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# Clinical impact of pulmonary sampling site in the diagnosis of ventilator-associated pneumonia: A prospective study using bronchoscopic bronchoalveolar lavage☆

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ABSTRACT

*Purpose:* It is unclear whether ventilator-associated pneumonia (VAP) is actually a bilateral and multifocal process. In addition, the diagnostic role of chest x-ray is under debate. Assuming a low microbiologic concordance between the left and right lungs, the reliability of a single pulmonary sampling becomes questionable. The purpose of this study was to determine whether the choice of the pulmonary sampling area is clinically relevant in the management of VAP.

*Methods:* In 79 patients admitted to a university general intensive care unit with clinically suspected VAP, right- and left-lung bronchoalveolar lavage (BAL) samples were taken with separate bronchoscopes and quantitatively cultured. Primary end-point variable was microbiologic concordance rate between right- and left-lung BAL cultures. Secondary outcomes included predictors of microbiologic concordance, rates of appropriate antibiotic treatment, and diagnostic accuracy of chest x-ray.

*Results:* BAL cultures were bilaterally negative in 21 (27%) of 79 patients, bilaterally positive in 36 (46%), and unilaterally positive (right in 12, left in 10) in 22 (28%). Intra-patient concordance was observed in 47 (59.5%) of 79 cases and independently associated with purulent secretions and bilateral infiltrates on chest x-ray. In simulated prescribing experiments, treatments chosen based on right or left cultures alone were as appropriate as those based on bilateral data in >90% of cases. The presence of a radiographic infiltrate in the sampling area predicted BAL culture positivity with a positive predictive value of only 61%.

*Conclusions:* In patients with clinically suspected VAP (especially those without purulent secretions or without radiographically documented bilateral infiltrates), quantitative culture of a single BAL sample may provide an incomplete assessment of lung microbiology, without having a relevant impact on the appropriateness of antimicrobial treatment. These findings suggest that single sampling of respiratory secretions, regardless radiographic opacity, seems to be a reliable diagnostic method in the management of VAP.



## 1. Introduction

Bronchoscopic sampling of lower respiratory tract secretions is widely used in intensive care units (ICUs) for the microbiologic diagnosis of ventilator-associated pneumonia (VAP). In addition, blind sampling with telescopic catheters is frequently used, but there is no guarantee that the material collected originates in the injured lung segments.

In guided procedures, the material for culture is generally collected at the site characterized by the most obvious infiltrate on chest radiography or the segment in which purulent secretions are encountered during bronchoscopy [1]. However, findings on portable anteroposterior chest x-ray have displayed limited accuracy in predicting the presence of VAP [2]. Additionally, post-mortem histologic studies have shown that VAP is often bilateral and multifocal, even when localized infiltrates are

*Abbreviations:* BAL, bronchoalveolar lavage; CFU, colony forming units; ICU, intensive care unit; VAP, ventilator-associated pneumonia.

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seen on thoracic imaging [3,4]. Consequently, the lung segment sampled would not be expected to play any major role in the microbiologic diagnosis of VAP. On this point, it is essential to note that postmortem histologic data are limited because they are likely to be more representative of terminally ill patients with VAP, where the possibility of a diffuse infectious process is higher. Therefore, while bilateral, diffuse pneumonia may well be common in this subset of patients, the presence of more localized lung involvement cannot be excluded in other types of patients.

In the presence of pneumonia, microbiologic concordance between the left and right lungs is crucial. If concordance is low, the reliability of a single pulmonary sampling becomes questionable.

When the bacterial distribution in the right and left lungs of VAP patients has been investigated using bronchoscopic sampling techniques [5–9], rates of microbiological concordance between the two specimens have varied widely (from 53% to 92%). The factors potentially associated with concordant culture yields have never been explored, and it is unclear whether choosing the pulmonary sampling site may affect the appropriateness of antibiotic treatment prescribed for patients with suspected VAP.

To address these questions, we conducted a prospective observational study of 79 patients with suspected VAP. Each underwent bilateral standardized bronchoscopic BAL performed with two different fiberoptic bronchoscopes, and samples were subjected to quantitative culture for bacteria.

The primary objective of the study was to assess the frequency of microbiologic concordance between the right- and left-lung samples. Secondary end-points included factors associated with such concordance, the suitability of treatments prescribed based on unilateral vs both lung BAL cultures, and the diagnostic accuracy of chest x-ray in the management of VAP.

## 2. Methods

### 2.1. Study design and patient selection

This prospective study was conducted in the 18-bed general ICU of the Agostino Gemelli University Hospital in Rome, Italy, between 1 February 2013 and 31 July 2014. The protocol was preapproved by the Ethical Committee of Università Cattolica del Sacro Cuore, and written informed consent was obtained from all enrolled patients or their next of kin.

