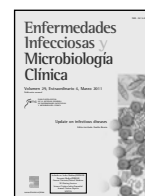




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Update on catheter-related bloodstream infections in ICU patients

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ABSTRACT

Keywords:

Catheter-related bacteremia
Intensive care unit
Risk factors

The present article is an update of the literature on catheter-related bloodstream infections in ICU patients. A multidisciplinary group of Spanish physicians with an interest in bloodstream infections selected the most important recently published papers produced in the field. One of the members of the group discussed the content of each of the selected papers, with a critical review by other members of the panel. After a review of the state of the art, papers from the fields of epidemiology, causative microorganisms (bacterial and fungal), risk factors and prognosis, pathogenesis, laboratory diagnosis and prevention were discussed by the group.

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Actualización en infecciones del torrente circulatorio relacionadas con catéteres en unidades de cuidados intensivos

RESUMEN

Palabras clave:

Bacteriemia asociada a catéter
Unidad de cuidados intensivos
Factores de riesgo

El artículo presente recoge una actualización bibliográfica de la bacteriemia relacionada con catéteres en unidades de cuidados intensivos. Un grupo multidisciplinario de clínicos españoles con experiencia en las infecciones relacionadas con catéteres seleccionó las publicaciones más importantes en este campo aparecidas recientemente. El contenido de cada uno de los artículos seleccionados fue expuesto y discutido por uno de los miembros del grupo, después de lo cual los miembros restantes efectuaron una revisión crítica. Tras la revisión de la situación actual, el grupo discutió las publicaciones procedentes de los campos de la epidemiología, la etiología, la detección de factores de riesgo, la evolución y el pronóstico, la patogénesis, el diagnóstico de laboratorio y la prevención.

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State of the art

Nosocomial bloodstream infections (BSIs) constitute a serious health problem worldwide and are associated with increased length of hospital stay and health-care costs, and, most importantly, with high morbidity and mortality^{1,2}. The incidence of hospital-acquired BSIs varies with the type of population studied, the size of the institution, and the ward location. Critically ill patients carry much higher rates of BSIs than those in general wards, with a reported incidence ranging from 3 to 10 episodes/100 intensive-care unit

(ICU) admissions and a mortality rate ranging from 32% to 82%¹⁻⁷. In the last 30 years, the frequency, etiology, and epidemiology of nosocomial BSI have changed with the evolution of medical care, particularly among the increasing number of hospitalized patients who require intensive care. Nearly 75% of primary bloodstream infections have been caused by Gram-negative bacilli. This is due to the development of potent anti-staphylococcal β -lactam agents. *Staphylococcus aureus* gave way to Gram-negative bacilli, however, by the early 1980s; Gram-positive cocci began to re-emerge as predominant nosocomial pathogens⁸. Mortality and morbidity from infections are greater when caused by antimicrobial-resistant bacteria. Enterobacteriaceae and non-fermentative Gram-negative bacilli are of great concern because antimicrobial therapy for infections due to these resistant pathogens remains a clinical

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dilemma in hospitalized patients⁹. It is also noted that there is an increase in the resistance among Gram-negative bacilli to third generation cephalosporins which is caused by the expression of extended-spectrum β -lactamase (ESBL) enzymes. Therefore infections due to ESBL isolates continue to pose a challenge to infection management worldwide¹⁰. The clinical significance of BSIs in ICU patients is controversial. Several studies have shown that bacteremic patients are at greater risk of death than those with comparable severity of underlying illness and without this complication^{3,11,12}. On the contrary, other studies did not find any significant difference in mortality between bacteremic and non-bacteremic critically ill patients^{13,14}. A recent study has demonstrated that the severity of illness on admission, as estimated by APACHE II score, the presence of acute respiratory distress syndrome, and a history of diabetes mellitus were risk factors for the occurrence of BSI whereas the development of an ICU-acquired BSI was an independent risk factor for death¹⁵.

Below, a group of Spanish physicians with an interest in the field of bloodstream infection (BSI) in the ICU discussed the most remarkable papers produced in this area during the last 3 years, particularly in those with origin in endovascular catheters. The following are the publications selected for discussion.

