Blood Cultures at Central Line Insertion in the Intensive Care Unit: Comparison with Peripheral Venipuncture[▽]

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Blood cultures are a key diagnostic test for intensive care unit (ICU) patients; however, contaminants complicate interpretations and lead to unnecessary antibiotic administration and costs. Indications for blood cultures and central venous catheter (CVC) insertions often overlap for ICU patients. Obtaining blood cultures under the strict sterile precautions utilized for CVC insertion might be expected to decrease culture contamination. This retrospective study compared the results of blood cultures taken at CVC insertion, at arterial line insertion, and from peripheral venipuncture in order to validate the advantage of CVC insertion cultures. Cultures from indwelling lines were excluded. Results of 14,589 blood cultures, including 2,736 (19%) CVC, 1,513 (10%) arterial line, and 10,340 (71%) peripheral cultures taken over 5.5 years in two ICUs (general and medical) were analyzed. CVC cultures were contaminated more frequently than arterial line or peripheral cultures (225/2,736 [8%] CVC, 48/1,513 [3%] arterial line, and 378/10,340 (4%) peripheral cultures [$P < 0.001$ for CVC versus peripheral and CVC versus arterial line cultures]). True pathogens were found more frequently in CVC insertion cultures (334/2,736 [12%] CVC, 155/1,513 [10%] arterial line, and 795/10,340 [8%] peripheral cultures [$P < 0.001$ for CVC versus peripheral cultures; $P = 0.055$ for CVC versus arterial line cultures; $P < 0.001$ for peripheral versus arterial line cultures]). Contamination and true-positive rates were similar for culture sets from the two ICUs for each given culture source. Despite superior sterile precautions, cultures taken at the time of central line insertion had a higher contamination rate than did either peripheral or arterial line blood cultures. This may be related to the increased manipulations required for CVC insertion.

Severe sepsis, defined as acute organ dysfunction secondary to infection, is the most common cause of death in noncardiac intensive care units (ICUs) (22). Blood cultures serve as a reliable, if imperfect, test for detecting the bacteremia often associated with sepsis and as a vital tool in tailoring antibiotic therapy (8, 36). However, blood culture contamination (with organisms that do not reflect true bacteremia) frequently complicates the interpretation of blood culture results (30), leading to unnecessary antibiotic administration (20) and adding significantly to the length of hospital stay and the cost of care (1).

Central lines are often inserted into unstable ICU patients when sepsis is suspected, in order to measure central venous pressure, direct fluid resuscitation, obtain venous oxygen saturation (33), and facilitate the safe administration of vasoactive drugs. The strict aseptic techniques and sterile-barrier precautions employed during central line insertion (in order to reduce the incidence of central line-associated bloodstream infections [28]) far exceed those taken when obtaining blood cultures from peripheral venipuncture. Since suspected sepsis is also an indication for obtaining blood cultures, and since central lines are inserted under strict sterile precautions, obtaining blood cultures during central line insertion presents an

attractive opportunity to minimize the risk of culture contamination. Indeed, this is a common ICU practice.

The principal hypothesis examined in this study was that the rate of contamination of blood cultures taken at central line insertion would be lower than that of blood cultures taken from peripheral venipuncture. This question is important in order to establish the validity of central line insertion blood cultures.

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MATERIALS AND METHODS

Setting and data collection. The Hadassah-Hebrew University Medical Centre is a 775-bed academic tertiary care hospital. Data on all blood cultures taken from patients in the 12-bed adult general (mainly surgical) ICU (GICU) and the 9-bed medical ICU (MICU) between January 2005 and June 2010 were obtained retrospectively from the computerized microbiological laboratory database. Cultures taken from existing lines (not at the time of insertion) were excluded. A waiver of informed consent was granted by the institutional research ethics committee, as this was considered a quality control initiative, and there were no patients identified or treatments given.

The following information was extracted for each blood culture: ICU of patient admission, date of specimen collection, culture result, and source of blood culture (peripheral venipuncture, central venipuncture during central venous catheter insertion, or arterial puncture during arterial catheter insertion). Central venous catheters included single-, double-, and triple-lumen catheters; temporary dialysis catheters; and pulmonary-artery catheters.

