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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 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 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. 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.

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 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 of 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 lack of universal agreement in terms of diagnostic criteria and optimal method for obtaining specimens for microbiological culture [3]. This intricateness is primarily due to huge diversity of pathologies which can cause radiological infiltrates . The high frequency of bacterial colonization in proximal respiratory tract of ventilated patients also add to this complexity [4]. Early accurate diagnosis is important in achieving favorable outcome without compromising the risk of antibiotic resistance. Investigators have proposed several criteria for diagnosing VAP in clinical settings which included 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 development of VAP with increasing degrees of loss of aeration. In a multicentre 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 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

To study the utility of chest ultrasound in diagnosis of ventilator associated pneumonia in critical care unit.

Study design

Prospective time bound observational study

Study participants

All consecutive patients mechanically ventilated in adult intensive care unit 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 ventilator associated pneumonia 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 h, with newly appeared/evolving CXR infiltrate, and two or more of the following clinical criteria:

1. Temperature more than or equal to 38.5 degree C or hypothermia (< 36.5 degree C)
2. Leucocytosis > 10^4/mL, or leukopenia < 4 x10^3/mL
3. Purulent tracheal secretions
4. PaO2/FIO2 < 300 mm Hg.

Final diagnosis of VAP was made when ETA or Bronchoalveolar lavage(BAL) culture was positive with a threshold of >10^5 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 in the inclusion criteria within the study period were planned to be included. Because of the restrictions due to 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 predesigned, 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 ventilator associated pneumonia (satisfying exclusion criteria) were included in the study.

On clinical suspicion of VAP, patients were subjected to ultrasound chest (lung) and endotracheal aspirate for gram stain and aerobic culture were sent within 6 hours. Ultrasonography of chest was performed by Sonosite M turbo ultrasound systems. A curvilinear low frequency probe (2–5 MHz) was used for LUS.

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

The following ultrasound findings were noted in each area.

1. Small subpleural consolidations (echo-poor regions >0.5cm in diameter).
2. 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 three year super speciality training in our institute , the resident underwent a 2 week training in the radiology department . He was trained in performing lung ultrasound and reading CT Thorax scans.

We calculated clinical-LUS score (ventilator-associated pneumonia lung ultrasound score [VPLUS]) as per the LUS findings which is a combination of ultrasound signs and purulent endotracheal aspirate.

2 areas with subpleural consolidations - 1 point;

1 area with dynamic arborescent/linear air bronchogram- 2 points

purulent EA- 1 point.

Endotracheal aspirate was collected through a single lumen sterile catheter passed through endotracheal/ tracheostomy tube. Bronchsocopy was done if clinically indicated and lavage taken. Samples were sent for gram stain and aerobic culture. Patients were subjected to antibiotic modification as per 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 was expressed in means and standard deviation, median and interquartile range (IQR). Statistical tests including Chi square test, t test for means, t test for proportions for quantitative data. For non-parametric data, Mann Whitney test was used. Diagnostic performance of risk factors for VAP were analyzed by parameters like Sensitivity, Specificity, Positive predictive value, Negative predictive value, Likelihood ratio (positive and negative). ROC curve analysis was also done and Area under curve (AUC) values for each parameters calculated. 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 $\pm$ standard deviation of patients in our study was 56.76 $\pm$ 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 that of PaO2/FiO2<300 and purulent tracheal secretions. This data is shown in Table 2. The microbiological yield in patients with VAP are shown in Table 3. Acinetobacter spp ,Klebsiella and Pseudomonas spp were the commonest organism in VAP patients.

Diagnostic performance of laboratory parameters and LUS score were studied in 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 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.

Discussion

Overall incidence of VAP in our study population was 62%. Another prospective study by Ranjan et al from Indian subcontinent also showed a higher incidence of VAP (57%) [7].Gram negative organisms were the predominant microbiological flora from endotracheal aspirate culture (96%) with Acinetobacter baumanii 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 lung ultrasound 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 ventilator associated pneumonia. 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 S et al. (81%) [5]. Lichtenstein et al assessed dynamic air bronchogram in mechanically ventilated patients with pneumonia or atelectasis and reported sensitivity of 61% and specificity of 95% in diagnosing pneumonia [11]. In our study in contrast to the study by Lichenstein et al, the positive predictive value of the ultrasound sign of dynamic air bronchogram was lower with respect to >2 subpleural consolidations (64% v/s 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 lower prevalence of dynamic air bronchogram. About 20% of lung surface is not visualized by LUS due to anatomical structures like clavicle and scapula [12]. Efficiency of LUS in VAP is also influenced by the lesion and lung surface. LUS is not efficient in detecting small consolidations < 20mm and away from the pleura [13]. These factors might have also contributed to 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 form 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 oedema , atelectasis , 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 diagnosis of VAP , found a pooled specificity of 85% and negative likelihood ratio of 0.05 [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 . Lung ultrasound becomes an important alternative by the virtue of being carried out bedside , 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 finding with a simple clinical criterion (purulent secretions) require less expertise and produced specificity and sensitivity (around 70%) in the study by Mongodi S 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 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 LUS score in our study and the study by Mongodi et al were similar (both 0.83).

