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Value of Superficial Cultures for Prediction of Catheter-Related Bloodstream Infection in Long-Term Catheters: a Prospective Study

M. Guembe,[a] P. Martín-Rabadán,[a] A. Echenagusia,[b] F. Camúñez,[b] G. Rodríguez-Rosales,[b] G. Simó,[b] M. Echenagusia,[b] E. Bouza,[a,b] on behalf of the GEIDI Study Group

Department of Clinical Microbiology and Infectious Diseases, Hospital General Universitario Gregorio Marañón, Instituto de Investigación Sanitaria del Hospital Gregorio Marañón, Universidad Complutense, Madrid, Spain[a]; Department of Vascular Interventional Radiology, Hospital General Universitario Gregorio Marañón, Madrid, Spain[b]

Cultures taken from the skin and from the hubs of short-term central venous catheters can help us to predict catheter-related bloodstream infections (C-RBSIs). The value of these cultures for such predictions has not been assessed in long-term catheters. Our objective was to assess the value of superficial cultures for the prediction of C-RBSI among patients with long-term catheters. Over a 2-year period, we prospectively obtained cultures from the skin overlying reservoir ports (group A) and from the skin insertion site and hubs of all tunneled catheters (group B). This routine was performed by vascular and interventional radiologists immediately before catheter removal (irrespective of the reason for withdrawal). Swabs were processed semiquantitatively. Catheter tips from both groups were cultured using Maki's semiquantitative technique and sonication. We also performed cultures of the reservoir ports at different sites. C-RBSI was defined as the isolation of the same species of microorganism(s) both in the colonized catheter and in at least 1 peripheral blood culture. We included 372 catheters (group A, 223; group B, 149) during the study period. The catheter colonization rate was 23.4% (87/372), and 28 patients had C-RBSI. Validity index values for the capacity of surface cultures to predict C-RBSI in groups A and B were, respectively, as follows: sensitivity, 23.5% and 45.5%; specificity, 59.7% and 63.0%; positive predictive value, 4.6% and 8.9%; and negative predictive value, 90.4% and 93.5%. Superficial cultures of patients with long-term catheters could help us to rule out the catheter as the portal of entry of bloodstream infections. Superficial cultures (from skin and hubs) proved to be a useful conservative diagnostic tool for ruling out C-RBSI among patients with long-term tunneled catheters and totally implantable venous access ports.

Catheter-related bloodstream infection (C-RBSI) is an important nosocomial entity with high rates of morbidity and mortality (1–5). Patients undergoing chemotherapy or hemodialysis are at risk of developing C-RBSI, as they need a permanent intravascular device. Although C-RBSI rates are low in these patients (6–12), the difficulties and complications attributable to catheter replacement require the use of alternative diagnostic tools which allow us to predict infection without having to withdraw the catheter.

Microorganisms colonizing skin, hubs, or both are considered the first step to catheter tip colonization and, consequently, to C-RBSI (13–15). Therefore, superficial cultures (skin and hubs) are good diagnostic tools for predicting catheter colonization and C-RBSI. However, they have been tested only in patients with short-term central venous catheters, who are mainly admitted to intensive care units (13, 16). Data on the usefulness of superficial cultures in a subpopulation using long-term catheters are scarce.

The purpose of our study was to assess the validity values of superficial cultures for the prediction of C-RBSI in patients with long-term tunneled catheters and totally implantable venous access ports.

MATERIALS AND METHODS

Setting. We performed a prospective study between July 2009 and April 2011 at a large tertiary institution in Madrid, Spain.

We included all long-term central venous catheters that were routinely removed in the Vascular and Interventional Radiology Department, irrespective of the reason for withdrawal. No antimicrobial-coated catheters were used during the study period.

Catheters were classified into two groups: group A, totally implantable venous access ports; and group B, tunneled central venous catheters.