Definitions. Each culture result was designated sterile, “contaminant,” or “noncontaminant.” Blood culture contamination was determined based on CDC definitions (18). Common skin contaminants (i.e., diphtheroids [*Corynebacterium* spp.], *Bacillus* spp., *Propionibacterium* spp., coagulase-negative staphylococci [including *Staphylococcus epidermidis*], viridans group streptococci, *Aerococcus* spp.,

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and *Micrococcus* spp.) were considered to reflect true infection if the same organism was isolated from two or more blood culture sets taken within 2 days of each other and with antibiograms that were different for fewer than two antimicrobial agents. All other organisms isolated from blood cultures were considered to be "noncontaminants" and, for the purposes of this study, to represent "true pathogens."

In order to further examine the results of central versus peripheral cultures, an analysis of blood culture sets taken in parallel from both sources within 24 h was performed. Contamination and true-pathogen isolation were compared in this subset of blood cultures.

Blood culture phlebotomy technique. Each blood culture set included an aerobic bottle and an anaerobic bottle. Bottles were used according to the manufacturer's instructions. Blood was either aspirated directly into aerobic and anaerobic culture bottles or drawn into a syringe and subsequently injected into culture bottles. Needle changes were not recommended. All blood culture bottle tops were swabbed with 70% isopropyl alcohol (Tyco Healthcare, Mansfield, MA) prior to blood inoculation.

Peripheral blood cultures were obtained from venipuncture following skin preparation with 70% isopropyl alcohol or 0.5% chlorhexidine in 70% alcohol using a 21-gauge or 23-gauge needle. Nonsterile gloves were used. Peripheral blood cultures from ICU patients were obtained and inoculated into blood culture bottles by physicians.

Central venous catheters were inserted by using the Seldinger catheter-over-wire technique. Maximal barrier precautions were employed in accordance with CDC guidelines (28) and included the use of a surgical cap and mask, hand disinfection with a 4% chlorhexidine scrub or 70% ethanol hand rub prior to the procedure, sterile gloves and gown, patient skin disinfection with 2% chlorhexidine (0.5% chlorhexidine until late 2006) in 70% alcohol, and whole-body sterile drapes. Blood cultures were obtained from the hub of the new catheter toward the end of the procedure. Blood was aspirated with a 20-ml syringe and passed to an assisting nurse, who attached a sterile needle and inoculated the blood into a pair of blood culture bottles.

Peripheral arterial catheters (e.g., radial artery) represented the majority of arterial access. They were inserted by using 20-gauge catheter-over-needle intravenous equipment following skin preparation similar to that used for peripheral venipuncture. Femoral arterial catheters were inserted using barrier precautions as described above for central line insertions. Catheters were inserted by physicians, and blood was inoculated into blood culture bottles by an assisting nurse as described above. Arterial cultures were drawn at the time of catheter insertion through either the fresh catheter or the previously unopened stopcock.

Obtaining blood cultures from indwelling central or arterial catheters, not at the time of insertion, was actively discouraged. In the event that such cultures were taken, they were recorded as such on the request form and excluded from the study.

Microbiological methods. Becton Dickinson Bactec Plus aerobic and anaerobic bottles (Becton Dickinson & Co., Sparks, MD) were used for all blood cultures and processed using the Bactec 9240 system. Bacteria were identified using standard microbiological techniques (27).

Statistical analysis. The proportions of cultures growing contaminants and true pathogens were calculated and compared for each blood culture source (central venous catheter insertion, peripheral venipuncture, and arterial line insertion) and each ICU using the chi-square test. Statistical significance was defined as a two-tailed *P* value of <0.05. All tests were performed by using SAS 8.02 (SAS Institute Inc., Cary, NC).

Data were also analyzed on a yearly basis and displayed graphically to identify changes occurring over time.

RESULTS

A total of 14,589 blood cultures (8,087 from the GICU and 6,502 from the MICU) were analyzed. Of these, 2,736 (19%) were taken during central line insertion, 1,513 (10%) were taken during arterial line insertion, and 10,340 (71%) were taken from peripheral venipuncture. Among these cultures, 12,654 (87%) were sterile, 1,284 (9%) grew true pathogens, and 651 (4%) grew contaminants.

Contaminants were found in 225/2,736 (8%) central line cultures, 378/10,340 (4%) peripheral cultures, and 48/1,513 (3%) arterial line cultures (*P* < 0.001 for central versus peripheral and central versus arterial cultures). True pathogens

were found in 334/2,736 (12%) central line cultures, 795/10,340 (8%) peripheral cultures, and 155/1,513 (10%) arterial line cultures (*P* < 0.001 for central versus peripheral and peripheral versus arterial cultures). The distribution of cultures by result, source, and ICU is shown in Tables 1 and 2. Blood cultures from GICU and MICU patients showed very similar distributions of contaminants and true pathogens across the different culture sources (Table 3).

