

Update in nosocomial infection

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Practical approach to the management of catheter-related bloodstream infection

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ABSTRACT

Catheter-related bloodstream infections (CRBSI) is a common cause of nosocomial infection associated resulting in substantial morbidity, mortality, increased length of hospital stays and health-care costs. New clinical practice guidelines for the management of adults with CRBSI have been published in 2018 by the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC) and the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC). This review focuses on updated recommendations for the diagnosis and management of CRBSI in adults. Prevention of CRBSI is excluded. Our aim is to show some of the key aspects concerning the following topics: diagnosis, empirical and targeted therapy.

Key words: Catheter-related bloodstream infection; guidelines; bacteremia.

INTRODUCTION

Nosocomial bloodstream infections (BSIs) have significant associated morbidity, incur increased hospital costs, and prolonged the length of stay [1]. Attributable mortality ranges between 12% and 25%. Most nosocomial BSIs are associated with intravascular (IV) catheters and central venous catheters (CVCs) in particular.

In the last years, intravascular device insertion has become a very common practice in the hospital and outpatient settings for various purposes, including hemodynamic monitoring, renal replacement therapy, nutritional support, as well as fluid and medication administration. According to national data facilitated by the study of the prevalence of

nosocomial infections in Spain (EPINE), it is estimated that approximately 70% of the patients admitted to Spanish hospitals will carry one of these devices at some moment during their stay [2].

Recently published Spanish clinical guidelines provide recommendations about diagnosis and management of catheter-related bloodstream infections (CRBSI) in adults [3]. The experts identified 39 questions being possible to define 103 recommendations with different levels of gradation. Thus, within category A there were 41 recommendations, 29 in category B and 23 C. However, it is worth noting that, regarding the categorization of the recommendation, only 10 could be placed with a quality of the evidence of AI [4]. Nevertheless, other aspects as prevention are therefore excluded. Nonetheless, a manuscript recently published provides a comprehensive review about aseptic measures recommended by scientific societies the insertion and manipulation of vascular catheters [5]. The aim of the present manuscript is to summarize the most relevant recommendations of this Spanish document updating with relevant information recently published.

CATHETER-RELATED BLOODSTREAM INFECTION DIAGNOSIS

It is essential to make an accurate diagnosis of CRBSI because there are serious consequences associated with inaccurate or failed diagnoses, such as unnecessary serious procedural complications and increased morbidity and mortality if the catheter origin of a BSI is not timely removed. The document defines the clinical characteristics and other factors in order to establishing a clinical suspicion and initiate a microbiological diagnostic, as well as, what conditions are needed to consider the CRBSI as complicated.

CRBSI should be clinically suspected in patients with intravenous catheters and onset of fever, chills or other signs of sepsis, even in the absence of local signs of infection, and

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especially if no alternative source is recognized. Several circumstances should increase suspicion such as local sign of infection at the catheter, metastatic infections caused by hematogenous spread of microorganisms or persistent blood cultures for particular microorganisms.

There are a variety of factors associated with poorer outcomes, which make CRBSI as complicated. Factors associated with complicated bacteremia are patients diagnosed with CRBSI and with endocarditis, suppurative thrombophlebitis, septic metastasis, extraluminal infections, septic shock, non-resolving CRBSI, or immunocompromised patients.

DIAGNOSIS CRBSI WITH OR WITHOUT (CONSERVATIVE DIAGNOSIS) CATHETER WITHDRAWAL

The guidelines emphasize the recommendation that a catheter culture must only be obtained when a CRBSI is suspected, thus avoiding unnecessary cultures [6]. Removal of catheter is the most suitable approach for the diagnosis of CRBSI at least in the critical care setting.

Nevertheless, removal of a suspected CVC, may not be feasible or practical for a variety of reasons, such as including limited alternative vascular access or unacceptable complications associated with removal and replacement.

