Comparison of utility of blood cultures from intravascular catheters and peripheral veins: a systematic review and decision analysis

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Blood cultures are sometimes obtained from intravascular catheters for convenience. However, there is controversy regarding this practice. The authors compared the diagnostic test characteristics of blood cultures obtained from intravascular catheters and peripheral veins. Relevant studies for inclusion in this review were identified through PubMed (January 1970–October 2005) and the Cochrane Central Register of Controlled Trials. Studies that reported clear definitions of true bacteraemia were included in the analysis. Two reviewers independently extracted the data. Six studies were included in the analysis, providing data for 2677 pairs of blood cultures obtained from an intravascular catheter and a peripheral venipuncture. A culture obtained from an intravascular catheter was found to be a diagnostic test for bacteraemia with better sensitivity (OR 1.85, 95% CI 1.14–2.99, fixed effects model) and better negative predictive value (almost with statistical significance) (OR 1.55, 95% CI 0.999–2.39, fixed effects model) but with less specificity (OR 0.33, 95% CI 0.18–0.59, random effects model) and lower positive predictive value (OR 0.41, 95% CI 0.23–0.76, random effects model) compared to a culture taken by peripheral venipuncture. In a group of 1000 patients, eight additional patients with true bacteraemia would be identified and 59 falsely diagnosed as having bacteraemia by a blood culture obtained from an intravascular catheter compared to results of the peripheral blood culture. Given the consequences of undertreating patients with bacteraemia, the authors believe that, based on the available evidence, at least one blood culture should be obtained from the intravascular catheter.

Background

The convenience of obtaining blood specimens from intravascular catheters for routine laboratory tests makes them a tempting method for the collection of blood culture specimens (Krüeger et al., 1981). However, this practice is controversial. A discouraging concern is that the proportion of false-positive results may increase (i.e. decrease of the specificity of the test in diagnosing true bacteraemia), resulting in unnecessary administration of costly and potentially toxic antibiotics to patients, and increased length of hospitalization, health care cost and antimicrobial resistance of micro-organisms (Bates et al., 1991; Bryant & Strand, 1987; Everts et al., 2001; Vaisanen et al., 1985). In addition, frequent manipulations of the intravascular devices may increase the potential for microbial colonization of the device and subsequently development of infection (O’Grady et al., 2002).

However, there is evidence deriving from published studies that blood cultures obtained from central vascular catheters are sufficiently sensitive for detection of bloodstream infection (Felices et al., 1979; Tonnesen et al., 1976; Wormser et al., 1990). Given their convenience, a clinically important question arises whether blood cultures obtained from intravascular catheters have such test characteristics (sensitivity, specificity, and positive and negative predictive value) in diagnosing bacteraemia to be considered equivalent or even better than blood cultures obtained by peripheral venipuncture. Thus we conducted a quantitative systematic review to critically evaluate the published data regarding performance characteristics of blood cultures obtained through intravascular devices compared to peripheral venipuncture.

Search of the literature

Two reviewers independently performed the literature search, identified the relevant studies to be included in the analysis, and extracted the data. Relevant studies for inclusion in this review were identified through PubMed (January 1970–October 2005) and the Cochrane Central Register of Controlled Trials, as well as from references of the initially found articles. The search terms we used were intravascular device, vascular catheter, peripheral vein,
venipuncture, blood culture, bacteraemia, bacteremia, bloodstream infection, performance characteristics, sensitivity, specificity and predictive value.

**Process of study selection**

Studies were included in the analysis if they provided data regarding the diagnostic utility of blood cultures drawn from central venous, peripheral arterial or Swan–Ganz catheters, compared to the standard peripheral venipuncture, in patients with suspected bacteraemia. Included studies should have reported clear definitions of true bacteraemia. Since the end points of interest were the diagnostic performance characteristics of the compared tests [sensitivity, specificity and positive and negative predictive value (PPV and NPV, respectively)], studies that did not report relevant results or the raw data that permitted the calculation of results for these characteristics were excluded from the analysis. Both studies with prospective and retrospective design were evaluated for possible inclusion in further analysis. Case–control studies, case series and case reports, as well as review articles and letters to the editor, were excluded from our analysis. Only studies in English language were evaluated.

**Data extraction**

Data extracted from the studies included in our analysis were the year of publication, the design of the study, the setting, patient population, details regarding the type of catheters used and the techniques of blood culture acquisition, the time allowed to elapse between obtaining the blood specimen from the intravascular catheter and a peripheral venipuncture for cultures, and the definition used for true bacteraemia. In addition, outcomes of interest achieved with each type of blood culture were extracted, namely sensitivity, specificity, PPV and NPV, as well as any increase in catheter colonization or catheter-related infections attributable to the use of intravascular catheters for obtaining blood cultures.

