Meta-analysis: methods for diagnosing intravascular device-related bloodstream infection

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CRD summary
This review aimed to identify the most accurate methods for diagnosing intravascular device-related bloodstream infection. The authors concluded that the most accurate test is paired quantitative blood culture, though most methods showed acceptable accuracy. These conclusions were based on pooled findings from a diverse group of studies, making clinical interpretation of the results difficult.

Authors' objectives
To identify the most accurate methods for the diagnosis of intravascular device (IVD)-related bloodstream infection.

Searching
The authors searched MEDLINE, Current Contents, PubMed and the Cochrane Library from their inception to July 2004; the search terms were reported. Conference abstracts were screened and references of recent reviews and meta-analyses were searched. Only studies published in English were included.

Study selection
Study designs of evaluations included in the review
Case reports and reviews were excluded. The majority of the included studies appeared to be diagnostic cohort studies.

Specific interventions included in the review
Studies were included if they evaluated any diagnostic method for IVD-related bloodstream infection. The review assessed the following diagnostic methods: qualitative, semi-quantitative or quantitative culture of catheter segment, IVD-drawn quantitative or qualitative blood culture, paired quantitative blood cultures, differential time to positivity, and acridine orange leukocyte cytopsin test. Studies of endoluminal brushing were excluded.

Reference standard test against which the new test was compared
Studies were included if they used a reference standard, though no single reference standard was specified. The reference standards used in the primary studies included: qualitative catheter segment culture (CSC) and qualitative peripheral blood culture (PBC); qualitative PBC and semi-quantitative CSC; primary bloodstream infection; semi-quantitative or quantitative CSC and qualitative PBC; culture isolates of hub, infusate, or catheter segment and bloodstream infection by DNA subtyping; qualitative and quantitative PBC; CSC with qualitative PBC and clinical symptoms and signs of infection; no other focus of infection with purulence at the insertion site with positive exudates and PBCs, or signs and symptoms of sepsis with positive quantitative CSC and positive PBC. Other combinations of these were used as the reference standard in the remaining studies (details provided in an online appendix).

Participants included in the review
The authors did not state any inclusion criteria relating specifically to the participants. The study populations varied widely, from infants to adults and from general in-patients to patients with end-stage renal disease and patients in intensive care units.

Outcomes assessed in the review
The studies had to include sufficient data for the calculation of the sensitivity and specificity. The authors reported 2x2 data for each study and used this to calculate sensitivities, specificities, predictive values and summary receiver operating characteristic (ROC) curves.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.
Assessment of study quality
The authors used the following criteria, based on the Standards for Reporting Diagnostic Accuracy statement, and other published criteria to assess the quality of the included studies: description of study sample; setting; type of IVD examined; methods used to recruit the patients; study design; reference standard; definition of cuff-off values for positivity; blinding of readers of test; methods used for statistical analysis; description of indeterminate results; subgroup analyses; and presence of bias. The authors did not state how the papers were assessed for quality, or how many reviewers performed the quality assessment.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data were extracted on the index test, criteria for positivity, reference standard, study design (prospective or retrospective), study population, number of participants, rationale for performing the diagnostic test, duration of catheterisation, prevalence of infection, and outcomes.

Methods of synthesis
How were the studies combined?
The sensitivities and specificities were pooled for each diagnostic test using a random-effects model. Summary ROC curves were constructed and the Q* value (where sensitivity equals specificity) was calculated along with its 95% confidence interval (CI).

How were differences between studies investigated?
Heterogeneity in the pooled sensitivities and specificities was assessed using the Pearson chi-squared test or the Fisher exact test. A subgroup analysis was conducted to compare the findings for short- versus long-term catheterisation, while the impact of the reference standard was investigated by comparing findings for studies using CSC in conjunction with a qualitative blood culture with those based on IVD-sparing blood culture. The influence of degree of quantification for methods of CSC and blood culture was also examined.

Results of the review
Fifty-one studies were included in the review (at least 5,552 patients; 23 studies did not report the number of patients). Several studies included more than one sample per patient.