Laboratory procedures. Catheter tips from groups A and B were analyzed using Maki's semiquantitative roll-plate technique and the sonication method in a random order (1:1). The roll-plate technique was applied by transferring each catheter tip to a plate with Columbia agar supplemented with 5% sheep blood and rolling the tip back and forth across the surface at least 3 to 4 times (17). Sonication was performed by placing the catheter tip in 10 ml of brain heart infusion broth, sonicating for 1 min (at 55,000 Hz and 125 W), and vortexing for 15 s. Then, 0.1 ml of the sonicated broth and 0.1 ml of a 1:100 dilution of the broth were streaked onto sheep blood agar plates. The plates were incubated aerobically for 48 h at 37°C. The colonies recovered were counted (18).

We performed venous access port cultures (Columbia blood agar) using the following samples and sites: port content aspirate before and after sonication, port sonication fluid, and port internal surface biofilm. The laboratory management of venous access port sites was as described in a previous study by our group (19).

The microorganisms recovered from catheter cultures were fully identified by standard microbiologic methods using an automated MicroScan system with POS Combo Panel Type 2S and NEG Combo Panel Type 1S (Dade Behring, Sacramento, CA).

Superficial cultures. Cultures from the skin insertion site (groups A and B) and all hubs (group B) were collected immediately before catheter withdrawal. For skin samples, a dry cotton swab was rubbed over a 2-cm^2 area around the insertion site. For hub samples, an alginate swab was

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Address correspondence to M. Guembe, mariaguembe@hotmail.com.

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TABLE 1 Patient and catheter characteristics[a]

Characteristic	Value(s)		
	Overall	Group A	Group B
No. of patients	360	222 (61.7)	138 (38.3)
Median age (IQR) in yr	56.19 (0–87)	54.27 (18.06)	58.2 (16–87)
Male	167 (44.9)	90 (40.5)	73 (52.9)
Underlying disease			
Cancer	303 (83.9)	223 (100)	80 (58.0)
Renal failure	58 (16.1)	0 (0.0)	58 (42.0)
Cumulative no. of days of catheter use	164,582	139,120	25,462
Median (IQR) no. of days of catheter use	270 (83.25–622.50)	440 (212–907)	137 (59–237)
Median (IQR) no. of times of catheter use	20 (0.0–50.0)	20 (1.75–50.0)	40 (20–72)
Type of catheter			
Port-A-Cath	223 (59.9)	223 (100)	0 (0.0)
Hickman	89 (23.9)	0 (0.0)	89 (59.7)
Permcath	60 (16.1)	0 (0.0)	60 (40.3)
Site of catheter insertion			
Jugular vein	335 (90.1)	202 (90.6)	133 (89.3)
Subclavian vein	37 (9.9)	21 (9.4)	16 (10.7)
Reason for catheter withdrawal			
End of use	220 (59.1)	135 (60.5)	85 (57.0)
Suspicion of bloodstream infection	84 (22.6)	44 (19.7)	40 (26.8)
Suspicion of local infection	37 (9.9)	22 (9.9)	15 (10.1)
Obstruction-malfunction	22 (5.9)	15 (6.7)	7 (4.7)
Thrombosis	6 (1.6)	4 (1.8)	2 (1.3)
Other	3 (0.8)	3 (1.3)	0 (0.0)
Appearance of insertion site			
Intact	316 (84.9)	192 (86.1)	124 (83.2)
Swollen	42 (11.3)	18 (8.1)	24 (16.1)
Ulcerated	11 (3.0)	10 (4.5)	1 (0.7)
Suppurative	3 (0.8)	3 (1.3)	0 (0.0)
Catheter colonization	87 (23.4)	48 (21.5)	39 (26.2)
Microorganisms isolated in colonized catheters			
Gram-positive bacteria	78 (72.9)	44 (74.6)	34 (70.8)
Gram-negative bacteria	18 (16.8)	8 (13.6)	10 (20.8)
Yeasts	11 (10.3)	7 (11.9)	4 (8.3)
Total	107	59	48