**Statistical analysis**

We calculated the pooled odds ratios (ORs) and 95 % confidence intervals (CIs) of the main indices of interest between each type of blood culture (obtained from an intravascular catheter or a peripheral vein). Indices of interest were the sensitivity, specificity, PPV and NPV of each method. In addition, we constructed a decision analysis tree by calculating the possible results of blood culture drawn through an intravascular catheter or a peripheral vein, using the diagnostic performance characteristics that we derived from the synthesis of data reported in the studies included in our analysis (Weinstein & Fineberg, 1980).

Statistical analyses were performed using the 'Meta-analyst' software (Joseph Lau, Tufts University School of Medicine, Boston, MA, USA). Pooled ORs and CIs for all the outcomes were calculated using the Mantel–Haenszel fixed effects and the DerSimonian–Laird random effects models. A finding was considered statistically significant if there was a $P$ value lower than 0.05 in the analysis of the outcomes. The results from the fixed effects models are presented when there was no heterogeneity between the analysed studies ($P$ value greater than 0.1).

**Analysed studies**

Our initial search retrieved 301 possibly relevant studies that included one or some of our search terms in their PubMed or Cochrane Central Register of Controlled Trials record. The majority of the initially identified studies were excluded due to the fact that they were either irrelevant to our main research question (222 studies), or they did not report comparative data (66 studies). We finally included six studies in our analysis, three of which were prospective (Beutz et al., 2003; Bryant & Strand, 1987; Tafuro et al., 1986) and three retrospective (DesJardin et al., 1999; Martinez et al., 2002; McBryde et al., 2005). The main characteristics of the eligible studies including details regarding their methodology are summarized in Table 1. Four of the six studies included in our analysis were performed in intensive care units (ICUs) whereas the rest examined patients in regular hospital wards.

There was some variability in the analysed studies regarding the types of intravascular catheters used. A total of 2677 cultures were obtained through catheters, the great proportion of which referred to temporary central venous catheters (50 %), Hickman catheters (18 %), port-A-caths (5.7 %) and arterial catheters (22.4 %) including the Swan–Ganz type (less than 9 % of the total). The site of catheter insertion was described in detail in only one study, in which central venous catheters in subclavian and internal jugular veins were mainly used (Beutz et al., 2003). Similar definitions of true bacteraemia, focusing on the number of positive cultures, the type of micro-organism isolated and the clinical evaluation of the patient, were used in the studies included in our analysis. The primary focus of infection in cases of true bacteraemias was not reported in any of the included studies.

The studies included in our analysis had some differences with reference to other methodological features, i.e. the method used for skin antisepsis and catheter preparation and the initial blood discard. The discard of blood prior to obtaining the specimen for culture was applied in three studies in an attempt to decrease the number of false-positive results due to colonization of the catheter. The rest of the studies avoided this technique, possibly trying to detect a common primary source of secondary bacteraemia. Skin antisepsis was usually performed with povidone iodine, and only in one study both an isopropyl alcohol solution and iodine tincture were sequentially used. In two of the studies, this parameter was not reported.
### Table 1. Main characteristics of the studies included in our analysis