Summary of main diagnostic methods for catheter-related bloodstream infections recommended by new guidelines for the different patient subgroups with suspected CRBSI are the following:

- Semiquantitative culture (roll plate) or quantitative culture performed after sonication or vortex washing the catheter tip are the preferred method for sampling long-term IV catheters. Lamentably, these culture techniques require removal of the catheter.
- In situations where catheter cannot be withdrawal, paired blood cultures obtained simultaneously from a catheter lumen and peripheral blood meets the criteria for CRBSI by quantitative blood cultures (a colony count 3 times greater in a sample drawn through a catheter than from the peripheral vein) or differential time to positivity (DTP) (positivity of blood cultures obtained through the catheter ≥ 120 min before those obtained from a peripheral vein). The role of DTP for the diagnosis of catheter related candidemia remains controversial.
- Other conservative techniques such as endoluminal brushing, superficial cultures or Gram stain-acridine orange leukocyte cytopsin (AOLC) of catheter blood are not widely used in clinical laboratories.

Although molecular-based rapid diagnostic testing has evolved recently for the early identification of microorganisms in BSIs, including infections resulting from vascular catheters [7], these guidelines contemplate the usefulness of these techniques as a potential for the improvement in the diagnosis CRBSI in patients undergoing antibiotic therapy, taken into account these techniques have not been standardized.

CATHETER RELATED BLOODSTREAM INFECTION TREATMENT

One of the most important contribution of this document refers to the no immediate and systematic removal of all catheters in patients with suspected related infection, establishing the criteria that must be fulfilled in order to take this clinical decision. This recommendation is based on two studies that found no differences in outcomes when early CVC removal was compared with a watchful waiting strategy for suspected CRBSI in patients with non-tunneled catheters [8, 9]. These studies excluded patients with neutropenia, solid organ or hematologic malignancy, immunosuppressive drugs or radiation therapy, organ transplants, intravascular foreign bodies, hemodynamic instability, suppuration or frank erythema/induration at the insertion site, as well as bacteremia or fungemia. However, the CVC should be removed early in patients with Gram-negative CRBSI, especially when multi-drug resistant isolates are prevalent [10].

Catheter exchange over a guide is not recommended because it is associated with a higher risk of associated infectious complications [11]. This strategy is contraindicated in patients with documented catheter related infections. Guidewire-assisted exchange to replace a catheter should be limited to patients with very difficult venous access (i.e., extensive burns, morbid obesity, or severe coagulopathy) and without documented catheter infection.

Empirical antimicrobial therapy. Once CRBSI is suspected, empiric antimicrobial therapy should be administered after appropriate cultures are obtained. These guidelines recommend choosing the empiric antimicrobial agent(s) based on an assessment of the risk factors for infection, the severity of the clinical picture and the likely pathogens based on local ecology and catheter site of insertion. Some considerations for appropriate antibiotic therapy are as follows: empiric antibiotics should always cover gram-positive organisms; based on the high frequency of *Staphylococcus* in this type of infections and its potential associated clinical severity. Coverage for other pathogens, gram-negative bacilli or fungi, should be considered especially in episodes presenting as septic shock. It is worth noting that these pathogens are more frequently involved when a femoral catheter is the BSI source [12, 13].

An interesting aspect of the document refers to the conservative management of CRBSI in patients with devices used for hemodialysis. The recommendation indicates that the use of combination antibiotic therapy (local and systemic) offers better results than exclusive systemic antibiotics, with the exception of cases produced by *S. aureus*, in which catheter exchange over a guidewire with systemic antibiotic therapy has been shown to be associated with higher cure rate than a strategy based on local plus systemic antibiotics [14].

