

Differential Time to Positivity: A Useful Method for Diagnosing Catheter-Related Bloodstream Infections

Issam Raad, MD; Hend A. Hanna, MD, MPH; Badie Alakech, MD; Ioannis Chatzinikolaou, MD; Marcella M. Johnson, MS; and Jeffrey Tarrand, MD

Background: Catheter-related bloodstream infections are associated with recognized morbidity and mortality, especially in critically ill patients. Accurate diagnosis of such infections results in proper management of patients and in reducing unnecessary removal of catheters.

Objective: To evaluate differential time to positivity as a method for diagnosing catheter-related bacteremias caused by both short-term and long-term use of central venous catheters.

Design: Prospective study design.

Setting: M.D. Anderson Cancer Center, Houston, Texas, a tertiary care cancer center.

Patients: All patients, between September 1999 and November 2000, who had the same organism isolated from blood cultures drawn simultaneously through the central venous catheter and the peripheral vein.

Measurements: Time necessary for the blood cultures from the central venous catheter and the peripheral vein to become positive, as well as other relevant patient information.

Results: 191 bloodstream infections with positive simultaneous central venous catheter and peripheral vein blood cultures were included. One hundred eight patients had catheter-related bacteremias, and 83 had non-catheter-related bacteremias. Catheter-related bacteremias were more frequently caused by staphylococci and less likely to be associated with underlying hematologic malignant conditions, neutropenia, and longer duration of hospitalization. As a diagnostic tool for catheter-related bacteremia (using a composite definition reference standard according to the Infectious Diseases Society of America guidelines), differential time to positivity of 120 minutes or more was associated with 81% sensitivity and 92% specificity for short-term catheters and 93% sensitivity and 75% specificity for long-term catheters.

Conclusion: Differential time to positivity of 120 minutes or more is highly sensitive and specific for catheter-related bacteremia in patients who have short- and long-term catheters.

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For author affiliations, see end of text.

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Catheter-related bloodstream infections are a common type of nosocomial bloodstream infections and are associated with the use of central venous catheters (1, 2). Kluger and Maki (3) estimated that more than 200 000 cases of catheter-related bloodstream infections occur annually in the United States, with an attributable mortality rate of 12% to 25% (3). However, despite their high frequency of occurrence and seriousness, such infections are often difficult to diagnose. Clinical manifestations of this type of infection, such as fever and chills, are sensitive but not specific for a diagnosis, whereas other manifestations, such as catheter-site inflammation, are specific but not sensitive.

For the past 25 years, semiquantitative (for example, the roll-plate technique) and quantitative (for example, sonication) methods of catheter culture have been used to establish the diagnosis of catheter-related bloodstream infection (4-6). However, because taking catheter cultures requires the removal or exchange of the catheter, it only minimally affects management of the infection (7). To avoid unnecessary removal of the central venous catheter, some researchers have suggested taking simultaneous quantitative blood cultures from the catheter and the peripheral vein (8, 9). This method has been limited because quantitative blood cultures are labor intensive and costly and therefore are not widely used in clinical microbiology laboratories.

Recently, Blot and colleagues (10, 11) reported that the measurement of differential time to positivity between

blood cultures drawn through the central venous catheter and those drawn from the peripheral vein is highly diagnostic of catheter-related bloodstream infection in patients with long-term catheters. The differential time to positivity was defined as the difference in the time it took for a blood culture drawn through the central venous catheter and a culture drawn from a peripheral vein to become positive. Other investigators did not show that this method is highly diagnostic of catheter-related bloodstream infection in patients with short-term (<30 days of dwell time) catheters. However, all of the studies reported so far have included a very small number of evaluable patients who had positive simultaneous blood cultures from both the central venous catheter and the peripheral vein (12-14). To investigate the diagnostic usefulness of differential time to positivity, we decided a priori to follow for a year patients who grew the same organism from blood cultures drawn simultaneously through the central venous catheter and peripheral vein. We hypothesized that the diagnostic utility of differential time to positivity would differ between patients who had short-term catheters and those who had long-term catheters.

