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## Predictive value of superficial cultures to anticipate tunneled hemodialysis catheter–related bloodstream infection $^{\stackrel{\sim}{\sim}}$ , $^{\stackrel{\sim}{\sim}}$

Emilio Bouza <sup>a,b,c,d,\*</sup>, Loreto Rojas <sup>a</sup>, María Guembe <sup>a,\*</sup>, Mercedes Marín <sup>a</sup>, Fernando Anaya <sup>b</sup>, José Luño <sup>b</sup>, Juan M. López <sup>b</sup>, Patricia Muñoz <sup>a,b,c,d</sup> and on behalf of the COCADI Study Group

- <sup>a</sup> Department of Clinical Microbiology and Infectious Diseases, Hospital General Universitario Gregorio Marañón, Madrid, Spain
- b Department of Nephrology, Hospital General Universitario Gregorio Marañón, Madrid, Spain
- <sup>c</sup> Universidad Complutense de Madrid, Madrid, Spain
- d Red Española de Investigación en Patología Infecciosa (REIPI), Sevilla, Spain

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### ABSTRACT

We performed a prospective study in patients with tunneled catheters to assess the validity of Gram stain and superficial culture for anticipating catheter exit-site infection and hemodialysis catheter–related bloodstream infection. The sensitivity and negative predictive value were high, and we succeeded in identifying a subpopulation at low risk of infection.

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Hemodialysis catheter-related bloodstream infection (HC-RBSI) is 1 of the most frequent causes of sepsis in patients under hemodialysis, and the incidence rates range from 0.5 to 7.6 episodes per 1000 catheter-days (Farinas et al., 2008; Grothe et al., 2010; Klevens et al., 2008; Lemaire et al., 2009; Powe et al., 1999; Saeed Abdulrahman et al., 2002).

Microorganisms colonizing skin, hubs, or both are considered the first step to catheter tip colonization and, consequently, to catheter-related bloodstream infection (C-RBSI) (Cercenado et al., 1990; Linares et al., 1985; Sherertz et al., 1997; Templeton et al., 2008).

Semiquantitative cultures from skin and hubs can anticipate catheter tip colonization and identify subpopulations at risk of C-RBSI. However, these findings are only from a general population and in patients admitted to intensive care units with short-term central venous catheters (Bouza et al., 2005; Cercenado et al., 1990).

In order to reduce HC-RBSI and its associated complications, we hypothesized that colonization of skin, hubs, or both in patients

undergoing hemodialysis with tunneled catheters could anticipate the risk of exit-site infection (ESI) and HC-RBSI.

We performed a prospective observational cohort study over an 8-month period in a large teaching institution. We selected adult patients with renal impairment who were undergoing hemodialysis and plasmapheresis. All patients who agreed to participate and signed a consent form were included in the study.

All catheters were non-antibiotic-coated (HemoStar® Long-term Haemodialysis Catheter and Bard® Hickman® Catheter; C.R. Bard, Inc Nordic, Helsingbord, Sweden) and were inserted by trained vascular interventional radiologists using ultrasound and a standardized aseptic technique (O'Grady et al., 2002).

Cultures from the skin insertion site and all hubs (superficial cultures) were collected every 15 days immediately before the hemodialysis session over a period of 6 months (March 1, 2010, to August 30, 2010). All samples were processed immediately at the microbiology laboratory.

Superficial cultures were considered positive when there were  $\geq$ 15 CFU/plate (Cercenado et al., 1990).

Peripheral blood cultures (BCs) were obtained when infection was suspected. In general, 2 or 3 BCs (from 2 or 3 different sites) were obtained.

Catheter tip culture was performed using the semiquantitative roll-plate technique (Maki) (Bouza et al., 2007; Maki et al., 1977).

In patients suspected of having HC-RBSI, the correlation between the microorganisms isolated in superficial cultures and those isolated

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<sup>\*</sup> Corresponding authors. Tel.: +34-91-586-84-53; fax: +34-91-504-49-06. E-mail addresses: ebouza@microb.net (E. Bouza), mariaguembe@hotmail.com (M. Guembe).

in BCs was determined using phenotypic identification to genus and species level and susceptibility testing. Susceptibility testing of the isolated microorganisms in both superficial cultures and BCs was performed following the recommendations of the Clinical Laboratory Standards Institute (Wayne, 2010). Molecular typing was performed by pulsed-field gel electrophoresis (PFGE) for *Staphylococcus* species isolates or Rep-PCR for Gram-negative isolates, as previously described (Cercenado et al., 2008; Sanz-Garcia et al., 2009). Results were considered concordant if the same organism (genus and species) was isolated from superficial cultures and BCs or if both cultures yielded negative results. If the same organism was present in both cultures, it was considered concordant, even if 1 of them was polymicrobial. Any other results were defined as discrepant.

Diagnosis of ESI and HC-RBSI was based on the intravascular catheter infection guidelines of the Infectious Diseases Society of America (Mermel et al., 2009).

