Invasive approaches to the diagnosis of ventilator-associated pneumonia: a meta-analysis
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CRD summary
This review found that invasive strategies for the diagnosis of ventilator-associated pneumonia did not affect mortality, but did result in changes to the prescribing of antibiotics. This was generally a well-conducted review and these conclusions are likely to be reliable.

Authors' objectives
To investigate whether invasive testing of patients with ventilator-associated pneumonia (VAP) affects antibiotic management and mortality.

Searching
MEDLINE (1966 to December 2003), EMBASE (1990 to December 2003) and the Cochrane Library were searched; key terms were reported. Abstracts from relevant conferences were handsearched, reference lists of retrieved studies screened, and experts in the area contacted to identify additional relevant studies. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and prospective observational studies were eligible for inclusion.

Specific interventions included in the review
Studies of invasive testing for the diagnosis of VAP were eligible for inclusion. The specific interventions evaluated by the included studies were protected specimen brush, with or without bronchoalveolar lavage, or mini-bronchoalveolar lavage.

Reference standard test against which the new test was compared
The review did not include any diagnostic accuracy studies that compared the performance of the index test with a reference standard of diagnosis.

Participants included in the review
Studies that evaluated patients for possible VAP were eligible for inclusion. Studies that included patients who underwent testing for the diagnosis of severe community-acquired pneumonia requiring mechanical ventilation were excluded. VAP was confirmed bronchoscopically in 44 to 69% of patients, Acute Physiology and Chronic Health Evaluation (APACHE) scores ranged from 15 to 46, and the duration of mechanical ventilation prior to enrolment ranged from 6 to 11 days.

Outcomes assessed in the review
Studies had to report data on the impact of testing on mortality in patients with VAP and on antibiotic prescribing to be included in the review. Mortality was the primary outcome; antibiotic management was the secondary outcome.

How were decisions on the relevance of primary studies made?
Two reviewers independently screened studies for inclusion in the review.

Assessment of study quality
Two reviewers independently assessed the methodological quality of included RCTs using the Jadad scale, which assigns studies a score of 0 to 5 according to how many of the five items they fulfil. The quality of the observational studies was not assessed.

Data extraction
Two reviewers independently extracted the data from the included studies. Changes in antibiotic management as a result of testing were considered to be either the addition or discontinuation of any anti-infective. Odds ratios (ORs), together
with 95% confidence intervals (CIs), were calculated for each individual study to quantify the effect of invasive testing on mortality and antibiotic prescribing.

**Methods of synthesis**

How were the studies combined?

ORs from RCTs were pooled using random-effects models. The data from observational studies were not pooled for mortality, but were pooled separately to investigate the effects of invasive testing on antibiotic prescribing. Publication bias was assessed through visual examination of a funnel plot and using Begg’s test.

How were differences between studies investigated?

Heterogeneity was investigated visually using Galbraith plots and assessed statistically using the Q statistic.

**Results of the review**

Four RCTs (n=628) and 5 prospective observational studies (n=635) were included.

The median Jadad score was 5 (range not reported). None of the trials was blinded. Only one of the observational studies included a control arm. There was no evidence of publication bias.

Mortality (4 RCTs).

Mortality ranged from 22 to 46% in patients randomised to receive invasive testing, and from 21 to 46% in patients randomised to noninvasive strategies. The ORs for the association of invasive testing with mortality ranged from 0.71 to 2.42; none of these showed a statistically significant association (p>0.05). The pooled OR was 0.89 (95% CI: 0.56, 1.41, p=0.62), suggesting no effect of invasive testing on mortality. There was no statistical evidence of heterogeneity (p=0.247).

Antibiotic management (3 RCTs, 5 observational studies).

All RCTs showed that antibiotics were more likely to be changed in patients who underwent invasive diagnostic testing than in those who underwent noninvasive strategies. The ORs ranged from 1.69 to 4.11. The pooled OR was 2.85 (95% CI: 1.45, 5.59, p=0.002), suggesting that antibiotics were more likely to be changed in patients who underwent invasive testing. There was no statistical evidence of heterogeneity (p=0.493). The observational studies showed that invasive sampling resulted in changes in antibiotic prescribing in more than half of the patients (pooled estimate 50.4%, 95% CI: 36, 65).

**Authors’ conclusions**

Invasive strategies for the diagnosis of VAP do not affect mortality, but do result in changes to antibiotic prescribing.

**CRD commentary**

This review addressed a focused question that was supported by clearly defined inclusion criteria. The search was adequate and included attempts to locate unpublished studies. Full details of the review process were reported and these included appropriate steps to minimise bias and errors. Quality was assessed using an accepted tool, but the results were only reported as a median summary score. This showed that the median score was 5, which is the maximum possible Jadad score, however, the authors also stated that none of the studies were blinded and so it should not have been possible for studies to score 5. Details of the individual studies were tabulated clearly and methods of analysis were appropriate. The authors’ conclusions are supported by the data presented and are likely to be reliable.

**Implications of the review for practice and research**

Practice: The authors stated that physicians should ensure that patients with VAP receive the appropriate antibiotic therapy initially; this may include the use of broad-spectrum agents. Bronchoscopy can be used to narrow the spectrum of antibiotics and reduce the duration of total antibiotic exposure.

Research: The authors stated that future studies should compare bronchoscopy with risk stratification strategies that
employ the clinical pulmonary infection score, and that formal economic analysis of the cost-savings of more appropriate antibiotic prescribing is required.

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