METHODS

Patients

The study took place at the University of Texas M.D. Anderson Cancer Center, in Houston, Texas, between 1

September 1999 and 1 November 2000. We evaluated the results of all blood cultures drawn simultaneously from the central venous catheter and peripheral vein and prospectively followed patients who had positive simultaneous blood cultures that grew the same organisms. Information obtained on these patients included age, sex, underlying disease, duration of hospitalization, duration of stay in the intensive care unit, history of bone marrow transplantation, type of catheter, number of catheter lumen, catheter insertion site, and duration of catheterization. We also evaluated patients for neutropenia, thrombocytopenia, concomitant infections, therapy with antimicrobial agents, and outcome of infections.

Definitions and Diagnosis

We defined differential time to positivity as the difference in time needed for blood cultures drawn simultaneously through the central venous catheter and from a peripheral vein to become positive. As in previous studies, differential time to positivity was considered positive (that is, suggestive of catheter-related bloodstream infection) if the blood culture drawn through the central venous catheter became positive at least 120 minutes earlier than a positive culture drawn simultaneously from a peripheral vein. Significant colonization of the catheter tip was defined as a positive semiquantitative catheter culture by the roll-plate method, whereby at least 15 colony-forming units (CFUs) of an organism were cultured from the catheter tip (4). We used 3 definitions of catheter-related bloodstream infection in this study to evaluate the diagnostic accuracy of differential time to positivity. All of the definitions included the presence of clinical signs and symptoms of bacteremia, such as fever and chills, in the absence of sources for the bacteremia other than the catheter. The definitions were as follows:

1. *Composite definition of catheter-related bloodstream infection as defined by the recent Infectious Disease Society of America (IDSA) guidelines (15):* Positive simultaneous blood cultures from the central venous catheter and peripheral vein yielding the same organism in the presence of either significant catheter-tip colonization with 15 CFUs or more of the same organism (same species and antibiogram) isolated from the blood cultures, or simultaneous quantitative blood cultures in which the number of CFUs isolated from the blood drawn through the central venous catheter was at least 5-fold greater than the number isolated from blood drawn percutaneously.

2. *Partial definition based on simultaneous quantitative blood cultures:* The presence of at least 5 times the number of CFUs from the central venous catheter blood culture compared with that the number from the peripheral vein blood culture.

3. *Partial definition based on semiquantitative catheter culture:* Catheter-tip culture with at least 15 CFUs of the same organism isolated from the peripheral vein blood culture.

Context

Diagnosing central venous catheter-related bloodstream infections may be difficult.

Contribution

This prospective study from a tertiary care cancer center examined 191 infections with the same organism detected from simultaneously drawn central and peripheral blood cultures. Catheter-tip colonization or quantitative blood cultures defined catheter-related bloodstream infection. When the culture drawn from the catheter became positive at least 120 minutes earlier than the peripherally drawn culture, the odds of catheter-related bloodstream infection increased by a factor of 5.9.

Implications

Differential time to positivity of at least 120 minutes between centrally and peripherally drawn blood cultures helps diagnose catheter-related bloodstream infection.

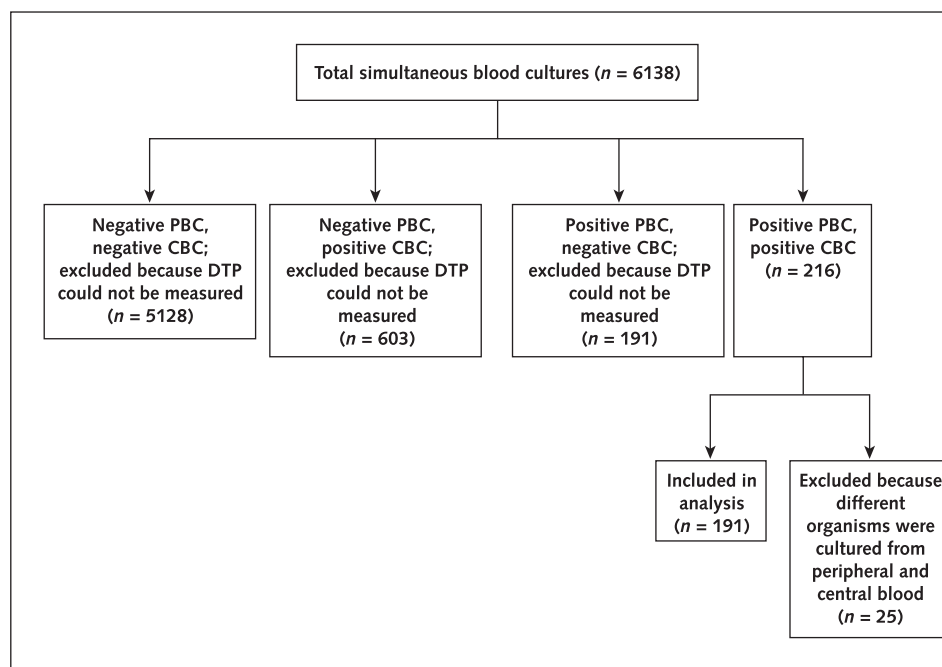
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A bloodstream infection originating from a noncatheter source was defined as one with positive blood cultures from the central venous catheter and peripheral vein that did not fulfill any of the criteria of quantitative catheter-related bloodstream infection or tip culture-based bloodstream infection, as defined earlier. Evaluable cases of bloodstream infection were those with positive simultaneous blood cultures of the same organisms from the central venous catheter and peripheral vein, in which it was possible to determine the source of the bloodstream infection (catheter or otherwise) on the basis of the definitions outlined earlier. Short-term central venous catheters were those with a dwell time of less than 30 days, and long-term central venous catheters were those with a dwell time of 30 days or more. The principal investigator determined whether infections were catheter related and had no knowledge of differential time to positivity at the time of adjudication of the reference standard definitions.