Definition

Worth LJ, Brett J, Bull AL, McBryde ES, Russo PL, Richards MJ. Impact of revising the National Nosocomial Infection Surveillance System definition for catheter-related bloodstream infection in ICU: reproducibility of the National Healthcare Safety Network case definition in an Australian cohort of infection control professionals. *Am J Infect Control.* 2009;37:643-8.¹⁶

Effective and comparable surveillance for central venous catheter-related bloodstream infections (CLABSIs) in the intensive care unit requires a reproducible case definition that can be readily applied by infection control professionals. Using a questionnaire containing clinical cases, reproducibility of the National Nosocomial Infection Surveillance System (NNIS) surveillance definition for CLABSI was assessed in an Australian cohort of infection control professionals participating in the Victorian Hospital Acquired Infection Surveillance System (VICNISS). The same questionnaire was then used to evaluate the reproducibility of the recently issued (2008) National Healthcare Safety Network (NHSN) surveillance definition for CLABSI. Target hospitals were defined as large metropolitan (1A) or other large hospitals (non-1A), according to the Victorian Department of Human Services. Questionnaire responses of Centers for Disease Control and Prevention NHSN surveillance experts were used as gold standard comparator. Eighteen of 21 eligible VICNISS centers participated in the survey. Overall concordance with the gold standard was 57.1%, and agreement was highest for 1A hospitals (60.6%). The proportion of congruently classified cases varied according to NNIS criteria: criterion 1 (recognized pathogen), 52.8%; criterion 2a (skin contaminant in 2 or more blood cultures), 83.3%; criterion 2b (skin contaminant in 1 blood culture and appropriate antimicrobial therapy instituted), 58.3%; non-CLABSI cases, 51.4%. When survey questions regarding identification of cases of CLABSI criterion 2b were removed (consistent with the current NHSN definition), overall percentage concordance increased to 62.5% (72.2% for 1A centers).

Comments. Further educational interventions are required to improve the discrimination of primary and secondary causes of bloodstream infection in Victorian intensive care units. Although reproducibility of the CLABSI case definition is relatively poor, adoption of the revised NHSN definition for CLABSI is likely to improve the concordance of Victorian data with international centers.

Prevention

Krein SL, Hofer TP, Kowalski CP, Olmsted RN, Kauffman CA, Forman JH, et al. Use of central venous catheter-related bloodstream infection prevention practices by US hospitals. *Mayo Clin Proc.* 2007;82:672-8.¹⁷

Between March 16, 2005, and August 1, 2005, questionnaires about regular use of 5 specific practices and a "composite" approach for preventing CR-BSIs, was mailed to infection control coordinators at 719 hospitals across the United States. They compared two kinds of hospitals: a total of Veterans Affairs medical centres (VA) with acute care beds (n=119), and a random sample of general medical and surgical hospitals (non-VA) with more than 50 beds and intensive care units (ICU) (n=600). The VA has a health care system with a centralized administration. The 5 specific practices were: maximal sterile barrier precautions, chlorhexidine gluconate for insertion site antisepsis, use of antimicrobial coated catheters, care with chlorhexidine dressing and avoidance of routine line changes. A composite approach was the concurrent use of maximal sterile barrier precautions, chlorhexidine gluconate for insertion site antisepsis and avoidance of routine line changes. Their survey also included questions regarding the infection control program, including the service of hospital epidemiologist and if the coordinator of infection control program (ICP) was certified in infection control and epidemiology. In addition, the survey also assessed the available expertise and hospital safety culture at the participating institutions. The average number of ICU beds, evidence-based practice support score, use of hospitalists, and participation in an infection-related collaborative were similar for both kinds of hospitals. VA hospitals had a higher registered nurse staffing ratio, were more likely to be approved to train residents and to have supervisory ICP certified in infection control. A higher percentage of VA compared to non-VA hospitals reported using maximal sterile barrier precautions (84% vs. 71%; $P=.01$), chlorhexidine gluconate for insertion site antisepsis (91% vs. 69%; $P<.001$), and a composite approach (62% vs. 44%; $P=.003$). In addition, hospitals having a higher safety culture score, having a certified infection control professional, and participating in an infection prevention collaborative study were more likely to use CR-BSI prevention practices.

Comments. Fewer than half of non-VA US hospitals reported concurrent use of maximal sterile barrier precautions, chlorhexidine gluconate, and avoidance of routine central line changes. Wider use of CR-BSI prevention practices by hospitals could be encouraged by fostering a culture of safety, participating in infection prevention collaborative studies, and promoting infection control professional certification.