The identity of contaminant organisms by ICU is shown in Table 4. Out of 697 culture sets growing common skin organisms (18), 46 (7%) cultures taken from 23 patients were defined as reflecting true infection and were analyzed as such. All these sets grew coagulase-negative staphylococci.

Blood cultures taken at the time of central line insertion on 903 occasions were matched to 1,420 peripheral blood cultures taken within 24 h. Among these parallel culture sets, contaminants grew in 72/903 (8%) central culture sets, versus 38/1,420 (3%, *P* < 0.001) peripheral cultures. True pathogens grew in 121/903 (13%) central culture sets, versus 84/1,420 (6%) peripheral cultures (*P* < 0.001).

The time-trend data show that although the overall rates of culture contamination changed over time for both GICU and MICU, the difference in contamination rates between central and peripheral cultures remained stable over time in both ICUs; that is, the proportion of contaminants in cultures obtained from central lines remained higher than the proportion of contaminants in cultures obtained from peripheral venipuncture at all time points (Fig. 1). Similarly, blood cultures obtained at the time of central line insertion were superior to those obtained from venipuncture for the detection of true pathogens at most time points (Fig. 2).

DISCUSSION

In complete contrast to the expected findings, blood cultures taken at the time of central line insertion using strict aseptic techniques yielded a higher rate of contaminants than did blood cultures obtained from peripheral venipuncture. Despite a gradual decrease in the overall rate of blood culture contamination over the study period, the rate of contamination of central line cultures remained consistently higher than that of venipuncture cultures. The study also demonstrated a higher yield of true pathogens in cultures drawn at the time of central line insertion than in those drawn from peripheral venipuncture. These findings, consistent over a 5.5-year period, were duplicated in two independent ICUs admitting different patient populations, staffed by different physicians and nurses and located in entirely different hospital locations.

The definition for blood culture contaminants used in this study was based on CDC criteria for bloodstream infection (18). Defining bloodstream infections caused by common skin organisms requires the isolation of identical organisms with similar antibiograms in two or more blood cultures over 48 h, coupled with signs of clinical infection. The retrospective nature of this study precluded the use of clinical patient data, so the study definition of a bloodstream infection was altered to include only the culture-based criteria. Using this broader definition, the presence of true bloodstream infections may have been overestimated, or, conversely, contamination by common skin organisms may have been underestimated. Despite this,

TABLE 1. Detection of contaminants and true pathogens by puncture site and ICU

Site of blood collection	No. of cultures (%)									
	Total				GICU				MICU	
	Contaminants	True pathogens	No growth	Total	Contaminants	True pathogens	No growth	Total	Contaminants	Total
Central	225 (8)	334 (12)	2,177 (80)	2,736 (100)	148 (8)	217 (12)	1,422 (80)	1,787 (100)	77 (8)	117 (12)
Peripheral	378 (4)	795 (8)	9,167 (88)	10,340 (100)	212 (4)	411 (8)	4,659 (88)	5,282 (100)	166 (3)	384 (8)
Arterial	48 (3)	155 (10)	1,310 (87)	1,513 (100)	30 (3)	113 (11)	875 (86)	1,018 (100)	18 (4)	42 (8)
Total	651 (4)	1,284 (9)	12,654 (87)	14,589 (100)	390 (5)	741 (9)	6,956 (86)	8,087 (100)	261 (4)	543 (8)
									5,698 (88)	6,502 (100)

TABLE 2. Statistical significance of differences in rates of detection of contaminants and pathogens by puncture site^a

Puncture site comparison	Total						GICU						MICU	
	% contaminants by puncture site comparison		P value for % contaminants		% true pathogens by puncture site comparison		% contaminants by puncture site comparison		P value for % contaminants		% true pathogens by puncture site comparison		P value for % contaminants	
	8 vs 4	<0.001	12 vs 8	<0.001	12 vs 8	<0.001	8 vs 4	<0.001	12 vs 8	<0.001	8 vs 3	<0.001	12 vs 8	<0.001
Central vs peripheral	8 vs 3	<0.001	12 vs 10	0.055	12 vs 11	0.410	8 vs 3	<0.001	12 vs 11	0.410	8 vs 4	0.001	12 vs 8	0.027
Central vs arterial	4 vs 3	0.346	8 vs 10	<0.001	8 vs 10	<0.001	4 vs 3	0.105	8 vs 11	<0.001	3 vs 4	0.674	8 vs 8	0.476

^a Percentages are duplicated from Table 1 for ease of reference.