Conclusions

In patients suspected of ventilator associated pneumonia, 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 is fundamental to monitor VAP.

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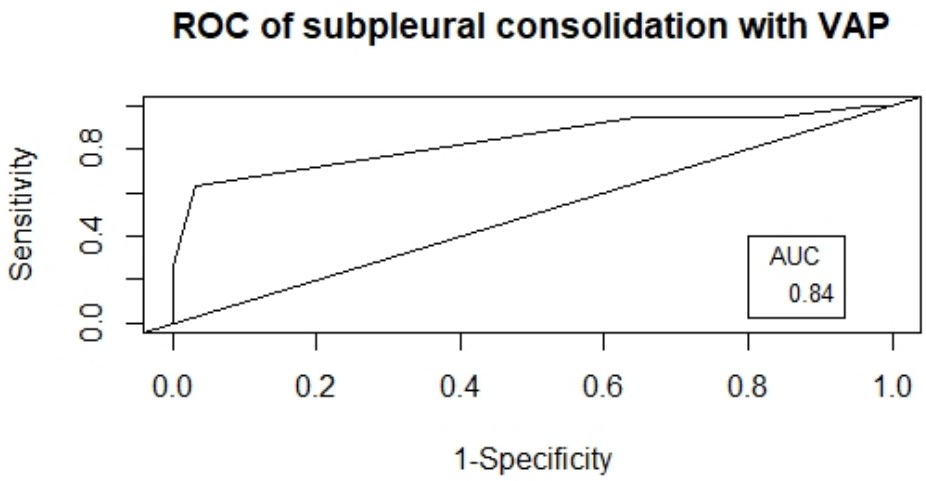

Figure 1. ROC of subpleural consolidation with VAP.

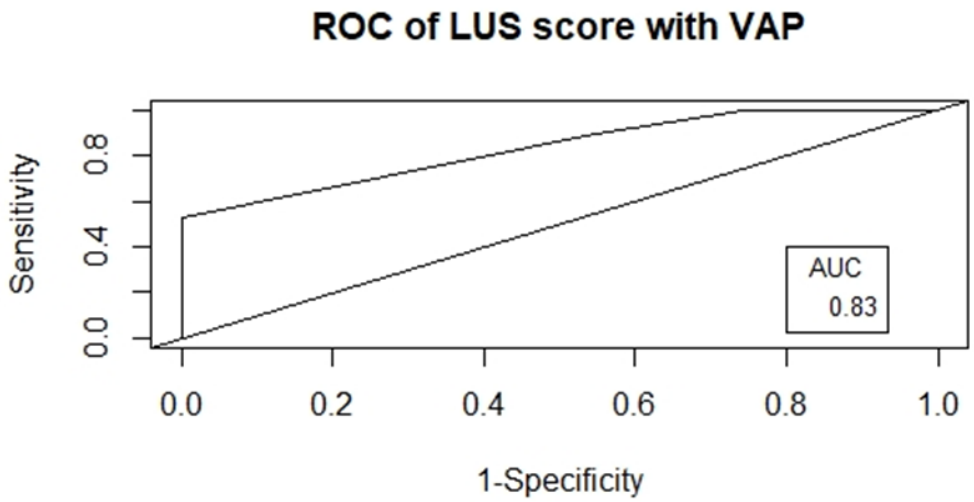

Figure 2. ROC of Clinical-LUS score with VAP.

Table 1. Clinical characteristics in study population.

Characteristic	VAP (n=31)	Non-VAP (n=19)	p-value	Statistical test used
Age (years), mean±SD	56.9±17.6	56.5±18.1	0.93	t test for means
Male	24(77%)	11(57%)	0.14	Chi square
Female	7(22%)	8(42%)		
Comorbidities				
Systemic hypertension	10(32%)	6(31%)	0.48	Chi square
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				
Medical	22 (70%)	15 (79%)	0.53	Chi square
Post-surgical	9 (30%)	4 (21%)		

Table 2. VAP suspicion criteria in the study population.

VAP suspicion criteria	VAP n=31 (%)	Non-VAP n=19 (%)	p-value	Test used
Temperature (degree Celsius) 38.5 or <36.5	6 (19%)	2(10%)	0.41	Fishers exact test
WBC count >10^4/mL or <$4x10^3$/mL	26(84%)	12(63%)	0.1	Chi square test
Purulent tracheal secretions	28(90%)	16(84%)	0.84	Chi square test
Pao2/Fio2 <300	30(97%)	16(84%)	0.11	Chi square test

Table 3. Microbiological data from positive endotracheal aspirate specimens.

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

Table 4. Diagnostic performance of laboratory parameters and LUS in the diagnosis of VAP.

Diagnostic performance of tracheal aspiration, laboratory and procalcitonin in diagnosis of VAP								
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)
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 $\geq$0.5ng/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)
Diagnostic performance of LUS signs in diagnosis of VAP								
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 $\geq$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 $\geq$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 $\geq$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 (LUS) 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)