Targeted antimicrobial therapy. Appropriate duration of antimicrobial therapy in CRBSI is based on the causative pathogen,

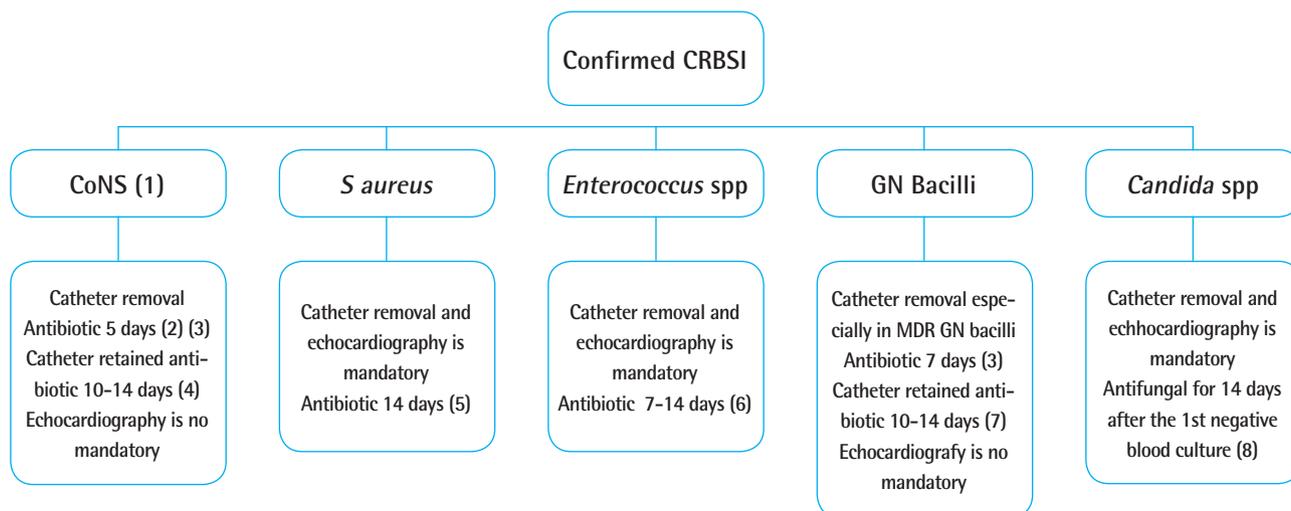


Figure 1 Approach to the treatment of a patient with confirmed CRBSI.

(1) Except *Staphylococcus lugdunensis*, which should be managed as for *Staphylococcus aureus*. (2) Vancomycin is the first option, cloxacillin or cefazolin are the alternatives for methicillin-susceptible strains. (3) In patients with intravascular devices, foreign bodies or in whom markers of inflammation persist after catheter removal therapy, antibiotic therapy for 10-14 days is recommended. (4) Vancomycin in the first option, ALT (Antibiotic Lock Therapy) with vancomycin for 10-14 days. (5) Cloxacillin or cefazolin are the alternatives for MSSA. Vancomycin or daptomycin are the alternatives for MRSA. Complicated episodes require longer courses of treatment (4-6 weeks). (6) Ampicillin is the drug of choice for susceptible strains Vancomycin is the alternative for strains resistant to ampicillin. (7) Only in immunocompetent patients without septic shock and when the isolate is susceptible to antibiotics that are available for ALT. (8) If metastatic complications have been ruled out.

presence of complications, and host factors. Figure 1 shows the approach to the treatment of a patient with confirmed CRBSI.

Guidelines supports the systematic treatment of CRBSI caused by coagulase-negative *Staphylococcus* (CoNS), although this decision does not provide of clear scientific evidence to support it. In fact, recent published studies concluded that inappropriate empirical therapy does not lead to poor outcomes in CoNS-CRBSI bacteremia [15].

One of the most important contributions of the document makes reference to indications for oral sequencing in the treatment of BRCVs. Clinical stability, negativization of blood cultures after catheter withdrawal and the possibility of using oral antibiotics with good bioavailability makes this alternative possible.