Falagas ME, Fragoulis K, Bliziotis IA, Chatzinikolaou I. Rifampicin-impregnated central venous catheters: a meta-analysis of randomized controlled trials. *J Antimicrob Chemother.* 2007;59:359-69.¹⁸

One of the most serious nosocomial infectious problems is catheter-related bloodstream infection (CR-BSI), which prolongs hospital stay, increases costs of hospitalization and may lead to death in selected patients. The use of antimicrobial-impregnated central venous catheters (CVCs) for the prevention of CR-BSI is still a matter of debate. The present manuscript reports the results of a meta-analysis of randomized controlled trials (RCTs) on rifampicin/minocycline-impregnated CVCs catheters examining the hypothesis that this strategy is effective in preventing CR-BSI and device colonization. One hundred and fifty-three potentially relevant studies were initially identified by this search although only seven RCTs were finally considered eligible for inclusion in the meta-analysis. All but one of the RCTs was of high quality (Jadad score >2). Only two of these studies were carried out in ICU patients (both with

Jadad score >2). The primary analysis demonstrated that rifampicin/minocycline-impregnated CVCs were associated with fewer CR-BSIs compared with catheters not impregnated with rifampicin/minocycline (odds ratio [OR]: 0.23; 95% confidence interval [CI], 0.14-0.40). The same result was found regarding colonization (OR: 0.46; 95%CI, 0.31-0.69). Moreover, the comparison of rifampicin-based CVCs with non-rifampicin-impregnated CVCs, demonstrated superiority of rifampicin-based CVCs in reducing colonization (OR: 0.38; 95%CI, 0.24-0.62) and CR-BSI (OR: 0.24; 95%CI, 0.14-0.40). Similarly, superiority of rifampicin/minocycline-impregnated CVCs were noted in a subgroup analysis of colonization and CR-BSIs in which rifampicin/minocycline-impregnated CVCs were compared with simple, non-tunnelled, non-antimicrobial impregnated CVCs, a subgroup analysis that was performed by including only high quality RCTs (Jadad score >2). A subgroup analysis for colonization comprising studies in which the sonication technique was used also concluded the superiority of rifampicin/minocycline-impregnated CVCs. No statistically significant difference in mortality between the two treatment arms was observed. Development of microbial resistance to the antibiotics used for catheter impregnation was not sufficiently evaluated in these trials.

Comments. The main findings of this well-performed meta-analysis that included 7 RCTs (six of them with high quality evaluated by Jadad score) show that non-tunnelled CVCs impregnated with rifampicin and minocycline are safe and effective in reducing the incidence of catheter colonization and CRBSI compared with non-impregnated catheters. Nevertheless, several important issues need further analysis: the possibility of development of antimicrobial resistance during treatment with impregnated catheters, the effectiveness of this strategy in critically ill patients with short-term catheterization, and, importantly, a cost analysis of this intervention to reduce CR-BSI.

Climo MW, Sepkowitz KA, Zuccotti G, Fraser VJ, Warren DK, Perl TM, et al. The effect of daily bathing with chlorhexidine on the acquisition of methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, and healthcare-associated bloodstream infections: results of a quasi-experimental multicenter trial. *Crit Care Med.* 2009;37**:1858-65.¹⁹**

Up to 20% of patients admitted to Intensive Care Units (ICUs) develop a healthcare-associated infection and many of those infections are caused by multidrug-resistant organisms resulting in substantial morbidity and mortality. Skin colonization may be the portal of entry of some of those infections and partially responsible for the development of bloodstream infections (BSI). This study sought to determine if the use of daily chlorhexidine bathing would decrease the incidence of colonization and (BSI) caused by methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) among ICU patients. The study was carried out in 6 ICUs at four academic centres and measured the incidence of MRSA and VRE colonization and BSI during a period of bathing with routine soap for 6 months and then compared results with a 6-month period where all admitted patients received daily bathing with a chlorhexidine solution. Changes in incidence were evaluated by Poisson and segmented regression modelling. Overall, acquisition of MRSA decreased 32% (5.04 vs. 3.44 cases/1,000 patient days; $P = .046$) and acquisition of VRE decreased 50% (4.35 vs. 2.19 cases/1,000 patient days; $P = .008$) following the introduction of daily chlorhexidine bathing. Segmented regression analysis demonstrated significant reductions in VRE bacteremia ($P = .02$) following the introduction of chlorhexidine bathing. VRE-colonized patients bathed with chlorhexidine had a lower risk of developing VRE bacteremia (relative risk [RR]: 3.35; 95%CI, 1.13-9.87; $P = .035$), suggesting that reductions in the level of colonization led to the observed reductions in BSI. Apparently no other interventions

intended to reduce the incidence of BSI were introduced during the study period

Comments. The study was not a randomized trial but a before and after sequential study. Unfortunately no typing of skin and blood isolates in patients with BSI was performed. The authors did not check for the development of chlorhexidine resistance, but the approach is simple to implement and inexpensive and may be an important adjunctive intervention to barrier precautions to reduce acquisition of VRE and MRSA and the subsequent development of healthcare-associated BSI.