[a] Values represent numbers (%) of patients except where otherwise indicated. Group A, totally implantable venous access ports; group B, long-term tunneled catheters; IQR, interquartile range.

introduced in each hub and rubbed 3 times against the inner surface. When swabs arrived at the laboratory, they were rubbed onto Columbia blood agar and incubated aerobically for 48 h at 37°C. The colonies recovered were counted. Cultures with ≥15 CFU/plate were considered positive (13). The microorganisms recovered from cultures were identified by their phenotypic characteristics.

Definitions. (i) Tunneled catheter colonization. Tunneled catheter colonization was defined as detection of the presence of a positive semiquantitative tip culture by either the roll-plate technique (≥15 CFU/plate) or the sonication method (≥100 CFU/plate) (20).

(ii) Venous access port colonization. Venous access port colonization was defined as detection of the presence of a positive semiquantitative tip culture by either the roll-plate technique (≥15 CFU/plate) or the sonication method (≥100 CFU/plate) and/or a positive quantitative culture (≥100 CFU/ml) of port content aspirate before or after sonication or of port sonication fluid or a positive qualitative culture of port internal surface biofilm.

(iii) Gold standard for C-RBSI. The gold standard for C-RBSI detection was defined as isolation of the same microorganism(s) in both the colonized catheter and at least 1 peripheral blood culture obtained 7 days before or after catheter withdrawal (21).

Statistical analysis. Qualitative variables are expressed as a frequency distribution and quantitative variables as means and standard deviations or median and interquartile ranges (nonnormal distribution).

Validity values were defined as follows: sensitivity, proportion of colonized catheters causing C-RBSI detected using the tested culture with respect to the total number of colonized catheters causing C-RBSI detected by the gold standard; specificity, proportion of noncolonized catheters not causing C-RBSI detected using the tested culture with respect to the total noncolonized catheters not causing C-RBSI detected by the gold

TABLE 2 Description of the 28 C-RBSI episodes[a]

Characteristic	Value(s)		
	Overall	Group A	Group B
No. of C-RBSI episodes	28	17 (60.7)	11 (39.3)
Median (IQR) age in yr	59.28 (47.03–67.86)	55.05 (18.75)	59.8 (42.5–68.6)
Male	15 (53.6)	11 (64.7)	4 (36.4)
Underlying disease			
Cancer	22 (78.6)	17 (100)	5 (45.5)
Renal failure	6 (21.4)	0 (0.0)	6 (54.5)
Median (IQR) Charlson comorbidity index	4 (2–5.75)	5 (2.0–7.5)	4 (2–5)
Mean (SD) McCabe-Jackson index	2.68 (0.670)	2.59 (0.712)	2.82 (0.603)
Cumulative no. of days of catheter use	13,838	12,303	1,535
Median (IQR) no. of days of catheter use	248 (55.75–726.75)	613 (163.50–1,082.50)	119.5 (37.8–246.3)
Site of catheter insertion			
Jugular vein	24 (85.7)	13 (76.5)	11 (100)
Subclavian vein	4 (14.3)	4 (23.5)	0 (0.0)
Time that blood cultures were drawn			
Before catheter withdrawal	25 (89.3)	15 (88.2)	10 (90.9)
At catheter withdrawal	1 (3.6)	0 (0.0)	1 (9.1)
After catheter withdrawal	2 (7.1)	2 (11.8)	0 (0.0)
Reason for catheter withdrawal			
Suspicion of bloodstream infection	23 (82.1)	13 (76.5)	10 (90.9)
Suspicion of local infection	5 (17.9)	4 (23.5)	1 (9.1)
Appearance of insertion site			
Intact	12 (42.9)	5 (29.4)	7 (63.6)
Ulcerated	6 (21.4)	6 (35.3)	0 (0.0)
Swollen	8 (28.6)	4 (23.5)	4 (36.4)
Suppurative	2 (7.1)	2 (11.8)	0 (0.0)
Median (IQR) DDDs	23.85 (10.63–55.50)	29.4 (18.05–63.20)	11 (4.80–50.00)
Median (IQR) total days of therapy	16 (10.25–27.75)	19 (14–28)	16 (6–27)
Microorganisms causing C-RBSI			
Gram-positive bacteria	18 (62.1)	11 (61.1)	7 (63.6)
Staphylococcus aureus	9 (31.3)	6 (33.3)	3 (27.3)
Staphylococcus epidermidis	7 (24.1)	3 (16.7)	4 (36.4)
Enterococcus faecalis	2 (6.9)	2 (11.1)	0 (0.0)
Gram-negative bacteria	7 (24.1)	4 (22.2)	3 (27.3)
Stenotrophomonas maltophilia	2 (6.9)	0 (0.0)	2 (18.2)
Proteus mirabilis	2 (6.9)	1 (5.6)	1 (9.1)
Escherichia coli	1 (3.4)	1 (5.6)	0 (0.0)
Enterobacter cloacae	1 (3.4)	1 (5.6)	0 (0.0)
Serratia marcescens	1 (3.4)	1 (5.6)	0 (0.0)
Yeasts	4 (13.8)	3 (16.7)	1 (9.1)
Candida parapsilosis	2 (6.9)	2 (11.1)	0 (0.0)
Candida glabrata	1 (3.4)	1 (5.6)	0 (0.0)
Candida tropicalis	1 (3.4)	0 (0.0)	1 (9.1)
Total	29	18	11