Enrollment was open to all patients ≥18 years of age who developed clinical signs of pneumonia after 48 hours or more of invasive mechanical ventilation. Pneumonia was suspected when the simplified Clinical Pulmonary Infectious Score (CPIS) [10] exceeded 6 or when chest radiographs revealed a new or progressive pulmonary infiltrate in a patient with at least 2 of the following: purulent respiratory secretions, temperature >38°C or <36°C, white blood cell count >12,000/$mm^3$ or <4000/$mm^3$ [11,12]. Exclusion criteria were: age <18 years; pregnancy; absence of informed consent; an arterial oxygen partial pressure to inspired oxygen fraction ratio ($Pao_2$:$Fio_2$) of ≤150; use of positive end-expiratory pressure (PEEP) >10 cm $H_2O$; active uncontrolled bronchospasm; unstable angina or recent (<6 weeks) myocardial infarction; unstable arrhythmia; intracranial hypertension; platelet count ≤20,000/$mm^3$; international normalized ratio or activated partial thromboplastin time (aPTT) ratio >1.5; or documented treatment-limitation orders in the patient's chart. In all enrolled patients, right and left-lung BAL samples were obtained with separate bronchoscopes and quantitatively cultured.

### 2.2. Fiberoptic bronchoscopy

Procedures were performed by two experienced endoscopists (GB and FDM) in strict accordance with consensus guidelines [1]. Before the examination, the portable chest radiograph was reviewed by the endoscopist. The left or right lung (randomly selected) was then examined with a flexible fiberoptic bronchoscope (4.9 mm BF-PE2; Olympus, Tokyo, Japan). After thorough tracheobronchial suctioning with a conventional suction catheter, the bronchoscope was inserted through the endotracheal tube (internal diameter ≥8 mm) via a sterile connector. If localized infiltrates were present on the chest radiograph, the tip of the scope was wedged into a subsegment of the area displaying the most marked opacity. In the presence of diffuse opacity or when no clear roentgenographic abnormalities were observed, the tip was positioned in the lingula or right middle lobe. Five 20-mL aliquots of sterile normal saline were then injected and reaspirated with a syringe. The first aliquot was discarded, and the remaining BAL fluid was pooled for microbiological analysis. Bronchoscopy was then repeated in the same manner in the contralateral lung with a second, sterile

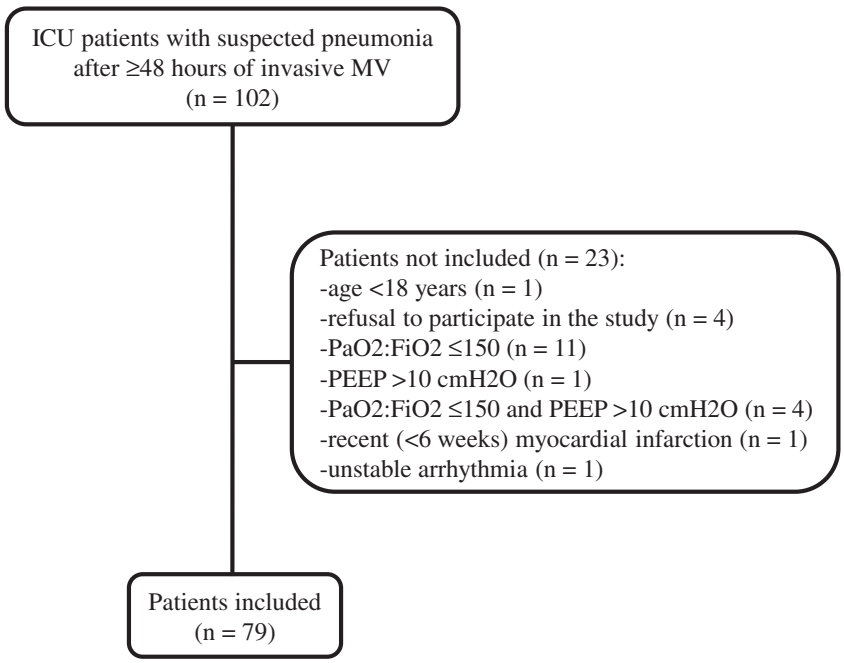


**Fig. 1.** Patient selection flow diagram. MV, mechanical ventilation; $Pao_2$:$Fio_2$, ratio of arterial oxygen partial pressure to inspired oxygen fraction; PEEP, positive end-expiratory pressure.