Culture Techniques

After rigorous antiseptic cleansing of the skin and the hub with 70% alcohol, we drew quantitative and qualitative blood cultures from the peripheral vein and central venous catheter hub simultaneously (maximum of 15 minutes apart). From the central venous catheter, we drew 7 to 10 mL of blood and then discarded the sample to avoid contamination with previously administered agents that could have antimicrobial activity. We subsequently drew 20 mL of blood through the central venous catheter and divided the sample into 2 portions. We placed 10 mL in isolator tubes (isolator 10, Wampole, Cranbury, New Jersey) for quantitative culturing by using the lysis centrifugation method, as described elsewhere (16). Another 10 mL of blood was placed in a regular aerobic blood culture

Figure 1. Flow diagram of blood cultures during the study period.



CBC = central blood culture; DTP = differential time to positivity; PBC = percutaneous blood culture.

bottle (aerobic 26+, Becton Dickinson DIS, Sparks, Maryland). We also drew 20 mL of blood percutaneously and processed the sample in the same manner as the blood culture from the central venous catheter. All blood culture bottles were taken promptly to the microbiology laboratory and placed in an automatic culture detector (Bactec 9240, Bactec Plus Aerobic/F, Becton Dickinson DIS, Sparks, Maryland), which records culture positivity every 15 minutes according to changes in fluorescence related to microbial growth. Catheters were removed aseptically, at the discretion of primary care physicians, if they were no longer needed or if infection was suspected. A 5-cm segment of the removed catheter tip was aseptically cut and delivered to the microbiology laboratory for culture by the semi-quantitative roll-plate method (4).

Statistical Analysis

We divided the study sample into 2 groups, those with catheter-related bloodstream infection and those without, on basis of the composite definition of catheter-related bloodstream infection according to IDSA guidelines (15). We determined the significance of the differences between the 2 study groups using the chi-square test or the Fisher exact test, as appropriate, for categorical variables. The Student *t*-test or Mann-Whitney test was used for continuous variables. All *P* values were based on 2-tailed tests (level of significance, $P \leq 0.05$). Sensitivity, specificity, and likelihood ratios, along with associated 95% CIs, were determined for differential time to positivity of 120 minutes or more. We constructed a receiver-operator characteristic (ROC) curve, using the composite definition of catheter-

related bloodstream infection, by plotting the true-positive rate (sensitivity) against the false-positive rate ($1 - \text{specificity}$) over a range of cutoff values of differential time to positivity. We estimated the ROC curve area with a non-parametric procedure. Statistical analyses were performed by using SPSS, version 11.0 for Windows (SPSS, Inc., Chicago, Illinois).