[a] Values represent numbers (%) of patients except where otherwise indicated. C-RBSI, catheter-related bloodstream infection, IQR, interquartile range; SD, standard deviation; DDDs, defined daily doses; Group A, totally implantable venous access ports; group B, long-term tunneled catheters.

standard; positive predictive value, proportion of colonized catheters causing C-RBSI detected using the tested culture matching colonized catheters causing C-RBSI detected by the gold standard with respect to the total colonized catheters causing C-RBSI detected by the tested culture; negative predictive value, proportion of noncolonized catheters not causing C-RBSI detected using the tested culture matching noncolonized catheters not causing C-RBSI detected by the gold standard with respect to the total noncolonized catheters not causing C-RBSI detected by the tested culture.

Statistical significance was set at $P \leq 0.05$.

The statistical analysis was performed using SPSS 16.0 and EPIDAT.

Ethics. The study was approved by the local ethics committee.

TABLE 3 Etiology of positive superficial cultures[a]

Microorganism	Value(s)			
	Group A (skin)	Group B		
		Global	Skin	Hubs
Gram-positive bacteria	133 (92.4)	68 (84.0)	67 (87.0)	1 (25.0)
CoNS	96 (66.7)	53 (65.4)	52 (67.5)	1 (25.0)
Corynebacterium spp.	15 (10.4)	5 (6.2)	5 (6.5)	0 (0.0)
Staphylococcus aureus	13 (9.0)	9 (11.1)	9 (11.7)	0 (0.0)
Micrococcus spp.	5 (3.5)	1 (1.2)	1 (1.3)	0 (0.0)
Enterococcus spp.	3 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)
Streptococcus viridans	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
Gram-negative bacteria	10 (6.9)	7 (8.6)	6 (7.8)	1 (25.0)
Enterobacteriaceae	4 (2.8)	5 (6.2)	4 (5.2)	1 (25.0)
NFGNB	6 (4.2)	2 (2.5)	2 (2.6)	0 (0.0)
Yeasts	1 (0.7)	6 (7.4)	4 (5.2)	2 (50.0)
Candida albicans	0 (0.0)	2 (2.5)	1 (1.3)	1 (25.0)
Candida parapsilosis	1 (0.7)	2 (2.5)	2 (2.6)	0 (0.0)
Candida glabrata	0 (0.0)	2 (2.5)	1 (1.3)	1 (25.0)
Total	144	81	77	4

[a] Values represent numbers (%) of patients except where otherwise indicated. CoNS, coagulase-negative staphylococci; NFGNB, nonfermenting Gram-negative bacilli; Group A, totally implantable venous access ports; group B, long-term tunneled catheters.

