Protected specimen brush or bronchoalveolar lavage to diagnose bacterial nosocomial pneumonia in ventilated adults: a meta-analysis

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Authors' objectives
To compare the diagnostic value for bacterial nosocomial pneumonia (BNP) of:

quantitative culture (colony-forming units per millilitre, CFU/mL) of respiratory secretions collected with a bronchoscopic protected specimen brush (PSB);

quantitative culture (CFU/mL) of a bronchoscopic bronchoalveolar lavage (BAL); and

the percentage of infected cells (IC) in BAL.

Searching

Study selection
Study designs of evaluations included in the review
Retrospective studies, animal studies and meta-analyses were excluded. All studies had to be published as an article or abstract in a peer-reviewed journal.

Specific interventions included in the review
Studies evaluating PSB or BAL were eligible for inclusion. The included studies looked at quantitative cultures of respiratory secretions collected with a bronchoscopic-protected specimen brush (CFU-PSB), quantitative cultures of a bronchoscopic bronchoalveolar lavage (CFU-BAL), or the percentage of infected cells in bronchoalveolar lavage (IC-BAL). The included studies incorporated at least one of the following reference standards: clinical data, chest radiograph, blood culture, pleural culture, protected specimen brush culture, biopsy, or autopsy.

Reference standard test against which the new test was compared
Acceptable reference standards of diagnosis were clinical data, radiologic data, blood culture, PSB culture if the test was CFU-BAL or IC-BAL, lung biopsy and autopsy.

Participants included in the review
The inclusion criteria were not stated. The characteristics of the participants in the included studies were as follows: the average age ranged from 42 to 63 years; all had been mechanically ventilated for at least 48 hours; almost all were immunocompetent; patients either had suspected BNP or were deemed at risk of BNP, or were scheduled for autopsy. Studies which included community-acquired pneumonia were excluded from the meta-analysis.

Outcomes assessed in the review
Studies from which 2x2 data could be extracted were eligible for inclusion. The outcome measures calculated in the review were sensitivity, specificity, and accuracy or ‘global value’ (calculated by dividing the sum of test results classified as true positives and true negatives by the total number of results).

How were decisions on the relevance of primary studies made?
Three reviewers independently determined whether a study met the defined inclusion criteria. Any disagreements were resolved through discussion, with inclusion and exclusion decisions being based upon the agreement of at least two
reviewers. The reviewers were not blinded to either the authorship or the results of a study.

Assessment of study quality
A set of criteria suggested by Chalmers et al. (see Other Publications of Related Interest no.1) for assessing the quality of clinical trials was adapted to assess the quality of studies evaluating the sensitivity and specificity of a diagnostic test. The criteria related to study protocol, statistical analysis and presentation of results, and were listed in detail in the paper. A criterion on reproducibility, as suggested by Cook et al. (see Other Publications of Related Interest no.2) was also added. Three reviewers independently evaluated the quality of the studies and each study was then given a mean quality score. The rate of agreement between the reviewers was expressed as a percentage and by using a weighted kappa score.

Data extraction
One of the authors extracted study data on the sensitivity and specificity of PSB or BAL. The data were recalculated and displayed in 2x2 contingency tables (positive or negative result versus presence or absence of disease). Four contingency tables were constructed for each study; these included:

(1) all patients;
(2) patients who were not receiving antibiotics when PSB or BAL was performed;
(3) patients who were receiving at least one antibiotic when PSB or BAL was performed; and
(4) patients for whom diagnosis of BNP was based on autopsy.

The study authors were contacted where insufficient information was available in the paper.

Methods of synthesis
How were the studies combined?
For each specific test (CFU-PSB, CFU-BAL, IC-BAL), an 'unweighted pooled global value' (UPGV) was calculated by dividing the sum of true positives and true negatives by the total number of cases across all studies.

Summary receiver operating characteristic (ROC) curves were calculated for each specific test (see other Publications of Related Interest no.3). Summary ROC curves were constructed exclusively for studies reporting a high true-positive rate (over 50%) and low false-positive rate (less than 50%). Where studies reported the sensitivity and specificity at many cut-off points, the threshold with the best global value was plotted on the ROC curve.

UPGVs and Q values from summary ROC curves were used to compare the overall diagnostic value of CFU-PSB, CFU-BAL and IC-BAL. UPGVs and ROC curves were also calculated to compare the diagnostic value of the tests for patients who had previously received antibiotics and patients who had not.