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Ward or ICU</th>
<th>Type of central vascular catheter (CVC)</th>
<th>Study population</th>
<th>Other study method characteristics</th>
<th>Definition of true bacteraemia ('gold standard')</th>
</tr>
</thead>
</table>
| McBryde et al.    | Retrospective    | All wards                 | Venous–arterial (9% arterial, 13% port-A-cath, 77% central venous line)                                 | Not reported     | Maximum time lag between samples: 2 h; Intravascular catheter preparation: 70% isopropyl alcohol swabs; Skin antisepsis prior to peripheral venipuncture: Data not reported; Initial blood discard: None | (1) Concordant positive central and peripheral culture  
(2) When discordant, pairs were assessed according to the following criteria: (i) evidence of sepsis (fever, high or low neutrophil count) and a localizing site; (ii) organisms unlikely to be contaminants; (iii) same organism found in other blood cultures taken from a separate site during the same episode of sepsis. |
| (2005)            | cohort study     |                           |                                                                                                           | 962              |                                                                                                                                                                                                                                        |                                               |
| Beutz et al.      | Prospective      | Medical ICU               | Venous (74.3% temporary multilumen CVCs, 11% Hohn catheters, 5% multilumen dialysis catheter, 4.3% Cordis catheter, 3.3% other types of multilumen catheter, 1.7% subcutaneous ports, 0.3% CVC placed from a peripheral site) | 119              | 70% isopropyl alcohol and Betadine pad; 70% isopropyl alcohol followed by 2% iodine tincture; Same definition as in DesJardin et al. (1999) | Same definition as in the study by DesJardin et al. (1999) |
| (2003)            | cohort study     |                           |                                                                                                           | 300              |                                                                                                                                                                                                                                        |                                               |
| Martinez et al.   | Retrospective    | Surgical and cardiothoracic ICU | Venous (temporary central venous 62%, arterial 33%, Hickman 5%)                                             | 271              | Either 75% isopropyl alcohol or povidone–iodine; Povidone–iodine; None | Same criteria as in DesJardin et al. (1999). When not applicable, evaluation of clinical and laboratory data by two physicians.                                                                                     |
| (2002)            | cohort study     |                           |                                                                                                           | 499              |                                                                                                                                                                                                                                        |                                               |
| DesJardin et al.  | Retrospective    | Haematology ward          | Venous (83% Hickman catheter, 5% port, 9% temporary central venous catheter)                             | 185              | Either 70% isopropyl alcohol or a povidone–iodine swab; Povidone–iodine; None | True bacteraemia or fungaemia criteria: (1) Certain pathogens (S. aureus, Gram (--), Candida spp.) (2) Common skin contaminants isolated from ≥ 2 cultures from different sites and associated with fever, rigors or hypotension (3) Polymicrobial infection with the same organisms in ≥ 1 culture and associated with fever, rigors or hypotension. When criteria not applicable, blinded determination by two infectious disease experts |
| (1999)            | cohort study     |                           |                                                                                                           | 552              |                                                                                                                                                                                                                                        |                                               |
Main outcomes of interest

Data for the main outcomes, including the prevalence of bacteraemia and the main diagnostic performance values, for each study analysed, as well as for all studies combined, are presented in Table 2. The sensitivity of cultures taken through intravascular catheters or by peripheral venipuncture ranged from 78% to 95% and from 64% to 95%, respectively (Table 2). The highest observed PPV of catheter-drawn cultures was 63.9% (range 17.2–63.9%, weighted mean 55.1), which was inferior even to the lowest PPV of the cultures drawn via peripheral vein (range 66.7–85.4%, weighted mean 79.3%). The lowest observed PPV of central vascular catheter culture was 17.2%. In that study, the sample size was relatively small (130 paired cultures), providing only six cases of true bacteraemia, and the prevalence of bacteraemia was also the lowest among the evaluated studies (4.6 versus a weighted mean of 11.6). The NPV was high for both central and peripheral drawn cultures in all studies.

Pooling the data from all the included studies showed that a culture obtained from an intravascular catheter is a test with better sensitivity (OR 1.85, 95% CI 1.14–2.99, fixed effects model) and better NPV (almost with statistical significance) (OR 1.55, 95% CI 0.999–2.39, fixed effects model) in diagnosing bacteraemia compared to a culture taken by peripheral venipuncture. On the contrary, it is a diagnostic test with less specificity (OR 0.33, 95% CI 0.18–0.59, random effects model) and lower PPV (OR 0.41, 95% CI 0.23–0.76, random effects model) compared to a culture obtained by peripheral venipuncture.

Decision analysis tree

Results from the calculated combined performance characteristics of cultures obtained from an intravascular catheter or by peripheral venipuncture are shown in a decision analysis tree, where the possible scenarios and the corresponding probabilities were assessed (Fig. 1). As shown in this figure, we assumed that 1000 blood cultures were obtained in an equal number of patients with suspected bacteraemia, through a peripheral vein or through an intravascular catheter. According to the performance characteristics derived from the combination of data from the individual studies, the catheter-drawn culture would result in 103 true-positive, 84 false-positive, 801 true-negative and 12 false-negative results. The results for the cultures drawn from peripheral vein would be 96, 25, 859 and 20, respectively. Under the assumption that the decision to administer antibiotics would be based only on the result of this culture, 96 patients from the first group versus 45 from the second would be inappropriately handled (12 versus 20 undertreated, and 84 versus 25 overtreated, for the intravascular catheter and the peripheral venipuncture group, respectively). From these estimates, it is derived that in a group of 1000 patients, compared with the results of the peripheral blood culture, eight additional patients with true bacteraemia would be
vascular catheter (CVC) or peripheral venipuncture (PV) would be detected in 104 patients compared to blood culture obtained from an intravascular catheter. True bacteraemia represents a medical emergency that requires prompt identification of its source, if possible, and institution of appropriate antimicrobial treatment. Thus the number of patients with contamination of blood cultures that would be needed to overtreat due to the lower specificity and PPV (i.e. false-positive results) of cultures drawn from intravascular catheters should be weighed against the higher number of true bacteraemias that are identified by this method.