TABLE 4 Validity values of superficial cultures for the prediction of catheter-related bloodstream infection[a]

Group	Parameter	Value (%)		
		Overall	Skin	Hubs
A	S		23.5	
	SP		59.7	
	PPV		4.6	
	NPV		**90.4**	
B	S	45.5	36.4	18.2
	SP	63.0	63.8	**98.6**
	PPV	8.9	7.4	50.0
	NPV	**93.5**	**92.6**	**93.8**

[a] S, sensitivity; SP, specificity; PPV, positive predictive value; NPV, negative predictive value; group A, totally implantable venous access ports; group B, long-term tunneled catheters. Values of >90% are shown in boldface type.

RESULTS

We included 372 long-term central venous catheters from 360 patients during the study period. Of these, 223 (59.9%) were venous access ports and 149 (40.1%) were tunneled catheters. The median catheter indwelling time was 270 days (interquartile range [IQR], 83.25 to 622.50). The main underlying disease was cancer (83.9%), followed by renal failure (16.1%). Most catheters were removed because of end of use (59.1%), followed by suspicion of bloodstream infection (22.6%). Other patient and catheter characteristics are detailed in Table 1.

The overall catheter colonization rate was 23.4% (87/372), and the distribution of the isolated microorganisms was as follows: Gram-positive bacteria, 72.9%; Gram-negative bacteria, 16.8%; and yeast species, 10.3% (Table 1).

During the total of 164,582 cumulative catheter days, we found 28 episodes of C-RBSI (incidence density, 0.17 episodes/1,000 catheter days). The main underlying disease with C-RBSI was cancer (78.6%), and many patients showed no external signs of infection (42.9%). The microorganisms isolated from the C-RBSI episodes were distributed as follows: Gram-positive bacteria, 62.1%; Gram-negative bacteria, 24.1%; and yeast species, 13.8%. The most frequently isolated microorganism causing C-RBSI was *Staphylococcus aureus* (31.0%) (Table 2).

The colonization rates of superficial cultures were 39.0% (86/223) and 37.6% (56/149) in groups A and B, respectively. The most predominant microorganisms were coagulase-negative staphylococci (66.7% in group A and 65.4% in group B) (Table 3). The validity values of superficial cultures for prediction of C-RBSI in groups A and B were, respectively, as follows: sensitivity, 23.5% and 45.5%; specificity, 59.7% and 63.0%; positive predictive value, 4.6% and 8.9%; and negative predictive value, 90.4% and 93.5% (Table 4).

In group B (patients with tunneled catheters), catheter hub cultures proved to have good (98.6%) specificity for the prediction of C-RBSI.

DISCUSSION

Our study showed that negative superficial cultures allow us to rule out C-RBSI in patients with long-term catheters. Long-term central venous catheters are widely used in patients with cancer or renal failure, as these populations need a permanent vascular access for chemotherapy and hemodialysis. Therefore, they are at risk of developing C-RBSI. Rates of C-RBSI range from 0.10 to 0.37 episodes/catheter days among patients undergoing chemotherapy and 0.5 to 7.6 episodes/1,000 catheter days among patients undergoing hemodialysis (6–8, 11, 22–27).