RESULTS

Between September 1999 and November 2000, we analyzed 6138 pairs of simultaneously drawn blood cultures. Of these, 5128 pairs (83.5%) had negative central venous catheter blood cultures and peripheral vein blood cultures, 603 pairs (9.8%) had positive central venous catheter blood cultures and negative peripheral vein blood cultures, and 191 pairs (3.1%) had negative central venous catheter blood cultures and positive peripheral vein blood cultures. We excluded these 5922 pairs of cultures from the analysis because the study's objective was to evaluate differential time to positivity when both cultures were positive. Another 216 pairs of cultures (3.5%) had positive results on both the central venous catheter blood cultures and peripheral vein blood cultures. Of these, we excluded 25 pairs because the central venous catheter blood cultures and peripheral vein blood cultures had different organisms. We included in the analysis the remaining 191 pairs, which were positive simultaneous blood cultures that grew the same organism (Figure 1).

Table 1 shows characteristics of patients during the

Table 1. Characteristics of Patients with Catheter-Related Bloodstream Infections*

Characteristic	Patients with CRBSI	Patients with Non-CRBSI	P Value
All patients, <i>n</i>	108	83	
Men, <i>n</i> (%)	73 (68)	61 (74)	>0.2
Age, <i>y</i>	50 ± 18	54 ± 15	>0.2
Underlying disease, <i>n</i> (%)			
Leukemia	30 (28)	47 (57)	<0.001
Lymphoma or myeloma	25 (23)	14 (17)	>0.2
Solid tumor	53 (49)	22 (27)	0.002
Hospitalization, <i>n</i> (%)	91 (84)	81 (98)	0.002
Duration of hospitalization, <i>d</i>	13 ± 16	15 ± 12	>0.2
Intensive care unit stay, <i>n</i> (%)	17 (16)	16 (19)	>0.2
Duration of stay in intensive care unit, <i>d</i>	8 ± 11	5 ± 5	>0.2
Bone marrow transplantation in previous year, <i>n</i> (%)	9 (8)	17 (21)	0.02
Neutropenia during study, <i>n</i> (%)†	40 (37)	57 (69)	<0.001
Duration of neutropenia, <i>d</i>	9 ± 9	19 ± 16	<0.001
Thrombocytopenia during study, <i>n</i> (%)‡	64 (59)	66 (80)	0.003
Duration of thrombocytopenia, <i>d</i>	27 ± 36	42 ± 38	0.02
Response, <i>n</i> (%)	103 (95)	73 (88)	0.06
Relapse, <i>n</i> (%)	2 (2)	5 (6)	0.1
Died during hospitalization, <i>n</i> (%)	7 (7)	15 (18)	0.01
Catheter type, <i>n</i> (%)			
Silicone percutaneous	98 (91)	60 (72)	0.001
Rigid wall or polyurethane	3 (3)	16 (19)	<0.001
Port	6 (6)	5 (6)	>0.2
Quinton	1 (1)	1 (1)	>0.2
Duration of catheter, <i>d</i>	91 ± 124	72 ± 103	>0.2
Long-term catheterization (>30 d)	72 (67)	44 (53)	0.06
Differential time to positivity, <i>min</i>	503 ± 628	−110 ± 1174	<0.001
Differential time to positivity ≥120 min, <i>n</i> (%)	96 (89)	14 (17)	<0.001
Blood culture organisms, <i>n</i> (%)			
Staphylococcal organisms	66 (60)	36 (43)	0.02
Gram-positive organisms	83 (77)	55 (66)	0.11
Gram-negative organisms	17 (16)	25 (30)	0.02

* Numbers in the table are based on the composite definition of CRBSI. Values presented with a plus/minus sign are means ± SD. CRBSI = catheter-related bloodstream infection.

† Defined as an absolute neutrophil count $<0.5 \times 10^9$ cells/L.

‡ Defined as a platelet count $<100 \times 10^9$ cells/L.

study period. We removed and cultured the central venous catheter in 119 patients (62%). We found 108 catheter-related bloodstream infections and 83 non-catheter-related bloodstream infections, according to the composite definition. Of the 108 patients with catheter-related bloodstream infection, 107 met the quantitative blood culture definition; of these, 33 also met the catheter culture definition. Patients with non-catheter-related bloodstream infections were more likely to have underlying hematologic