TABLE 3. Comparison of GICU and MICU data^a

Site of blood collection	% contaminants for GICU vs MICU	P value for % contaminants for GICU vs MICU	% true pathogens for GICU vs MICU	P value for % true pathogens for GICU vs MICU
Central	8 vs 8	0.879	12 vs 12	0.888
Peripheral	4 vs 3	0.047	8 vs 8	0.718
Arterial	3 vs 4	0.473	11 vs 8	0.115
Total	5 vs 4	0.019	9 vs 8	0.085

^a Percentages are duplicated from Table 1 for ease of reference.

central blood cultures were contaminated more frequently than were peripheral cultures.

The susceptibility of central cultures to contamination was further described by analyzing separately only central blood cultures taken in parallel with peripheral venipuncture, allowing a direct comparison of central and peripheral cultures drawn from the same patients at similar points in time. Even among the parallel sets, contaminants were significantly more common in central line sets, suggesting that these sets were indeed more susceptible to contamination. Furthermore, among parallel cultures, central cultures were positive for true pathogens significantly more frequently than were peripheral cultures, suggesting a greater sensitivity of central cultures for true pathogens.

The process of obtaining blood cultures can be divided broadly into three parts: preparing the phlebotomy site, drawing the blood, and inoculating the blood into the culture bottles. All three parts can be sources of blood culture contamination. Preparation (of both the physician and the patient) for central line insertion is far more extensive than the nonsterile gloves and alcohol skin swab used for peripheral venipuncture. It is thus unlikely that this phase accounts for the higher rate of contamination of central vein insertion cultures.

Significant differences exist, however, in the process of drawing blood between central and peripheral blood cultures. Central line insertion involves the use of a larger needle (18 gauge versus 21 gauge or 23 gauge for peripheral blood cultures), involves considerable manipulation of the skin and subcutaneous tissues during catheter insertion (management of the introducer needle, guide wire, dilator, catheter, and, more recently, ultrasound probe), and takes longer than venipuncture. Approximately 20% of skin bacteria live within the deeper

TABLE 4. Contaminant organisms by ICU

Parameter	Value for group	
	GICU	MICU
Total no. of cultures	8,087	6,502
Total no. (%) of contaminated cultures	390 (4.8)	261 (4.0)
No. of contaminated cultures (% of total no. of contaminants)		
<i>Staphylococcus</i> species	370 (94.8)	249 (95.4)
<i>Streptococcus</i> species	18 (4.6)	10 (3.8)
<i>Bacillus</i> species	1 (0.3)	0
<i>Corynebacterium</i> species	1 (0.3)	1 (0.4)
<i>Micrococcus</i> species	0	1 (0.4)

GICU - Contaminants

MICU - Contaminants

FIG. 1. Comparison of contamination rates over time for blood cultures obtained at the time of central line insertion (central) and from peripheral venipuncture (peripheral) for the general ICU (GICU) and medical ICU (MICU). The numbers of contaminants and total numbers of cultures taken per year for each source are shown under the graphs.

layers of the dermis and subcutaneous tissue, into which topical antiseptics cannot penetrate (3, 35), and these bacteria could be contaminating centrally drawn cultures. Skin flakes drawn through large needles are thought to account for a significant proportion of blood product contamination, and the diversion of initial volumes of donated blood products has reduced contamination by 40 to 90% (23, 29). Similarly, discarding the initial blood volume at phlebotomy for blood cultures decreased blood culture contamination (29). The manipulations involved in inserting a central line might increase the risk of skin flakes or of bacteria from deep subcutaneous tissues contaminating a blood culture. The longer time required for central line insertion also increases exposure to environmental (airborne) contaminants, including *Staphylococcus epidermidis* (16). The source of these bacteria may be the patient, the medical staff, or the environment (16). These bacteria are particularly attracted to statically charged plastics (6, 17) (possibly including the central catheter hub) and are known to be a source of infusion equipment colonization (17).