The most appropriate procedure for confirming an episode of C-RBSI is microbiological culture, which requires the catheter to be withdrawn (20). However, in this subpopulation of patients, catheter replacement is not always possible, since it involves severe complications during the surgical insertion procedure (28–30). Therefore, conservative methods may be required for the diagnosis of C-RBSI. Evaluation of differential times to positivity (DTTP) has proven effective for the diagnosis of C-RBSI in the general population (16, 31–33). However, it requires drawn blood from all catheter hubs and from a peripheral vein, which in most cases represents a great amount of blood. This, particularly, represents a big problem in the neonatal population and in patients whose catheters have persistent occlusion. Moreover, the application of DTTP evaluation for catheter-related candidemia has not been already established (34, 35). Therefore, the use of a rapid and easy-to-perform technique such as superficial culture analysis may allow us to solve these problems.

Superficial culture analyses have proven to be useful diagnostic methods that do not require the catheter to be withdrawn, as they are performed by taking cultures from the skin around the catheter insertion site and from the internal surface of all hubs (superficial cultures). However, studies evaluating this method have been tested mainly in critical ill patients with short-term central venous catheters (13, 16). We provide novel data regarding the validity values of superficial cultures tested in patients with long-

term catheters. We demonstrate that superficial cultures had a good (93.5%) negative predictive value for C-RBSI in long-term catheters and could help us to rule out the catheter as the origin of the bacteremia without needing to remove it. Moreover, long-term catheters are colonized mainly by the intraluminal route (36), and our data showed that hub cultures from tunneled catheters had high (98.6%) specificity for predicting C-RBSI. This may enable C-RBSIs to be managed by combining systemic and lock antimicrobial therapy, thus obviating the need for catheter withdrawal.

The main limitations of our study were the low number of C-RBSI episodes and that we performed only superficial cultures before catheter withdrawal. Besides, we have no data available regarding antibiotic use before catheter withdrawal, which could partially explain the low sensitivity and the low positive predictive value. Moreover, our results may not be entirely applicable to all patients with long-term tunneled catheters or port reservoirs, as we did not include patients whose device was removed because of failure of conservative treatment. Future studies must evaluate the validity of superficial cultures while the catheter is being used as a surveillance measure.

In conclusion, superficial cultures performed on long-term central venous catheters may be useful for ruling out an episode of C-RBSI.

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We declare that we have no conflicts of interest.

