Epidemiology of Ventilator-Associated Pneumonia*

Donald E. Craven, MD, FCCP

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Abbreviations: MDR = multidrug-resistant; MRSA = methicillin-resistant Staphylococcus aureus; VAP = ventilator-associated pneumonia

Despite remarkable progress in our understanding of ventilator-associated pneumonia (VAP) over the past decade, controversy persists over the optimal method of diagnosis. Accurate diagnosis is critical for identifying specific etiologic agents, for implementing appropriate therapy, and for prevention strategies.

Currently, there is no well-accepted “gold standard” for diagnosis, but, rather, there is a variety of diagnostic procedures with variable sensitivity and specificity. Bronchoscopy with the use of BAL or a protected-specimen brush has greater specificity than a clinical diagnosis, which has been used more commonly over the past decade. Nonbronchoscopic methods, such as blinded BAL or quantitative endotracheal aspiration, with and without the clinical pulmonary infection score, are more specific than clinical diagnosis. Regardless of the diagnostic method used, the American Thoracic Society Consensus Group suggested empirical initial therapy, based on the severity of the patient’s disease and the stage of onset, using antibiotics to cover specific pathogens in patients with specific risk factors.

To date, no study has demonstrated the superiority of a specific diagnostic method in terms of better patient outcomes, reduced hospital costs, or a lower incidence of complications, such as fewer infections with multidrug-resistant (MDR) nosocomial pathogens. With the evolution of managed care and health-care cost-containment efforts in the United States, it is important to examine the benefits, risks, and costs of each diagnostic procedure and to measure effectiveness in terms of outcomes rather than in terms of sensitivity and specificity. Outcomes include morbidity and mortality, total hospital costs, total days receiving mechanical ventilation, and duration of stay in the hospital or ICU. Other important considerations include the amount and duration of antibiotic therapy and the effect of such therapy on the emergence of MDR pathogens.

This section uses evidence-based techniques to summarize the current literature on the diagnosis of VAP caused by bacterial pathogens, excluding Legionella pneumophila. These data emphasize the limitations of existing knowledge and underscore the need for future diagnostic studies comparing critical outcomes rather than the sensitivity and specificity of diagnostic methods.

Bacterial Pathogens Associated With VAP

The etiology of VAP varies by the method of diagnosis and patient population studied. Nosocomial pathogens may be part of the host’s endogenous flora, or may be acquired from other patients, staff, devices, or the hospital environment.

Conceptually, VAP can be divided into early-onset and late-onset disease. Early-onset VAP occurs during the first 4 days that the patient receives mechanical ventilation and is often caused by Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, or, uncommonly, anaerobes. By comparison, late-onset VAP, occurring >4 days after admission, is more commonly caused by Pseudomonas aeruginosa, Acinetobacter or Enterobacter spp, or methicillin-resistant Staphylococcus aureus (MRSA).

Many aerobic Gram-negative bacilli, such as P aeruginosa, Acinetobacter spp, and S aureus, are resistant to many antibiotics or have MDR strains. S aureus is isolated in approximately 20 to 40% of cases and is particularly common in persons taking drugs by injection, in patients with neurologic disease, thermal injury, or wound infection, and in patients who have received prior antibiotic therapy or have had a prolonged stay in the ICU. Compared to patients with VAP caused by methicillin-sensitive S aureus, those in whom the causative agent is MRSA are often older and are significantly more likely to have had previous chronic lung disease, antibiotic therapy, steroid therapy, and >6 days of mechanical ventilation. Bacteremia, shock, and mortality are usually higher in the MRSA group.

In most patients, VAP is caused by multiple organisms. Aerobic Gram-negative bacilli, including Escherichia coli, Klebsiella pneumoniae, Enterobacter spp, Serratia spp, P aeruginosa, and Acinetobacter spp, are most frequently isolated, particularly in patients with late-onset disease or a serious underlying disease. VAP caused by L pneumophila is not discussed in this report.

Epidemiology

Rates of pneumonia are increased 6- to 21-fold for intubated patients and show a further rise with the duration of mechanical ventilation. The incidence of VAP ranges from 6 to 52 cases per 100 patients, depending on the population studied. Rates of VAP are usually 1 to 3% per day of intubation and mechanical ventilation. Rates per 1,000 ventilator days provide the best comparison. In the National Nosocomial Infections Study, rates of VAP varied from 5 cases per 1,000 days in pediatric patients to 35 cases per 1,000 days in patients with thermal injury. Overall rates are most commonly 10 to 15 cases per 1,000 ventilator days for ICU patients, depending on the population studied. Also, rates are generally higher in surgical ICU patients than in medical ICU patients.

Mortality

In the ICU, the risk of mortality appears to be 2- to 10-fold higher in patients with nosocomial pneumonia.
than in those without. In a case-control study of 200 patients who died in the hospital, nosocomial pneumonia was a contributing factor in 60% of patients with infection-related mortality. In addition, a review of 1,000 autopsy reports showed that pneumonia was associated with 7.5% of the deaths and was the most common nosocomial infection contributing to death.

Crude mortality rates are generally higher in patients with VAP than in those without. Mortality rates in patients with VAP due to *P. aeruginosa*, to bacterial strains resistant to many drugs, or with secondary bacteremia often have significantly higher rates of bacteremia than patients without these risk factors.58,64,74,76–79

In contrast to crude mortality rates, the mortality rate attributable to VAP (or “attributable mortality”), using a case-control methodology, was 27%. The mortality rate increased to 45% when the causative agent was *P. aeruginosa* or *Acinetobacter* spp.6 Lower rates have been reported in selected populations of patients and the selection of “controls.”80,81

## Costs

Several investigators have reported that nosocomial pneumonia increased the duration of hospitalization two- to threefold compared to patients without pneumonia.4,64,76,82 Fagon and coworkers6 found the mean length of stay was 34 days for patients with VAP and 21 days for matched ventilator-assisted patients without VAP.7 Although more specific data are needed, hospital costs are dramatically increased in survivors of nosocomial pneumonia.

## Summary

In summary, the method of diagnosis used for VAP accounts for reported differences in etiology, pathogenesis, and outcomes. Further studies are needed to assess outcomes related to various diagnostic methods rather than to assess the sensitivity and specificity of these methods.