The higher yield of true pathogens among central cultures may reflect a difference in blood volumes sampled between central and peripheral cultures, or it may reflect sampling bias. Blood volume is positively and consistently correlated with the yield of blood cultures for both adults (26) and children (5, 13),

FIG. 2. Comparison of rates of isolation of true pathogens over time for blood cultures obtained at the time of central line insertion (central) and from peripheral venipuncture (peripheral) for the general ICU (GICU) and medical ICU (MICU). The numbers of true pathogens and total numbers of cultures taken per year for each source are shown under the graphs.

with the yield increasing by approximately 3% per additional milliliter of blood (26). Peripheral venipuncture frequently results in underfilled culture bottles (26) due to difficulties in aspirating blood. This may be particularly pronounced in critically ill and often edematous ICU patients, for whom peripheral phlebotomy is challenging. Blood aspiration at the time of central line insertion is essentially unlimited, potentially providing enough blood to adequately fill each bottle.

Regarding sampling bias, central lines are often inserted for the administration of inotropes or to direct fluid resuscitation, indications commonly associated with septic shock. Blood cultures obtained under these circumstances have a greater likelihood of detecting true bacteremia. In contrast, cultures obtained by peripheral venipuncture are often drawn for investigations of fever or leukocytosis, possibly associated with a lower pretest probability of bacteremia. The analysis of parallel central and peripheral blood culture sets may limit this bias, as the culture sets are obtained at the same time. However, even among parallel sets, central cultures were positive for true pathogens significantly more frequently than were peripheral cultures. This does not, however, exclude a blood volume effect.

The data from the arterial line cultures may shed light on these differences. Peripheral arterial lines (which account for

the vast majority of arterial lines inserted) are inserted using aseptic techniques similar to those for venipuncture, smaller needles (20 gauge) than those used for central lines, and a catheter-over-needle technique that does not require guide-wire manipulation. Blood cultures are, however, inoculated by an assisting nurse (similar to central line cultures). The contamination rate for arterial cultures was similar to that of peripheral cultures, indicating that differences in the blood inoculation phase of the procedure (nurse for arterial and central line insertion versus physician for peripheral venipuncture) likely did not account for differences in the contamination rates. The arterial contamination rate was lower than that for central lines, possibly due to the minimal manipulation required for arterial line insertion. In contrast, blood is easily drawn from arterial lines (similar to central lines), suggesting that the blood volume in arterial line cultures should be similar to that in central line cultures and higher than that in peripheral cultures. However, arterial lines are an almost universal part of intensive care, and their use is not limited to unstable or septic patients. Thus, as might be predicted, more true pathogens were found in arterial line cultures than in peripheral cultures (due to higher blood volumes) but fewer than in central line cultures (due to less selection bias).

The overall blood culture contamination rate in this study, 4%, lies within the wide range (0.42% to 15.1%) reported previously for various settings (1, 2, 4, 10, 11, 15, 19, 24, 31, 32, 34, 38) and is close to that of other ICU populations (5.5% [7]). The overall blood culture rate of detection of true pathogens is similarly consistent with those reported previously for other ICU patient series, 4.6% (7) to 12.8% (21). The decrease in blood culture contamination demonstrated over time in this study (Fig. 1) may be due to a general increase in infection control awareness and a stricter implementation of "central line bundle" elements.

Cultures in this study were not drawn from indwelling lines, either central or arterial. Such cultures are unable to reflect reliably the presence or absence of true bacteremia (12, 15, 25, 37) and often represent line colonization rather than patient infection (15). Furthermore, the disinfection of these devices may be more difficult than the disinfection of skin before blood cultures are drawn (37).

This study is subject to the limitations of a retrospective analysis. First, owing to the large number of cultures included, there was no possibility of obtaining clinical data for correlation. Second, cultures were not always obtained from central lines and peripheral venipuncture in parallel pairs. Third, some blood cultures may have been mislabeled regarding the source (central, arterial, or peripheral). Furthermore, the labeling system did not distinguish among internal jugular, subclavian, or femoral venous lines, nor did it distinguish between peripheral and femoral arterial lines. Different sites may be associated with different rates of catheter colonization (9, 14, 28). Finally, there were no observations of clinician technique.

The strengths of the study lie in the large number of blood cultures surveyed, the uniformity of the findings between two independent ICUs, and the consistency of the results over time. Moreover, the present study is the first to analyze specifically the contamination rates and yields of blood cultures obtained from central venipuncture at the time of central line insertion.

Conclusion. Despite superior aseptic techniques, cultures taken at central line insertion had a higher contamination rate than did either peripheral or arterial line insertion blood cultures. These data were consistent between two completely independent ICUs and for cultures obtained over 5.5 years. The higher contamination rate may be related to the increased skin and soft tissue manipulations performed during central line insertion. This should be considered in interpreting the results of cultures taken at the time of central line insertion and may limit the utility of such cultures.

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