Continuous variables for the comparison of the patients' characteristics in the univariate analysis were assessed using the Mann–Whitney test, and qualitative variables were assessed using the Fisher exact test or  $\chi^2$  test. A P value <0.05 was considered significant. All statistical tests were 2-tailed.

The statistical analysis was performed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA).

Patients were monitored during the study period and followed for 2 months.

We included 115 catheters from 98 patients (95, hemodialysis; 3, plasmapheresis). The main population characteristics are described in Table 1. A total of 1845 superficial cultures were performed. The total number of positive superficial cultures was 267 (43.4%), and the colonization rate was 15.6 episodes per 1000 catheter-days.

ESI was present in 17 patients, with an incidence rate of 1 episode per 1000 catheter-days. The median (interquartile range [IQR]) number of positive samples per patient with ESI was higher than in the other patients: 7 (3.5-7.0) versus 1 (0-4) (P < 0.01).

The validity values of surveillance samples for Gram stain/culture to predict ESI were as follows: sensitivity, 94.1%/100%; specificity, 33.3%/43.2%; positive predictive value, 22.9%/27%; negative predictive value, 96.4%/100%; positive likelihood ratio, 1.4/1.8; and negative likelihood ratio, 0.2/0.0 (Table 2).

HC-RBSI was present in 6 (6.1%) patients with an incidence rate of 0.35 episodes per 1000 catheter-days. Of the 6 patients, 2 (33.3%) had tunnel infection by *Serratia marcescens* and methicillin-sensitive *Staphylococcus aureus* (MSSA), whereas 2 patients (33.3%) had left-side endocarditis by *Staphylococcus lugdunensis* and MSSA affecting the aortic valve. The mortality rate of patients with C-RBSI was 16.7%, which was higher than in the other patients (6.5%). The median (IQR) number of positive samples per patient with HC-RBSI was higher than in the other patients, 5.5 (1.0–7.5) versus 1.5 (0–4.8) (P < 0.01).

The accuracy of Gram stain/superficial cultures for predicting HC-RBSI was as follows: sensitivity, 66.7%/100%; specificity, 28.3%/38.0%; positive predictive value, 5.7%/9.5%; negative predictive value, 92.9%/100%; positive likelihood ratio, 0.9/1.6; and negative likelihood ratio, 1.2/0 (Table 2).

Our study shows that superficial Gram stain and cultures had excellent sensitivity and negative predictive values, which could be useful when identifying patients who will not develop infection. The most important issue is to know which patients will benefit from preventive measures in order to avoid infectious complications.

Other studies of colonization of skin and hubs in patients undergoing major heart surgery or in the general population showed that all episodes of C-RBSI occurred in the colonized population (Bouza et al., 2005; Cercenado et al., 1990); (Rodriguez-Aranda et al., 2010).

In conclusion, superficial cultures are very useful for identifying patients with chronic kidney failure receiving hemodialysis or apheresis via a tunneled catheter who are at high risk of