Epidemiology

Blot S, Cankurtaran M, Petrovic M, Vandijck D, Lizy C, Decruyenaere J, et al. Epidemiology and outcome of nosocomial bloodstream infection in elderly critically ill patients: a comparison between middle-aged, old, and very old patients. *Crit Care Med.* 2009;37**:1634-41.²⁰**

The number of elderly patients admitted to Intensive Care Units (ICUs) has grown steadily in the past decades and varies between 12 and 58%. Bloodstream infections (BSI) are among the most common nosocomially-acquired infections and have subsequent increases in morbidity, mortality and cost. The authors of this paper investigated the epidemiology of nosocomial BSIs in elderly ICU patients comparing middle-aged (45-64 years; $n=524$), old (65-74 years; $n=326$), and very old ICU patients (>75 years; $n=134$) who developed a nosocomial BSI during their ICU stay. Although the total number of ICU admissions decreased by approximately 10%, the number of very old patients increased by 33% between the periods 1992-1996 and 2002-2006. The prevalence of bloodstream infection (per 1,000 ICU admissions) increased significantly over time among old ($P = .001$) and very old patients ($P = .002$), but not among middle-aged patients ($P = .232$). Yet, this trend could not be confirmed with the incidence data expressed per 1,000 patient days ($P > .05$). Among patients with BSI the proportion of very old patients increased significantly with time from 7.2% (1992-1996) to 13.5% (1997-2001) and 17.4% (2002-2006) ($P < .001$). The incidence of bloodstream infection (per 1,000 patient days) decreased with age: 8.4 per thousand in middle-aged, 5.5 per thousand in old, and 4.6 per thousand in very old patients ($P < .001$). Mortality rates increased with age: 42.9%, 49.1%, and 56.0% for middle-aged, old, and very old patients, respectively ($P = .015$). Regression analysis revealed that the adjusted relationship with mortality was borderline significant for old age (hazard ratio [HR]: 1.2; 95%CI, 1.0-1.5) and significant for very old age (HR: 1.8; 95%CI, 1.4-2.4).

Comments. This is a historical cohort study that reveals that the incidence of BSI is lower in the very-old population but has a significant higher risk of death in this subgroup of patients. Over the past 15 years, an increasing number of elderly patients are admitted to ICU's but not all elderly patients are similar and it makes sense to differentiate the population with more than 65 years in different age groups.

Etiology

Lorente L, Jiménez A, Santana M, Iribarren JL, Jiménez JJ, Martín MM, et al. Microorganisms responsible for intravascular catheter-related bloodstream infection according to the catheter site. *Crit Care Med.* 2007;35**:2424-7.²¹**

This single-centre prospective study was carried out during 4 years to evaluate whether the microorganisms responsible for intravascular catheter-related bloodstream infection (IVC-RBSI) have any relation to catheter site. The authors diagnosed 88 IVC-RBSIs, including 36 femoral catheter sites and 52 other catheter sites. No

differences were found between IVC-RBSI of femoral vs. other catheter sites for age, sex, APACHE II, diagnosis at admission, and use of antimicrobials. The proportion of IVC-RBSI due to Gram-negative bacteria was higher in femoral (38.89%), than in the other catheter sites, (7.69%) (OR: 7.48; 95%CI, 2.19-25.54; $P=0.001$). The proportion of IVC-RBSIs due to yeasts was higher in femoral (16.67%) than in other catheter sites (1.92%) (OR: 10.20; 95%CI, 1.17-88.85; $P=0.035$).

Comments. The authors conclude that empirical antifungal therapy would seem to be indicated in patients with suspected femoral catheter-related bloodstream infection.