REFERENCES

- Olaechea PM, Palomar M, Álvarez-Lerma F, Otañal JJ, Insausti J, López-Pueyo MJ, et al. Morbidity and mortality associated with primary and catheter-related bloodstream infections in critically ill patients. *Rev Esp Quimioter*. 2013; 26:21-9. PMID: 23546458
- Sociedad Española de Medicina Preventiva, Salud Pública e Higiene. Estudio EPINE-EPPS 2018. Informe global de España. [Internet]. Available from: <https://www.epine.es/docs/public/reports/esp/2018%20EPINE%20Informe%20España.pdf>.
- Chaves F, Garnacho-Montero J, del Pozo JL. Diagnosis and Treatment of Catheter-Related Bloodstream Infection: Clinical Guide-
- Almirante B. Diagnosis, treatment of bacteremia associated with the use of, vascular catheters: That provides a new clinical practice guide. *Med Intensiva*. 2018; 42: 1-4. doi: 10.1016/j.medint.2017.12.009.
- Lorente L. Antiseptic measures during the insertion and manipulation of vascular catheters. *Med Intensiva*. 2019;43 Suppl 1:39-43. doi: 10.1016/j.medint.2018.09.012.
- Pascual A, Cercenado E, Salavert M, Elías García-Sánchez J, Eiros JM, Liñares J, et al. Update on pathogenesis and diagnosis of intravascular catheter-related infections. *Enferm Infecc Microbiol Clin*. 2011;29 Suppl 4:16-21. doi: 10.1016/S0213-005X(11)70032-5.
- Zhang L, Rickard CM. Non-culture based diagnostics for intravascular catheter related bloodstream infections. *Expert Rev Mol Diagn*. 2017;17(2):181-188. doi: 10.1080/14737159.2017.1275964.
- Rijnders BJ, Peetermans WE, Verwaest C, Wilmer A, Van Wijngaerden E. Watchful waiting versus immediate catheter removal in ICU patients with suspected catheter related infection: a randomized trial. *Intensive Care Med*. 2004; 30:1073-80. doi: 10.1007/s00134-004-2212-x
- Lorente L, Martín MM, Vidal P, Rebollo S, Ostabal MI, Solé-Violán J, et al. Should central venous catheter be systematically removed in

- patients with suspected catheter related infection? Crit Care. 2014; 18:564. doi: 10.1186/s13054-014-0564-3.
10. Lee YM, Moon C, Kim YJ, Lee HJ, Lee MS, Park KH. Clinical impact of delayed catheter removal for patients with central-venous-catheter-related Gram-negative bacteraemia. J Hosp Infect. 2018; 99: 106-113. doi: 10.1016/j.jhin.2018.01.004.
 11. Garnacho-Montero J, Aldabó-Pallás T, Palomar-Martínez M, Vallés J, Almirante B, Garcés R, Grill F, Pujol M, Arenas-Giménez C, Mesalles E, Escosca-Ortega A, de Cueto M, Ortiz-Leyba C. Risk factors and prognosis of catheter-related bloodstream infection in critically ill patients: a multicenter study. Intensive Care Med. 2008; 34(12):2185-93. doi: 10.1007/s00134-008-1204-7
 12. Lorente L, Jiménez A, Santana M, Iribarren JL, Jiménez JJ, Martín MM, Mora ML. Microorganisms responsible for intravascular catheter-related bloodstream infection according to the catheter site. Crit Care Med. 2007;35(10):2424-7. doi: 10.1097/01.CCM.0000284589.63641.B8
 13. Nagao M, Hotta G, Yamamoto M, Matsumura Y, Ito Y, Takakura S, et al. Predictors of *Candida* spp. as causative agents of catheter-related bloodstream infections. Diagn Microbiol Infect Dis. 2014; 80: 200-3. doi: 10.1016/j.diagmicrobio.2014.08.003
 14. Langer JM, Cohen RM, Berns JS, Chittams J, Cooper ET, Trerotola SO. *Staphylococcus*-infected tunneled dialysis catheters: is over-the-wire exchange an appropriate management option? Cardiovasc Intervent Radiol. 2011; 34: 1230-5. doi: 10.1007/s00270-011-0180-4.
 15. Hebeisen UP, Atkinson A, Marschall J, Buetti N. Catheter-related bloodstream infections with coagulase-negative staphylococci: are antibiotics necessary if the catheter is removed? Antimicrob Resist Infect Control. 2019;8:21. doi: 10.1186/s13756-019-0474-x.