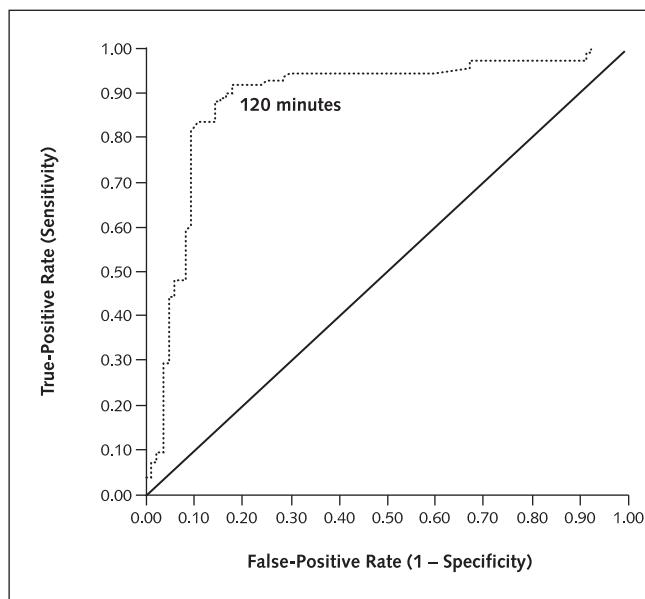
malignant conditions with previous bone marrow transplantation and a longer duration of hospitalization, as well as a higher frequency and longer duration of neutropenia and thrombocytopenia. In addition, as shown in Table 1, patients with non-catheter-related bloodstream infections were more likely to have rigid-wall polyurethane central venous catheters and gram-negative bacillary bacteremia, whereas patients with catheter-related bloodstream infections tended to have a higher frequency of silicone percu-

Table 2. Different Threshold Values for Differential Time to Positivity*

Differential Time to Positivity	CRBSI		Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
	Yes	No				
	<i>n</i>		%			
≥150 min	94	12	87 (81–93)	86 (78–93)	6.02 (3.55–10.21)	0.15 (0.09–0.25)
120–149 min	2	2	89 (83–95)	83 (75–91)	5.27 (3.25–8.54)	0.13 (0.08–0.23)
100–119 min	1	1	90 (84–96)	82 (74–90)	4.97 (3.13–7.89)	0.12 (0.07–0.22)
60–99 min	2	3	92 (86–97)	78 (69–87)	4.23 (2.80–6.39)	0.11 (0.06–0.20)
30–59 min	3	12	94 (90–99)	64 (54–74)	2.61 (1.96–3.49)	0.09 (0.04–0.19)
15–29 min	0	13	94 (90–99)	48 (37–59)	1.82 (1.47–2.25)	0.12 (0.05–0.26)
<15 min	6	40	–	–	–	–
Total	108	83				

* CRBSI = catheter-related bloodstream infection, using the composite definition.

Figure 2. A receiver-operating characteristic curve showing the accuracy of differential time to positivity of 120 minutes or more as a diagnostic test for catheter-related bloodstream infection.



taneous catheters and staphylococcal bacteremia. When the composite definition of catheter-related bloodstream infection was used, patients with this type of infection were significantly more likely to have a differential time to positivity of 120 minutes or more than were patients with non-catheter-related bloodstream infections ($P < 0.001$). We estimated the mean area under the ROC curve (\pm SE) as 0.89 ± 0.03 (95% CI, 0.83 to 0.94). Table 2 shows different threshold values for differential time to positivity and corresponding likelihood ratios, and Figure 2 shows the ROC curve.

Differential time to positivity of 120 minutes or more was associated with high sensitivity and specificity, based on the composite definition of catheter-related bloodstream infection as shown in Table 3. Differential time to positivity of 120 minutes or more was also associated with high sensitivity and specificity according to the partial definition, based on positive simultaneous quantitative blood cultures with at least 5 times the number of CFUs from central venous catheter blood cultures compared with peripheral vein blood cultures. Among patients whose catheters were removed and cultured during the 1-month follow-up, a differential time to positivity of 120 minutes or more was associated with low specificity according to another definition of catheter-related bloodstream infection based on a positive catheter-tip culture with at least 15 CFUs in the presence of a positive peripheral vein blood culture with the same organism (Table 3). The high frequency of false-positive results, in which 56% of patients with a non-catheter-related bloodstream infection (36 of 64), based on the partial catheter-tip culture definition,

had a positive differential time to positivity of 120 minutes or more, contributed to the low specificity.

Table 4 shows that a differential time to positivity of 120 minutes or more was associated with high sensitivity and specificity for short-term catheters (<30 days) and long-term catheters (≥ 30 days). The sensitivity and specificity of differential time to positivity for short-term catheters were 81% and 92%, respectively. For long-term catheters, the specificity was lower at 75% but sensitivity was higher at 93% (Table 4).