Burton DC, Edwards JR, Horan TC, Jernigan JA, Fridkin SK. Methicillin-resistant *Staphylococcus aureus* central line-associated bloodstream infections in US intensive care units, 1997-2007. *JAMA.* 2009; 301:727-36.²²

Healthcare-associated infections, particularly central line-associated bloodstream infections (CL-BSIs) and invasive infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA), have received much attention in recent years. Now, to examine trends in the incidence of MRSA CL-BSIs in U.S. ICUs, researchers have analyzed CDC surveillance system data for 1997 through 2007.

During this period, 1684 ICUs reported 33,587 CL-BSIs, of which 2498 (7.4%) were caused by MRSA and 1590 (4.7%) were caused by methicillin-susceptible *S. aureus*. Overall, the proportion of *S. aureus* CL-BSIs caused by MRSA increased from 47.9% in 1997 to 64.5% in 2007. However, although the annual incidence of MRSA CL-BSIs increased from 1997 through 2001, it then declined significantly through 2007, resulting in an overall 49.6% decrease in rates during the study period. The decrease in MRSA CL-BSIs after 2001 was seen in all six adult ICU types that were evaluated, and it paralleled a similar decline in overall ICU CL-BSIs during this period.

Comments. Although the proportion of *S. aureus* CL-BSIs attributable to MRSA has increased during the past decade, the rates of CL-BSIs in general and of MRSA CL-BSIs in particular have declined significantly in U.S. ICUs since 2001. As suggested by an editorialist, the findings call into question the usefulness of performing active surveillance for MRSA rather than focusing on decreasing healthcare-acquired infections in general.

Pathogenesis

Hamilton HC, Foxcroft DR. Central venous access sites for the prevention of venous thrombosis, stenosis and infection in patients requiring long-term intravenous therapy. *Cochrane Database Syst Rev.* 2007;(3):CD004084.²³

Central venous access (CVA), in which a large bore catheter is routed through a vein in the neck, upper chest or femoral area, is needed to give drugs that cannot be given by mouth or via a conventional cannula in the arm. The objectives of this study were to establish whether either the jugular, subclavian or femoral CVA routes result in a lower incidence of venous thrombosis, venous stenosis or infection related to CVA devices, and to determine whether the circumference of a long-term central venous access device influences the incidence of venous thrombosis, venous stenosis or infection related to CVA devices. The authors searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2006, Issue 4), MEDLINE, CINAHL, EMBASE (from inception to December 2006), reference lists of identified trials, and bibliographies of published reviews. They also contacted researchers in the field. There were no language restrictions. For selection criteria, they included randomized controlled trials comparing central venous catheter insertion routes. For data collection and analysis, two authors assessed potentially relevant studies. They resolved disagreements by

discussion. Relevant outcomes were: venous thrombosis, venous stenosis, infection related to CVA devices, mechanical complications (e.g., misplaced catheter, minor bleeding, haematoma).

The authors considered 83 studies for inclusion in the review. Six studies appeared eligible but five were subsequently excluded because they did not randomize participants for either site of access or catheter circumference size. One study was a high quality block randomized controlled trial. Allocation concealment was good and randomization was by a central computer. In all, 293 patients were randomized to a femoral or a subclavian CVA group. Results from this one trial were as follows: *a*) catheter-related infectious complications: Infectious complication (colonization with or without sepsis): the RR was 4.57 (95%CI, 1.95-10.71) favouring subclavian over femoral access. Major infectious complications (sepsis with or without bacteremia): the RR was 3.04 (95%CI, 0.63-14.82) favouring subclavian access. Colonized catheter (greater than 103 colony-forming units/mL of gram positive microorganisms): the RR was 3.65 (95%CI, 1.40-9.56) favouring subclavian access. Colonized catheter (greater than 103 colony-forming units/mL of Gram negative microorganisms): the RR was 5.41 (95%CI, 1.61-18.15) favouring subclavian access; *b*) catheter-related mechanical complications: overall complications (arterial puncture, minor bleeding, haematoma, misplaced catheter): the RR was 0.92 (95%CI, 0.56-1.51) favouring subclavian access; *c*) catheter-related thrombotic complications: catheter-related thromboses (fibrin sleeves, major and complete thrombosis): the RR was 11.53 (95%CI, 2.80-47.52) favouring subclavian access.

Comments. Subclavian CVA is preferable to femoral CVA. Further trials of subclavian versus femoral or jugular CVA are needed. Research on the impact of catheter circumference on catheter-related complications is required.

