our study can be due to the higher prevalence of purulent secretions (84%) in patients without VAP. These patients were already on antibiotics at the time of clinical suspicion, which might have led to culture negativity. Secondly, the growth of colonies after culture did not cross the threshold for pathogenicity due to antibiotic exposure. However, the AUC of the LUS score in our study and the study by Mongodi *et al.* were similar (both 0.83).



## Conclusions

In patients suspected of VAP, LUS can be helpful for early diagnosis. A linear/arborescent air-bronchogram or subpleural consolidation confirms the diagnosis of VAP. In experienced hands, a normal LUS rules out the diagnosis of VAP. The appearance of ultrasound signs of VAP could be assessed with daily ultrasound monitoring even in the absence of signs and symptoms. However, daily monitoring with different operators might influence the results of the LUS. Further clinical studies are needed to understand whether this new approach that integrates LUS with culture examination on bronchial aspirate leads to an appropriate and timely prescription of antibiotics and prevents the broad use of antibiotics in patients who do not develop VAP, thus helping to limit resistance. We would emphasize that LUS, in expert hands, has a potential role in the diagnosis of VAP, but the presence of pulmonary fibrosis and post-tuberculosis sequelae could influence the clinical considerations based on LUS. Adequate training and expertise in LUS are fundamental to monitoring VAP.

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Availability of data and materials: raw data with an excel sheet will be made available upon request.

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