A post hoc subanalysis was performed to evaluate the utility of differential time to positivity of 120 minutes or more in diagnosing catheter-related bloodstream infection (using the composite definition) if patients were receiving antibiotics when simultaneous blood cultures were drawn. As shown in Table 4, of the 173 patients who did not receive antibiotics, the sensitivity and specificity of a differential time to positivity of 120 minutes or more were 89% and 88%, respectively. However, for the 18 patients who were receiving antibiotics when the simultaneous blood cultures were done, the specificity was only 29% and the sensitivity remained high at 91%.

DISCUSSION

This study supports the findings of Blot and colleagues (10, 11) that the differential time to positivity of 120 minutes or more is sensitive, specific, and predictive of catheter-related bloodstream infection. Unlike previous studies that have used differential time to positivity to diagnose catheter-related bloodstream infection, our study is unique in 3 aspects. First, it included a large number of patients ($n = 191$) who had positive simultaneous blood cultures; the number of patients included in our study exceeds the total sum of all patients included in the previous 5 studies (Table 5). Second, we relied on a composite definition of catheter-related bloodstream infection proposed by the IDSA (15), which, in the absence of any other probable source of bacteremia, includes simultaneous quantitative blood cultures (≥ 5 -fold greater number of CFUs in the central venous catheter blood cultures compared with the peripheral vein blood cultures) or semiquantitative catheter-tip culture (tip growing ≥ 15 CFUs or more of the same organism isolated from a peripheral vein blood culture). As shown by the ROC curve analysis, the cutoff value of differential time to positivity of 120 minutes fulfills the optimal interplay between high sensitivity and high specificity required of reliable diagnostic tests. Previous studies have relied mostly on a partial definition of catheter-related bloodstream infection that was based only on a quantitative catheter-tip culture (10–13), whereas Seifert and coworkers (14) relied only on simultaneous quantitative blood cultures. Third, we included a subanalysis on the diagnostic utility of differential time to positivity for short-term (<30 days) and long-term (≥ 30 days) catheters as well as a post hoc subanalysis of patients who re-

Table 3. Diagnostic Utility of Differential Time to Positivity According to Various Definitions of Catheter-Related Bloodstream Infection*

Definition	DTP Results	CRBSI		Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
		Yes	No				
		<i>min</i>	<i>n</i>				
Composite†	≥120	96	14	89 (83–95)	83 (75–92)	5.27 (3.25–8.54)	0.13 (0.08–0.23)
	<120	12	69				
Partial quantitative blood culture‡	≥120	99	11	90 (84–96)	86 (79–94)	6.63 (3.81–11.52)	0.11 (0.07–0.20)
	<120	11	70				
Partial catheter-tip culture§	≥120	32	36	73 (60–86)	45 (32–56)	1.29 (0.98–1.71)	0.62 (0.36–1.09)
	<120	12	28				

* CRBSI = catheter-related bloodstream infection; DTP = differential time to positivity.

† Simultaneous quantitative blood cultures in which the colonies isolated from the central venous catheter blood culture are > 5-fold greater than those isolated from the peripheral vein blood culture or significant catheter-tip colonization with ≥ 15 colony-forming units of the same blood organism, or both.

‡ ≥ 5-to-1 ratio of colony-forming units from a central venous catheter blood culture compared with a peripheral vein blood culture.

§ Tip culture with ≥ 15 colony-forming units of the same organism isolated from the peripheral vein blood culture.

ceived or did not receive antibiotics at the time of the first positive simultaneous blood cultures.

Data from our study show that a differential time to positivity of 120 minutes or more is highly sensitive and specific in diagnosing catheter-related bloodstream infection associated with the use of short- and long-term catheters. Rijnders and coworkers (12) recently published a study evaluating the differential time to positivity in the diagnosis of catheter-related bloodstream infections in critically ill patients and concluded that this method is associated with a low specificity and predictive value in patients with short-term catheters. However, the low specificity and predictive values in that study may be attributed to 2 factors: the small number of patients with positive simultaneous blood cultures ($n = 10$) and the larger number (most of the patients studied) who were receiving antibiotics when the simultaneous blood cultures were drawn. In addition, Rijnders and colleagues relied on a partial definition involving a positive quantitative culture from the cen-