REFERENCES

1. **Blot SI, Depuydt P, Annemans L, Benoit D, Hoste E, De Waele JJ, Decruyenaere J, Vogelaers D, Colardyn F, Vandewoude KH.** 2005. Clinical and economic outcomes in critically ill patients with nosocomial catheter-related bloodstream infections. Clin. Infect. Dis. **41:**1591–1598.
2. **Dimick JB, Pelz RK, Consunji R, Swoboda SM, Hendrix CW, Lipsett PA.** 2001. Increased resource use associated with catheter-related bloodstream infection in the surgical intensive care unit. Arch. Surg. **136:**229–234.
3. **Maki DG, Kluger DM, Crnich CJ.** 2006. The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. Mayo Clin. Proc. **81:**1159–1171.
4. **Renaud B, Brun-Buisson C; ICU-Bacteremia Study Group.** 2001. Outcomes of primary and catheter-related bacteremia. A cohort and case-control study in critically ill patients. Am. J. Respir. Crit. Care Med. **163:**1584–1590.
5. **Warren DK, Quadir WW, Hollenbeak CS, Elward AM, Cox MJ, Fraser VJ.** 2006. Attributable cost of catheter-associated bloodstream infections among intensive care patients in a nonteaching hospital. Crit. Care Med. **34:**2084–2089.
6. **Biffi R, de Braud F, Orsi F, Pozzi S, Mauri S, Goldhirsch A, Nole F, Andreoni B.** 1998. Totally implantable central venous access ports for long-term chemotherapy. A prospective study analyzing complications and costs of 333 devices with a minimum follow-up of 180 days. Ann. Oncol. **9:**767–773.
7. **Crisinel M, Mahy S, Ortega-Debalon P, Buisson M, Favre JP, Chavanet P, Piroth L.** 2009. Incidence, prevalence and risk factors for a first infectious complication on a totally implantable venous-access port. Med. Mal. Infect. **39:**252–258. (In French.)
8. **Groeger JS, Lucas AB, Thaler HT, Friedlander-Klar H, Brown AE, Kiehn TE, Armstrong D.** 1993. Infectious morbidity associated with long-term use of venous access devices in patients with cancer. Ann. Intern. Med. **119:**1168–1174.
9. **Hoen B, Paul-Dauphin A, Hestin D, Kessler M.** 1998. EPIBACDIAL: a multicenter prospective study of risk factors for bacteremia in chronic hemodialysis patients. J. Am. Soc. Nephrol. **9:**869–876.
10. **Kessler M, Hoen B, Mayeux D, Hestin D, Fontenaille C.** 1993. Bacteremia in patients on chronic hemodialysis. A multicenter prospective survey. Nephron **64:**95–100.
11. **Kuizon D, Gordon SM, Dolmatch BL.** 2001. Single-lumen subcutaneous ports inserted by interventional radiologists in patients undergoing chemotherapy: incidence of infection and outcome of attempted catheter salvage. Arch. Intern. Med. **161:**406–410.
12. **Wisplinghoff H, Seifert H, Wenzel RP, Edmond MB.** 2003. Current trends in the epidemiology of nosocomial bloodstream infections in patients with hematological malignancies and solid neoplasms in hospitals in the United States. Clin. Infect. Dis. **36:**1103–1110.
13. **Cercenado E, Ena J, Rodriguez-Creixems M, Romero I, Bouza E.** 1990. A conservative procedure for the diagnosis of catheter-related infections. Arch. Intern. Med. **150:**1417–1420.
14. **Liñares J, Sitges-Serra A, Garau J, Pérez JL, Martín R.** 1985. Pathogenesis of catheter sepsis: a prospective study with quantitative and semiquantitative cultures of catheter hub and segments. J. Clin. Microbiol. **21:**357–360.
15. **Templeton A, Schlegel M, Fleisch F, Rettenmund G, Schobi B, Henz S, Eich G.** 2008. Multilumen central venous catheters increase risk for catheter-related bloodstream infection: prospective surveillance study. Infection **36:**322–327.
16. **Bouza E, Alvarado N, Alcala L, Perez MJ, Rincon C, Munoz P.** 2007. A randomized and prospective study of 3 procedures for the diagnosis of catheter-related bloodstream infection without catheter withdrawal. Clin. Infect. Dis. **44:**820–826.
17. **Maki DG, Weise CE, Sarafin HW.** 1977. A semiquantitative culture method for identifying intravenous-catheter-related infection. N. Engl. J. Med. **296:**1305–1309.
18. **Sherertz RJ, Heard SO, Raad II.** 1997. Diagnosis of triple-lumen catheter infection: comparison of roll plate, sonication, and flushing methodologies. J. Clin. Microbiol. **35:**641–646.
19. **Guembe M, Marin M, Martin-Rabadan P, Echenagusia A, Camunez F, Rodriguez-Rosales G, Simo G, Echenagusia M, Bouza E.** 2013. Use of universal 16S rRNA gene PCR as a diagnostic tool for venous access port-related bloodstream infections. J. Clin. Microbiol. **51:**799–804.
20. **Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, Raad II, Rijnders BJ, Sherertz RJ, Warren DK.** 2009. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. Clin. Infect. Dis. **49:**1–45.
21. **O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, Lipsett PA, Masur H, Mermel LA, Pearson ML, Raad II, Randolph AG, Rupp ME, Saint S; Healthcare Infection Control Practices Advisory Committee (HICPAC).** 2011. Guidelines for the prevention of intravascular catheter-related infections. Clin. Infect. Dis. **52:**e162–e193.
22. **Chang L, Tsai JS, Huang SJ, Shih CC.** 2003. Evaluation of infectious complications of the implantable venous access system in a general oncologic population. Am. J. Infect. Control **31:**34–39.
23. **Fariñas MC, García-Palomo JD, Gutiérrez-Cuadra M.** 2008. Infection associated with hemodialysis and peritoneal dialysis catheters. Enferm. Infecc. Microbiol. Clin. **26:**518–526. (In Spanish.)
24. **Grothe C, da Silva Belasco AG, de Cassia Bittencourt AR, Vianna LA,**

