

# Invasive diagnosis for ventilator-associated pneumonia reduced 14-day mortality and antibiotic use

Fagon J-Y, Chastre J, Wolff M, et al., for the VAP Trial Group. Invasive and noninvasive strategies for management of suspected ventilator-associated pneumonia. A randomized trial. *Ann Intern Med*. 2000 Apr 18;132:621-30.

## QUESTION

In patients in the intensive care unit (ICU) who are suspected of having ventilator-associated pneumonia (VAP), is an invasive diagnostic strategy more effective than a clinical, noninvasive strategy for improving clinical outcomes?

## DESIGN

Randomized {allocation concealed\*}†, blinded {statisticians}†, \* controlled trial with 28-day follow-up.

## SETTING

31 ICUs in France.

## PATIENTS

413 patients (mean age 63 y, 70% men) in the ICU who had received  $\geq 48$  hours of mechanical ventilation and were clinically suspected of having VAP. Exclusion criteria were pregnancy, enrollment in another study, low likelihood of survival, or introduction or modification of antibiotic therapy in the 3 days before collection of respiratory samples. Follow-up was complete.

## INTERVENTION

Patients were allocated to a clinical-management strategy ( $n = 209$ ) or to an invasive-management strategy ( $n = 204$ ). Clinical management involved clinical evaluation, examination of Gram-stained endotracheal aspirates, and adherence to the American

Thoracic Society (ATS) guideline recommendations for choosing antibiotics. Invasive management involved fiberoptic bronchoscopy to obtain protected specimen-brush samples or bronchoalveolar lavage samples to guide treatment.

## MAIN OUTCOME MEASURES

All-cause mortality, antibiotic use, and organ failure at 14 days. Secondary outcomes were the same end points at 28 days.

## MAIN RESULTS

Analysis was by intention to treat. At 14 days, fewer patients who had received invasive management died than did those who received clinical management ( $P = 0.022$ ) (Table). Patients in the invasive-management group also had more antibiotic-free days and took fewer antibiotics per day ( $P < 0.001$  for both) (Table). The groups did not differ for organ failure ( $P > 0.2$ ). At 28 days, differences between groups

remained for antibiotic-free days and number of antibiotics per day ( $P < 0.001$  for both). After multivariate analysis that controlled for variables known to affect mortality was done, a survival benefit was shown in the invasive management group.

## CONCLUSION

In patients in the intensive care unit who are suspected of having ventilator-associated pneumonia, an invasive strategy was effective for reducing death and antibiotic use.

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*For correspondence:* Dr. J.-Y. Fagon, Service de Réanimation Médicale, Hôpital Européen Georges Pompidou, 20 rue Leblanc, 75015 Paris, France. FAX 33-156093202. ■

\*See Glossary.

†Information provided by author.

## Invasive vs clinical management for intensive-care-unit patients with suspected ventilator-associated pneumonia at 14 days‡

Outcomes	Invasive management	Clinical management	RRR (95% CI)	NNT (CI)
Mortality	16%	26%	37% (8.2 to 58)	11 (6 to 56)
			<b>Difference (CI)</b>	
Mean antibiotic-free d	5.0	2.2	2.8 (1.9 to 3.6)	
Mean antibiotics/d	1.2	1.5	0.3 (0.2 to 0.5)	

‡Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

## COMMENTARY

This excellent, landmark trial by Fagon and colleagues is the first with adequate power to answer the question, Does the method used to diagnose VAP affect outcome? This question has been hotly debated in critical care medicine. The finding that patients who were investigated for VAP with invasive measures had improved survival forces many of us to stop and rethink our approach to patients with suspected VAP.

Although this study is internally valid, how generalizable are its findings? To expect to achieve similar benefit, one must practice in a similar environment. Physicians skilled in bronchoscopy must be available once clinical suspicion arises. Similarly, skilled technicians and appropriate laboratory facilities must also be available. Can we expect a similar survival advantage in ICUs with such lower levels of multiresistant bacteria as have been found in many ICUs in Europe?

Part of the survival benefit may be because fewer patients in the invasive-strategy group were treated with inappropriate antibiotics

(resistant organisms) than were those in the clinical-management group. It is tempting to wonder whether the responsibility for this imbalance lies with the reliance on the ATS guidelines for antibiotic selection in the clinical-management group. Perhaps the use of North American guidelines for antibiotic selection is inappropriate in some European ICUs, and the physicians who practice in these centers, if allowed to choose antibiotic coverage, may select agents that cover multiresistant organisms.

Despite these concerns, it is worth considering the adoption of an invasive strategy to diagnose VAP. It would be useful to see a similarly designed North American study to ensure that these results can be replicated on this side of the Atlantic Ocean.

Sean P. Keenan, MD  
Royal Columbian Hospital  
New Westminster, British Columbia, Canada