Risk factors and outcome

Garnacho-Montero J, Aldabó-Pallás T, Palomar-Martínez M, Vallés J, Almirante B, Garcés R, et al. Risk factors and prognosis of catheter-related bloodstream infection in critically ill patients: a multicenter study. *Intensive Care Med.* 2008; 34:2185-93.²⁴

The objective of this study was to assess the risk factors associated with CR-BSI development in critically ill patients with non-tunneled, non-cuffed central venous catheters (CVC) and the prognosis of the episodes of CR-BSI. This was a prospective, observational, multicenter study in nine Spanish Hospitals. All subjects admitted to the participating ICUs from October 2004 to June 2005 with a CVC were included. Overall, 1,366 patients were enrolled and 2,101 catheters were analyzed. Sixty-six episodes of CR-BSI were diagnosed. The incidence of CR-BSI was significantly higher in CVC compared with peripherally inserted central venous catheters (PICVC) without significant differences among the three locations of CVC. In the multivariate analysis, duration of catheterization and change over a guidewire were the independent variables associated with the development of CR-BSI whereas the use of a PICVC was a protective factor. Excluding PICVC, 1,598 conventional CVC were analyzed. In this subset, duration of catheterization, tracheostomy and change over a guidewire were independent risk factors for CR-BSI. A multivariate analysis of predictors for mortality among 66 patients with CRSI showed that early removal of the catheter was a protective factor and APACHE II score at the admission was a strong determinant of in-hospital mortality.

Comments. Peripherally inserted central venous catheters are associated with a lower incidence of CR-BSI in critically ill patients. Exchange over a guidewire of CVC and duration of catheterization are strong contributors to CR-BSI. The author's results reinforce the importance of early catheter removal in critically ill patients with CR-BSI.

Sreeramoju PV, Tolentino J, Garcia-Houchins S, Weber SG. Predictive factors for the development of central line-associated bloodstream infection due to gram-negative bacteria in intensive care unit patients after surgery. *Infect Control Hosp Epidemiol.* 2008; 29:51-6.²⁵

The objective of this study was to examine the relative proportions of central line-associated bloodstream infection (BSI) due to gram-negative bacteria and due to gram-positive bacteria among patients who had undergone surgery and patients who had not. The study also evaluated clinical predictive factors and unadjusted outcomes associated with central line-associated BSI caused by gram-negative bacteria in the postoperative period. This was an observational, case-control study based on a retrospective review of medical records, carried out at the University of Chicago Medical Center, a 500-bed tertiary care center located on Chicago's south side. All adult intensive care unit (ICU) patients who developed central line-associated BSI were included. There were a total of 142 adult patients who met the Centers for Disease Control and Prevention National Nosocomial Infection Surveillance System definition for central line-associated BSI. Of those, 66 patients (46.5%) had infections due to gram-positive bacteria, 49 patients (34.5%) had infections due to gram-negative bacteria, 23 patients (16.2%) had infections due to yeast, and 4 patients (2.8%) had mixed infections. Patients who underwent surgery were more likely to develop central line-associated BSI due to gram-negative bacteria within 28 days of the surgery, compared with patients who had not had surgery recently (57.6% vs 27.3%; $P = .002$). On multivariable logistic regression analysis, diabetes mellitus (adjusted OR: 4.6; 95%CI, 1.2-18.1; $P = .03$) and the presence of hypotension at the time of the first blood culture positive for a pathogen (adjusted OR: 9.8; 95%CI, 2.5-39.1; $P = .001$) were found to be independently predictive of central line-associated BSI caused by gram-negative bacteria. Unadjusted outcomes were not different in the group with BSI due to gram-negative pathogens, compared to the group with BSI due to gram-positive pathogens.

Comments. Clinicians caring for critically ill patients after surgery should be especially concerned about the possibility of central line-associated BSI caused by gram-negative pathogens. The presence of diabetes and hypotension appear to be significant associated factors.

Chin BS, Han SH, Lee HS, Jeong SJ, Choi H, Kim CO, et al. Risk factors for recurrent catheter-related infections after catheter-related bloodstream infections. *Int J Infect Dis.* 2010; 14:e16-21.²⁶