tral venous catheter tip (12). Similarly, Mermel and colleagues (13) included a small number of evaluable patients ($n = 22$) and used a partial definition that relied on central venous catheter tip cultures (Mermel LA. Personal communication). Mermel and colleagues (13) reported a low specificity of 69% and a negative predictive value of 56% (Table 5). In our study, when we used a definition of catheter-related bloodstream infection based on semiquantitative catheter-tip cultures, the specificity of differential time to positivity was only 45% (Table 3). Furthermore, when we determined the diagnostic utility of differential time to positivity in patients who were receiving antibiotics when the first positive simultaneous blood cultures were drawn, the specificity was only 29% (Table 4). Once these factors (limited definition, small number of patients, and antibiotic use) are accounted for, a differential time to positivity of 120 minutes or more may still prove to be a reliable method in diagnosing catheter-related bloodstream infections in patients with short-term catheters.

Table 4. Diagnostic Utility of Differential Time to Positivity in Determining Catheter-Related Bloodstream Infection in Short-Term and Long-Term Catheters*

Variable	DTP Results	CRBSI†		Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
		Yes	No				
		<i>min</i>	<i>n</i>				
Catheter type							
Short-term (<30-d dwell time)	≥120	29	3	81 (68–93)	92 (84–100)	10.47 (3.49–31.43)	0.21 (0.11–0.41)
	<120	7	36				
Long-term (≥30-d dwell time)	≥120	67	11	93 (87–99)	75 (62–88)	3.72 (2.22–6.23)	0.09 (0.04–0.22)
	<120	5	33				
Antibiotic status‡							
Did not receive antibiotics	≥120	86	9	89 (82–95)	88 (81–95)	7.49 (4.04–13.88)	0.13 (0.07–0.23)
	<120	11	67				
Received antibiotics	≥120	10	5	91 (74–100)	29 (0–62)	1.27 (0.77–2.11)	0.32 (0.04–2.89)
	<120	1	2				

* CRBSI = catheter-related bloodstream infection; DTP = differential time to positivity.

† As defined by the composite definition.

‡ Received antibiotics before the first positive blood culture.

this diagnostic test in a broader, heterogeneous patient population.

In conclusion, the differential time to positivity of 120 minutes or more for positive simultaneous blood cultures was significantly associated with catheter-related bloodstream infection defined according to a composite definition suggested by the IDSA guidelines. This method was highly sensitive and specific for diagnosis of catheter-related bloodstream infections in patients with cancer who had short-term and long-term catheters. However, this method was associated with low specificity in patients who received antibiotics before simultaneous blood cultures were obtained. Because only a few patients were included in this post hoc subanalysis, the effect of antibiotics needs to be investigated further in well-designed prospective studies. This method does not correlate well with the results of semiquantitative catheter cultures performed more than 1 day after obtaining simultaneous blood cultures. Finally, the accuracy of this method requires accurate tracking of the source of blood cultures (central venous catheter vs. peripheral vein), as well as simultaneous placement of the cultures in the automated machine.

From University of Texas M.D. Anderson Cancer Center, Houston, and Texas Tech University Medical School, Lubbock, Texas.

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Requests for Single Reprints: Hend Hanna, MD, Department of Infectious Diseases, Infection Control and Employee Health, University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard (Unit 402), Houston, TX 77030; e-mail, hhanna@mdanderson.org.

Current author addresses and author contributions are available at www.annals.org.

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Current Author Addresses: Drs. Raad, Hanna, Alakech, Chatzinikolaou, and Tarrand and Ms. Johnson: Department of Infectious Diseases, Infection Control and Employee Health, University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard (Unit 402), Houston, TX 77030.

Author Contributions: Conception and design: I. Raad, H.A. Hanna. Analysis and interpretation of the data: I. Raad, H.A. Hanna. Drafting of the article: I. Raad, H.A. Hanna.

Critical revision of the article for important intellectual content: I. Raad, H.A. Hanna.

Final approval of the article: I. Raad, H.A. Hanna, B. Alakech, I. Chatzinikolaou, M.M. Johnson, J. Tarrand.

Provision of study materials or patients: J. Tarrand.

Statistical expertise: H.A. Hanna, M.M. Johnson.

Collection and assembly of data: H.A. Hanna, B. Alakech, I. Chatzinikolaou.