How were differences between studies investigated?
No formal test of heterogeneity was carried out. However, the authors discussed potential sources of heterogeneity. The tests PSB and BAL were not performed in exactly the same way in the different studies, and the number and type of reference standard(s) used to confirm the diagnosis varied between studies. The authors stated that, owing to their inclusion criteria, heterogeneity between patient populations was unlikely.

The authors did not consider the variation in quality scores to be a significant source of heterogeneity. The studies were not weighted according to quality score in the analysis.

Results of the review
Twenty-six studies were included in the meta-analysis. Eighteen studies (795 participants) looked at CFU-PSB; 11 studies (447 participants) looked at CFU-BAL; and 11 studies (766 participants) looked at IC-BAL. The total number
of participants was not made clear in the article.

The overall mean quality score for the included studies was 42%. The authors considered that the quality of the majority of studies included in the meta-analysis was good, although the range of quality scores was wide (range: 19 to 64%).

The overall UPGVs were 0.83 (standard deviation, SD=0.13) for CFU-PSB, 0.76 (SD=0.16) for CFU-BAL, and 0.85 (SD=0.08) for IC-BAL. There were no significant differences in the summary ROC curves between CFU-PSB (Q value 0.8608) and CFU-BAL (Q value, 0.8373), or between CFU-BAL (Q value 0.8373) and IC-BAL (Q value 0.8852).

The UPGV of CFU-PSB went from 90% in patients who did not receive antibiotics to 73% among those who did. The same was true for CFU-BAL (89 to 72%) and IC-BAL (85 to 80%). There was a significant difference (P=0.0002) in the ROC curves for CFU-PSB between patients who had received antibiotics (Q value 0.6612) and those who had not (Q value 0.9120). There was no significant difference (P=0.3928) in the ROC curves for CFU-BAL between patients who had received antibiotics (Q value 0.8388) and those who had not (Q value 0.8870). Neither was there a significant difference (P=0.8202) for IC-BAL between patients who had received antibiotics (Q value 0.8273) and those who had not (Q value 0.8068).

**Authors' conclusions**
Both PSB and BAL are reliable to diagnose BNP. Since CFU-BAL and IC-BAL seemed more resistant to the effects of antibiotics, BAL is recommended rather than PSB if the patient is already receiving antibiotics.

**CRD commentary**
This was, on the whole, a methodologically sound review, although some oversights may have been made. The review question was clearly stated and was well supported by the inclusion criteria. The literature search was appropriate, although an attempt to search databases other than MEDLINE could have been made. Although only published studies were included in this meta-analysis, publication bias was not investigated. The validity assessment was appropriately performed by more than one reviewer, using an adapted version of a validated scale. However, there appeared to be some variation in study quality, the potential impact of which was not assessed during the analysis.

The authors recognised that there were potential sources of heterogeneity between the studies (i.e. the different studies did not perform PSB and BAL in exactly the same way, and they used different reference standards to diagnose nosocomial pneumonia), although these were not examined statistically. The reported values of sensitivity and specificity appeared to vary widely between tests, making the value of pooling accuracy to derive UPGVs and of generating summary ROC curves to derive Q values questionable. The authors' conclusions seem to follow from the evidence presented, but should be interpreted with caution given the limitations outlined.

**Implications of the review for practice and research**
Practice: The authors recommended BAL over PSB. They stated that with BAL, one can estimate infected cells in broncholar lavage (IC-BAL) as well as perform a culture of lower respiratory tract secretions. The immediate diagnosis of nosocomial pneumonia is possible with IC-BAL, and culture allows the identification of the causative germ(s) in the following days.

Research: The authors stated that the decision to perform bronchoscopic PSB or BAL should consider both their risks (e.g. pneumothorax or bleeding) and benefits (e.g. a decrease in mortality rate or in the length of stay in an intensive care unit). They concluded that only an outcome analysis could clarify whether PSB and BAL are useful in the clinical setting.

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Bibliographic details

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Other publications of related interest

S. Evaluation of the protected brush catheter and bronchoalveolar lavage in the diagnosis of nosocomial pneumonia. J
diagnostic test into a summary ROC curve: data analytic approaches and some additional considerations. Stat Med

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