This study was performed to identify the risk factors for recurrent catheter-related infections (CRIs) following non-tunneled central venous catheter (CVC) reinsertion after catheter-related bloodstream infections (CRBSIs). A retrospective cohort was constructed from a computer database for patients who underwent reinsertion of a non-tunneled CVC after a CRBSI during the period January 2004 to December 2007. Among these patients, recurrent CRI cases were selected through an electronic chart review, and the risk factors for recurrent CRI were investigated. Fifty-three patients who had had a reinserted non-tunneled CVC after a CRBSI were analyzed and 22 patients were considered as having recurrent CRIs (41.5%). Recurrent/persistent CRBSI after catheter reinsertion was observed in 16 patients, and six patients with systemic inflammatory response syndrome revealed positive results of an identical organism with the initial CRBSI in semi-quantitative reinsertion-catheter tip cultures. In multivariate analysis, fungal CRBSI compared with bacterial infection (adjusted HR: 7.77; 95%CI, 1.71-35.36) and CRBSI occurrence during intensive care unit (ICU) care (adjusted HR: 5.20; 95%CI 1.41-19.18) were revealed as independent risk factors for recurrent CRIs after catheter reinsertion on account of CRBSIs.

Comments. A substantial proportion of the patients with CRBSIs revealed recurrent CRIs after catheter reinsertion. Fungal CRBSIs

when compared with bacterial infections and CRBSI occurrence during ICU care were independent risk factors for recurrent CRIs following catheter reinsertion after a CRBSI.

Diagnosis

Lee A, Mirrett S, Reller LB, Weinstein MP. Detection of bloodstream infections in adults: how many blood cultures are needed? *J Clin Microbiol.* 2007;45:3546-8.²⁷

In this study the authors analyzed data at two university hospitals using the medical records of patients during a 2-year study period. Data were analyzed to determine the cumulative sensitivity of blood cultures obtained sequentially during the 24-h time period. Of 629 monomicrobial episodes with ≥ 3 blood cultures obtained, 73.1% were detected with the first blood culture, 89.7% were detected with the first two blood cultures, 98.2% were detected with the first three blood cultures, and 99.7% with the first four blood cultures. Among monomicrobial episodes, *Staphylococcus aureus* was more likely to be detected with the first blood culture.

Comments. This study indicates that two blood cultures sets in a 24-h period will detect approximately 90% of bloodstream infections. To achieve a detection rate of $> 99\%$, as many as four blood cultures will be needed. This results don't hold the axiom that virtually all bloodstream infections can be detected with two to three blood cultures.

Conflict of interest

The authors declare they have not any conflict of interest.

References

- Wenzel RP, Edmond MB. The impact of hospital-acquired bloodstream infections. *Emerg Infect Dis.* 2001;7:174-7.
- Pittet D, Li N, Woolson RF, Wenzel RP. Microbiological factors influencing the outcome of nosocomial bloodstream infections: a 6-year validated, population-based model. *Clin Infect Dis.* 1997;24:1068-78.
- Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infection in critically ill patients: excess length of stay, extra costs, and attributable mortality. *JAMA.* 1994;271:1598-601.
- Rello J, Ricart M, Mirelis B, Quintana E, Gurgui M, Net A, et al. Nosocomial bacteremia in a medical-surgical intensive care unit: epidemiologic characteristics and factors influencing mortality in 111 episodes. *Intensive Care Med.* 1994; 20:94-8.
- Vallès J, León C, Álvarez-Lerma F. Nosocomial bacteremia in critically ill patients: a multicenter study evaluating epidemiology and prognosis. *Clin Infect Dis.* 1997;24:387-95.
- Brun-Buisson C, Doyon F, Carlet J. Bacteremia and severe sepsis in adults: a multicenter prospective survey in ICUs and wards of 24 hospitals. *Am J Respir Crit Care Med.* 1996;154:617-24.
- Harbarth S, Ferrière K, Hugonnet S, Ricou B, Suter P, Pittet D. Epidemiology and prognostic determinants of bloodstream infections in surgical intensive care. *Arch Surg.* 2002;137:1353-9.
- Karchmer AW. Nosocomial bloodstream infections: organism, risk factors, and implications. *Clin Infect Dis.* 2000;31:39-43.
- Hsueh P, Chen W, Luh K. Relationships between antimicrobial use and antimicrobial resistance in Gram-negative bacteria causing nosocomial infections from 1991-2003 at a university hospital in Taiwan. *Int J Antimicrob Agents.* 2005;26:463-72.
- Ndugulile F, Jureen R, Harthug S, Urassa W, Langeland N. Extended spectrum beta-lactamases among Gram-negative bacteria of nosocomial origin from an intensive care unit of a tertiary health facility in Tanzania. *BMC Infect Dis.* 2005;5:85-91.
- Routsi C, Pratikaki M, Sotiropoulou C, Platsouka E, Markaki V, Paniara O, et al. Application of the sequential organ failure assessment (SOFA) score to bacteremic ICU patients. *Infection.* 2007;35:240-4.
- Laupland KB, Kirkpatrick AW, Church DL, Ross T, Gregson DB. Intensive care unit acquired bloodstream infections in a regional critically ill population. *J Hosp Infect.* 2004;58:137-45.
- Rello J, Ochagavia A, Sabanes E, Roque M, Mariscal D, Reynaga E, et al. Evaluation of outcome of intravenous catheter-related infections in critically ill patients. *Am J Respir Crit Care Med.* 2000;162:1027-30.
- Blot S, Vandewoude K, Colardyn F. Nosocomial bacteremia involving *Acinetobacter baumannii* in critically ill patients. *Intensive Care Med.* 2003;29:471-5.
- Pratikaki M, Platsouka E, Sotiropoulou C, Vassilakopoulos T, Paniara O, Roussos C, et al. Risk factors for and influence of bloodstream infections on mortality: a