**Table 1** Characteristics of the 98 patients included.

Characteristics         No. of patients (%)           Median age (QR)         75 (65–81)           Malae sex         49 (50)           McCabe and Jackson index         8           Non-fatal         58 (59-2)           Ultimately fatal         40 (40.8)           Rapidly fatal         40 (40.8)           Rapidly fatal         20 (29.6)           Median Charlson index (IQR)         8 (7-10.3)           Type of CKD or indication for apheresis         Diabetic nephropathy         10 (10.2)           Vascultis         7 (7.1)         Portical control of the control	Characteristics of the 98 patients included.	
Male sex         49 (50)           McCabe and Jackson index         Non-fatal           Non-fatal         40 (40.8)           Rapidly fatal         -           Median Charlson index (IQR)         8 (7-10.3)           Type of CKD or indication for apheresis         Diabetic nephropathy         29 (29.6)           Glomerulonephritis         12 (12.2)           Obstructive uropathy         10 (10.2)           Vasculitis         7 (7.1)           Nephrosclerosis         6 (6.1)           Ischemic nephropathy         4 (4.1)           Polycystic renal diseases         2 (2)           Chronic pyelonephritis         1 (1)           Unknown         18 (18.4)           Other         6 (6.1)           Underlying conditions         1 (1)           Chronic pyelonephritis         2 (2)           Underlying conditions         86 (87.8)           Chronic pelonephritis         1 (1)           Underlying conditions         86 (87.8)           Chronic pelonephritis         2 (2)           Underlying conditions         86 (87.8)           Chronic pelonephritis         1 (1)           Underlying conditions         86 (87.8)           Chronic pelonephritis         2 (	Characteristics	No. of patients (%)
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Non-fatal		49 (50)
Ultimately fatal		58 (59.2)
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HIV       1 (1)         Immunosuppressive therapy       11 (11.2)         Laboratory parameters       11 (11.2)         Kt/V       1.56 (1.3-1.8)         Albumin       3.8 (3.4-4.1)         Hemoglobin       11.9 (10.9-12.8)         Creatinine       6.5 (4.9-8)         Calcium       8.8 (8.3-9.2)         Phosphorus       4.2 (3.4-5.5)         CRP       4 (1-16.3)         Ferritin       233 (116-395)         iPTH       248 (149-437)         Median no. of sessions per week (IQR)       3 (3-3)         History of previous C-RBSI       11 (11.2)         Catheter replacement       10 (10.2)         Median no. of catheter replacements (IQR)       1 (1-1)         Catheter characteristics (days)       1 (1-1)         Median days of catheter use (IQR)       214 (121-230)         Nasal colonization culture       Positive with MRSA       6 (6.1)         Positive with MRSA       8 (8.2)         Negative       84 (85.7)         Superficial samples       Positive superfficial Gram stain       70 (71.4)         Positive skin Gram stain       50 (51)         Positive skin Gram stain       50 (51)         Positive bub Gram stain       39 (39.8)		4 (4.1)
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Laboratory parameters       Kt/V       1.56 (1.3-1.8)         Albumin       3.8 (3.4-4.1)         Hemoglobin       11.9 (10.9-12.8)         Creatinine       6.5 (4.9-8)         Calcium       8.8 (8.3-9.2)         Phosphorus       4.2 (3.4-5.5)         CRP       4 (1-16.3)         Ferritin       233 (116-395)         iPTH       248 (149-437)         Median no. of sessions per week (IQR)       3 (3-3)         History of previous C-RBSI       11 (11.2)         Catheter replacement       10 (10.2)         Median no. of catheter replacements (IQR)       1 (1-1)         Catheter characteristics (days)       1 (1-1)         Median days of catheter use (IQR)       214 (121-230)         Nasal colonization culture       Positive with MRSA       6 (6.1)         Positive with MRSA       8 (8.2)         Negative       84 (85.7)         Superficial samples       70 (71.4)         Positive skin Gram stain       70 (71.4)         Positive skin Gram stain       50 (51)         Positive shin Gram stain       39 (39.8)         Positive shin cultures       63 (64.3)         Positive skin cultures       61 (62.2)         Positive hub Cultures performed		, ,
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Creatinine         6.5 (4.9-8)           Calcium         8.8 (8.3-9.2)           Phosphorus         4.2 (3.4-5.5)           CRP         4 (1-16.3)           Ferritin         233 (116-395)           iPTH         248 (149-437)           Median no. of sessions per week (IQR)         3 (3-3)           History of previous C-RBSI         11 (11.2)           Catheter replacement         10 (10.2)           Median no. of catheter replacements (IQR)         1 (1-1)           Catheter characteristics (days)         1 (1-1)           Median days of catheter use (IQR)         214 (121-230)           Nasal colonization culture         Positive with MRSA         6 (6.1)           Positive with MRSA         8 (8.2)           Negative         84 (85.7)           Superficial samples         Positive superficial Gram stain         70 (71.4)           Positive skin Gram stain         50 (51)           Positive hub Gram stain         39 (39.8)           Positive superficial cultures         63 (64.3)           Positive skin cultures         61 (62.2)           Positive hub cultures performed         0.35 (0.0-0.8)           Insertion site findings         Erythema         12 (12.2)           Purulent secretion <td< td=""><td>Albumin</td><td>3.8 (3.4-4.1)</td></td<>	Albumin	3.8 (3.4-4.1)
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Catheter characteristics (days)       214 (121–230)         Median days of catheter use (IQR)       214 (121–230)         Nasal colonization culture       6 (6.1)         Positive with MRSA       8 (8.2)         Negative       84 (85.7)         Superficial samples       70 (71.4)         Positive superficial Gram stain       70 (71.4)         Positive skin Gram stain       50 (51)         Positive hub Gram stain       39 (39.8)         Positive superficial cultures       63 (64.3)         Positive skin cultures       61 (62.2)         Positive hub cultures       9 (9.2)         Positive cultures/cultures performed       0.35 (0.0-0.8)         Insertion site findings       Erythema         Erythema       12 (12.2)         Purulent secretion       7 (7.1)         No abnormalities       79 (80.6)		, ,
Nasal colonization culture         Positive with MRSA       6 (6.1)         Positive with MSSA       8 (8.2)         Negative       84 (85.7)         Superficial samples	Catheter characteristics (days)	
Positive with MRSA         6 (6.1)           Positive with MSSA         8 (8.2)           Negative         84 (85.7)           Superficial samples         70 (71.4)           Positive superficial Gram stain         50 (51)           Positive skin Gram stain         39 (39.8)           Positive superficial cultures         63 (64.3)           Positive skin cultures         61 (62.2)           Positive hub cultures         9 (9.2)           Positive cultures/cultures performed         0.35 (0.0-0.8)           Insertion site findings         Erythema           Purulent secretion         7 (7.1)           No abnormalities         79 (80.6)		214 (121–230)
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Purulent secretion 7 (7.1) No abnormalities 79 (80.6)		12 (12 2)
No abnormalities 79 (80.6)		

CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; Kt/V = number for measuring the dose of dialysis; CRP = C-reactive protein; iPTH = intact parathyroid hormone; MRSA = methicillin-resistant Staphylococcus aureus.

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