Since the blood cultures drawn through an intravascular catheter or a peripheral vein sometimes yield divergent results that lead to different diagnostic performance characteristics, a dilemma is posed about what the best choice would be if we had to obtain only one culture, considering the difference in failure to treat and excessive antibiotic use. Using the results presented in Fig. 1, the following conclusions can be made. In the group where a culture through the catheter, true bacteraemia would be detected in 104 patients compared to 96 patients of the other group. That means missing eight incidents of true bacteraemia, if only one culture from a peripheral vein was obtained. As an offset to that, in 59 additional patients of the catheter group, antibiotics would be unnecessarily administered. In other words, for every one patient who would be accurately diagnosed with bacteraemia due to the relative advance in sensitivity when culture is drawn from the catheter, in more than seven patients antibiotics would be inappropriately administered. However, when evaluating overtreatment one may presume that a significant proportion of these patients would receive antibiotics before the results of the culture were available, and that in practice, in some of them the antibiotics would be continued, even with negative blood culture results, so that finally the difference in the proportion of the overtreated patients between the two groups would decline.

Thus based on the aforementioned model, about 5% more patients would be overtreated if the diagnostic test used was a culture from an intravascular catheter compared to a peripheral venipuncture. Cost-effectiveness analysis is beyond the scope of this study but it is rather unlikely for the extra cost in antibiotic usage to be more than the cost that results from the missed diagnosis of bacteraemia in the extra 0.8% of the patients of our model. Another important factor that could not be evaluated by this analysis is the possible increase in the emergence of antimicrobial resistance that could be the result of the overuse of antibiotics. Finally, there may be some chance of introducing microbes into the intravascular line while attempting to obtain blood for culture but the exact probability of this occurring is not known. Nevertheless, bacteraemia is an infection associated with considerable morbidity and mortality and subsequently identifying a patient with true bacteraemia is unquestionably very important and may prove life-saving. Thus, ultimately,

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**Table 2. Prevalence of bacteraemia and diagnostic performance characteristics of blood cultures obtained through a central vascular catheter (CVC) or peripheral venipuncture (PV)**

Numbers in parentheses represent the proportion of cultures.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Bacteraemia prevalence (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CVC</td>
<td>PV</td>
<td>CVC</td>
<td>PV</td>
<td>CVC</td>
</tr>
<tr>
<td>McBryde et al. (2005)</td>
<td>15.9</td>
<td>94.8</td>
<td>95.4</td>
<td>84.5</td>
<td>96.9</td>
</tr>
<tr>
<td>Beutz et al. (2003)</td>
<td>11.3</td>
<td>82.4</td>
<td>64.7</td>
<td>92.5</td>
<td>95.9</td>
</tr>
<tr>
<td></td>
<td>(34/300)</td>
<td>(28/34)</td>
<td>(22/34)</td>
<td>(246/266)</td>
<td>(255/266)</td>
</tr>
<tr>
<td>Martinez et al. (2002)</td>
<td>9.0</td>
<td>77.8</td>
<td>64.4</td>
<td>95.6</td>
<td>98.2</td>
</tr>
<tr>
<td>DesJardin et al. (1999)</td>
<td>8.3</td>
<td>89.1</td>
<td>78.3</td>
<td>95.3</td>
<td>97.4</td>
</tr>
<tr>
<td></td>
<td>(46/552)</td>
<td>(41/46)</td>
<td>(36/46)</td>
<td>(482/506)</td>
<td>(493/506)</td>
</tr>
<tr>
<td>Tafuro et al. (1986)</td>
<td>11.1</td>
<td>88.5</td>
<td>73.1</td>
<td>93.8</td>
<td>96.2</td>
</tr>
<tr>
<td>Bryant &amp; Strand (1987)</td>
<td>4.6</td>
<td>83.3</td>
<td>66.7</td>
<td>80.6</td>
<td>98.4</td>
</tr>
</tbody>
</table>
the use of intravascular catheters for obtaining at least one blood culture may be the preferred method.