de Castro Cintra Sesso R, Barbosa DA. 2010. Incidence of bloodstream infection among patients on hemodialysis by central venous catheter. Rev. Lat. Am. Enfermagem. **18:**73–80.
25. **Klevens RM, Edwards JR, Andrus ML, Peterson KD, Dudeck MA, Horan TC.** 2008. Dialysis surveillance report: National Healthcare Safety Network (NHSN)—data summary for 2006. Semin. Dial. **21:**24–28.
26. **Powe NR, Jaar B, Furth SL, Hermann J, Briggs W.** 1999. Septicemia in dialysis patients: incidence, risk factors, and prognosis. Kidney Int. **55:** 1081–1090.
27. **Saeed Abdulrahman I, Al-Mueilo SH, Bokhary HA, Ladipo GO, Al-Rubaish A.** 2002. A prospective study of hemodialysis access-related bacterial infections. J. Infect. Chemother. **8:**242–246.
28. **Eastridge BJ, Lefor AT.** 1995. Complications of indwelling venous access devices in cancer patients. J. Clin. Oncol. **13:**233–238.
29. **Silas AM, Perrich KD, Hoffer EK, McNulty NJ.** 2010. Complication rates and outcomes of 536 implanted subcutaneous chest ports: do rates differ based on the primary operator's level of training? Acad. Radiol. **17:**464–467.
30. **Walser EM.** 2012. Venous access ports: indications, implantation technique, follow-up, and complications. Cardiovasc. Intervent. Radiol. **35:** 751–764.
31. **Blot F, Nitenberg G, Chachaty E, Raynard B, Germann N, Antoun S, Laplanche A, Brun-Buisson C, Tancrede C.** 1999. Diagnosis of catheter-related bacteraemia: a prospective comparison of the time to positivity of hub-blood versus peripheral-blood cultures. Lancet **354:**1071–1077.
32. **Catton JA, Dobbins BM, Kite P, Wood JM, Eastwood K, Sugden S, Sandoe JA, Burke D, McMahon MJ, Wilcox MH.** 2005. In situ diagnosis of intravascular catheter-related bloodstream infection: a comparison of quantitative culture, differential time to positivity, and endoluminal brushing. Crit. Care Med. **33:**787–791.
33. **Raad I, Hanna HA, Alakech B, Chatzinikolaou I, Johnson MM, Tarrand J.** 2004. Differential time to positivity: a useful method for diagnosing catheter-related bloodstream infections. Ann. Intern. Med. **140:**18–25.
34. **Ben-Ami R, Weinberger M, Orni-Wasserlauff R, Schwartz D, Itzhaki A, Lazarovitch T, Bash E, Aharoni Y, Moroz I, Giladi M.** 2008. Time to blood culture positivity as a marker for catheter-related candidemia. J. Clin. Microbiol. **46:**2222–2226.
35. **Bouza E, Alcala L, Munoz P, Martin-Rabadan P, Guembe M, Rodriguez-Creixems M.** 2013. Can. microbiologists help to assess catheter involvement in candidaemic patients before removal? Clin. Microbiol. Infect. **19:**E129–E135.
36. **Raad I, Costerton W, Sabharwal U, Sacilowski M, Anaissie E, Bodey GP.** 1993. Ultrastructural analysis of indwelling vascular catheters: a quantitative relationship between luminal colonization and duration of placement. J. Infect. Dis. **168:**400–407.