- 1-year prospective study in a Greek intensive-care unit. *Epidemiol Infect.* 2009;137:727-35.
16. Worth LJ, Brett J, Bull AL, McBryde ES, Russo PL, Richards MJ. Impact of revising the National Nosocomial Infection Surveillance System definition for catheter-related bloodstream infection in ICU: reproducibility of the National Healthcare Safety Network case definition in an Australian cohort of infection control professionals. *Am J Infect Control.* 2009;37:643-8.
 17. Krein SL, Hofer TP, Kowalski CP, Olmsted RN, Kauffman CA, Forman JH, et al. Use of central venous catheter-related bloodstream infection prevention practices by US hospitals. *Mayo Clin Proc.* 2007;82:672-8.
 18. Falagas ME, Fragoulis K, Bliiziotis IA, Chatzinikolaou I. Rifampicin-impregnated central venous catheters: a meta-analysis of randomized controlled trials. *J Antimicrob Chemother.* 2007;59:359-69.
 19. Climo MW, Sepkowitz KA, Zuccotti G, Fraser VJ, Warren DK, Perl TM, et al. The effect of daily bathing with chlorhexidine on the acquisition of methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, and healthcare-associated bloodstream infections: results of a quasi-experimental multicenter trial. *Crit Care Med.* 2009;37:1858-65.
 20. Blot S, Cankurtaran M, Petrovic M, Vandijck D, Lizy C, Decruyenaere J, et al. Epidemiology and outcome of nosocomial bloodstream infection in elderly critically ill patients: a comparison between middle-aged, old, and very old patients. *Crit Care Med.* 2009;37:1634-41.
 21. Lorente L, Jiménez A, Santana M, Iribarren JL, Jiménez JJ, Martín MM, et al. Microorganisms responsible for intravascular catheter-related bloodstream infection according to the catheter site. *Crit Care Med.* 2007;35:2424-7.
 22. Burton DC, Edwards JR, Horan TC, Jernigan JA, Fridkin SK. Methicillin-resistant *Staphylococcus aureus* central line-associated bloodstream infections in US intensive care units, 1997-2007. *Jama.* 2009;301:727-36.
 23. Hamilton HC, Foxcroft DR. Central venous access sites for the prevention of venous thrombosis, stenosis and infection in patients requiring long-term intravenous therapy. *Cochrane database of systematic reviews (Online).* 2007(3):CD004084.
 24. Garnacho-Montero J, Aldabo-Pallas T, Palomar-Martínez M, Vallès J, Almirante B, Garcés R, et al. Risk factors and prognosis of catheter-related bloodstream infection in critically ill patients: a multicenter study. *Intensive Care Med.* 2008;34:2185-93.
 25. Sreeramou PV, Tolentino J, García-Houchins S, Weber SG. Predictive factors for the development of central line-associated bloodstream infection due to gram-negative bacteria in intensive care unit patients after surgery. *Infect Control Hosp Epidemiol.* 2008;29:51-6.
 26. Chin BS, Han SH, Lee HS, Jeong SJ, Choi H, Kim CO, et al. Risk factors for recurrent catheter-related infections after catheter-related bloodstream infections. *Int J Infect Dis.* 2010;14:e16-21.
 27. Lee A, Mirrett S, Reller LB, Weinstein MP. Detection of bloodstream infections in adults: how many blood cultures are needed? *J Clin Microbiol.* 2007;45:3546-8.