A major concern regarding obtaining cultures through an intravascular catheter is the possibility of introducing an infection via the catheter. However, the results of a literature search for data concerning the increased risk of infection attributed to frequent manipulations of the catheter were controversial. This parameter was examined only in one of the studies included in our analysis, which concluded that frequent manipulation of lines did not significantly increase the rate of recovery of contaminants (Tafuro et al., 1986). However, other studies regard frequent manipulation as one of the important risk factors for the development of catheter-related bloodstream infection and emphasize the need of limiting catheter manipulation to decrease the rate of catheter colonization and secondary bacteraemia (Adal & Farr, 1996; Lange et al., 1997; Raad, 1994).

We identified eight other studies, seven prospective and one retrospective, relevant to our research question, which provided us useful information but could not be included in our analysis due to their design or reported data (Bozzetti et al., 1984; Everts et al., 2001; Felices et al., 1979; Juste et al., 2000; Vaisanen et al., 1985; Levin et al., 2000; Tonnesen et al., 1976; Wormser et al., 1990). They were also conducted in patients hospitalized in ICU or oncology wards who had pairs of blood cultures obtained from the intravascular catheter and by peripheral venipuncture. In addition to the studies included in our analysis, these studies that examined the comparative characteristics of blood cultures obtained from an intravascular catheter and a peripheral vein also suggested that the first test has higher sensitivity in diagnosing true bacteraemia than the second (Felices et al., 1979; Tonnesen et al., 1976; Juste et al., 2000). Some of the studies suggested that blood culture through intravascular catheters might be both sensitive and sufficiently specific for the diagnosis of bacteraemia (Felices et al., 1979; Tonnesen et al., 1976; Wormser et al., 1990). It is also supported that when cultures obtained from arterial lines and peripheral venipuncture are compared, the results of cultures from both sources are in most cases equivalent (Levin et al., 2000). In a study of paired cultures from arterial line and peripheral vein, the results were concordant in the majority of the cases, and when they were discordant, the culture from the arterial line was more commonly positive (Levin et al., 2000). Also, in another study where the result of the catheter tip culture was used in the identification of true bacteraemia, a good diagnostic performance of the blood culture obtained from the catheter was found (Juste et al., 2000). However, another study showed higher PPV of the blood culture drawn from a peripheral vein (Bozzetti et al., 1984) whereas other researchers supported that line blood cultures were a less reliable method that could not replace culture from venipuncture samples for the diagnosis of bacteraemia (Vaisanen et al., 1985).
Limitations

Our work is not without limitations. First, we performed analyses by pooling the data from the individual studies. It should be noted that the unit of analysis in the reviewed studies was the pair of blood cultures obtained from a central catheter and a peripheral vein. However, subsequent paired cultures from the same patient may not be handled as measurements that are independent from each other. Second, there was some variability regarding the setting of the studies, the patient population, the year of the study, and the types of central venous catheters examined. Third, we did not perform comparative analysis of the diagnostic performance characteristics of two sets of blood cultures, which is a common practice in an attempt to increase the sensitivity and specificity of the tests in diagnosis of true bacteraemia (Aronson & Bor, 1987; Tabriz et al., 2004; Tokars, 2004). Fourth, the results of our analyses, including the diagnostic characteristics of blood cultures, are influenced considerably by the prevalence of bacteraemia. We used in our calculations the weighted mean of the prevalence of true bacteraemia reported in the studies included in our analysis. It should be emphasized that the PPV and NPV would increase and decrease, respectively, as the prevalence of bacteraemia increases for both tests (blood cultures obtained from an intravascular catheter and a peripheral vein). Fifth, antibiotic therapy may be a cause of difference regarding isolation of microorganisms from blood cultures taken from peripheral veins and central venous catheters, since micro-organisms in the latter are frequently in biofilms and thus protected to some degree from the effect of antibiotics.

A major shortcoming of all studies evaluating the basic diagnostic performance characteristics (sensitivity, specificity, PPV and NPV) of blood cultures for the detection of bacteraemia is that there is no independent ‘gold standard’ test to evaluate blood culture results (Aronson & Bor, 1987). The relevant studies utilize physician evaluation of records to determine whether a positive culture represents a true-positive or a false-positive result, i.e. a method that is subjective. Thus sensitivity cannot be expressed, as there is no definitive way to identify false-negative results.

Conclusions

Although our study has some limitations, we believe that for various patient populations who have an intravascular catheter, our analysis offers additional support for the use of the intravascular catheter for obtaining at least one blood culture, when clinically indicated.

References