A majority of the included studies provided information on the composition of the sample (57%) and eligibility criteria (92%), but incorporation bias was present in 51% of studies and only 8% provided CIs or standard errors.

All pooled estimates were statistically heterogeneous.

Qualitative culture of catheter segment (6 studies): the sensitivity was 0.87 (95% CI: 0.79, 0.96), the specificity was 0.75 (95% CI: 0.72, 0.78) and Q* was 0.76 (95% CI: 0.64, 0.88).

Semi-quantitative culture of catheter segment (19 studies): the sensitivity was 0.83 (95% CI: 0.79, 0.87), the specificity was 0.86 (95% CI: 0.85, 0.87) and Q* was 0.84 (95% CI: 0.80, 0.88).

Quantitative culture of catheter segment (14 studies): the sensitivity was 0.82 (95% CI: 0.78, 0.86), the specificity was 0.89 (95% CI: 0.87, 0.91) and Q* was 0.87 (95% CI: 0.81, 0.93).

IVD-drawn qualitative blood culture (7 studies): the sensitivity was 0.91 (95% CI: 0.84, 0.98), the specificity was 0.86 (95% CI: 0.83, 0.89) and Q* was 0.86 (95% CI: 0.80, 0.92).

IVD-drawn quantitative blood culture (7 studies): the sensitivity was 0.84 (95% CI: 0.80, 0.89), the specificity was 0.90 (95% CI: 0.88, 0.92) and Q* was 0.89 (95% CI: 0.79, 0.99).

Paired quantitative blood cultures (10 studies): the sensitivity was 0.79 (95% CI: 0.74, 0.84), the specificity was 0.99 (95% CI: 0.98, 1.0) and Q* was 0.94 (95% CI: 0.88, 1.0).
Acridine orange leukocyte cytospin test (5 studies): the sensitivity was 0.87 (95% CI: 0.80, 0.94), the specificity was 0.93 (95% CI: 0.89, 0.97) and $Q^*$ was 0.89 (95% CI: 0.79, 0.91).

Differential time to positivity (10 studies): the sensitivity was 0.89 (95% CI: 0.86, 0.92), the specificity was 0.83 (95% CI: 0.79, 0.87) and $Q^*$ was 0.85 (95% CI: 0.81, 0.97).

The overall sensitivities and specificities were also reported.

**Authors' conclusions**
Paired quantitative blood culture is the most accurate test for the diagnosis of IVD-related bloodstream infection. However, most other methods studied showed acceptable sensitivity and specificity and negative predictive value. The positive predictive value of all tests increased greatly with high pre-test clinical probability.

**CRD commentary**
This review was based on a reasonable search of the literature and a fairly broadly defined question, although the inclusion of only English language studies might have resulted in the omission of other relevant reports. Some aspects of study quality were discussed in the review, while other relevant characteristics of the included studies were tabulated. It was unclear what attempts were made to minimise error or bias in the selection and assessment of studies for the review. The authors used established methods to calculate several different summary measures of diagnostic accuracy. However, the inclusion of studies was not limited by reference standard, participant characteristics or study design, which might have contributed to the significant statistical heterogeneity observed in the majority of the reported pooled estimates. A subgroup analysis indicated that the type of reference standard can influence summary sensitivity and specificity values. Although the authors' conclusions follow from the results presented, the summary results themselves may be of limited clinical value.

**Implications of the review for practice and research**
Practice: The authors stated that catheters should not be cultured routinely but rather only if IVD-related bloodstream infection is suspected clinically.

Research: The authors stated that larger higher quality studies are required to provide more reliable estimates of the accuracy of methods for diagnosing IVD-related bloodstream infection, particularly IVD-sparing techniques.

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**Other publications of related interest**
This additional published commentary may also be of interest. O'Grady NP. Review: Paired quantitative blood cultures most accurately detect intravascular device-related bloodstream infection. ACP J Club 2005;143:77.
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