

## Effectiveness of surveillance cultures for high priority multidrug-resistant bacteria in hematopoietic stem cell transplant units

Elisa Teixeira Mendes<sup>1</sup>, Matias Chiarastelli Salomão<sup>2</sup>, Lísia Moura Tomichi<sup>3</sup>, Maura Salaroli Oliveira<sup>2</sup>, Mariana Graça<sup>4</sup>, Flavia Rossi<sup>5</sup>, Fernanda Sapadao<sup>2</sup>, Thais Guimarães<sup>2</sup>, Vanderson Rocha<sup>6</sup>, Silvia Figueiredo Costa<sup>2,4</sup>

### ABSTRACT

Surveillance strategies to detect colonization are an important tool to prevent and control the spread of microorganisms in hematopoietic stem cell transplant (HSCT) units. The aim of this study was to evaluate routine surveillance cultures for screening colonization and infection by carbapenem-resistant Enterobacteriaceae (CRE), carbapenem-resistant *Pseudomonas aeruginosa* (CRPa), and vancomycin-resistant enterococci (VRE). Surveillance cultures were collected (1,323 samples) from 200 patients admitted to an HSCT unit over one year; swabs were taken on admission and then weekly. We compared the positivity of cultures for each site, agent, clinical and epidemiological data according to the colonization status. Infection due to multidrug-resistant organisms (MDROs) occurred in 52 (21.5%) patients, 45 (86.5%) due to blood stream infection; 12 (23%) patients had a positive surveillance culture before the infection. Cultures of 554 (41.8%) samples were performed for CRPa, 413 (31.2%) for VRE and 356 (27%) for CRE. Of these, 179 (13.5%) were positive. Colonization by any MDRO, CRE or CRPa was associated with increased risk of infection ( $P < 0.05$ ), but not with death. Previous colonization by an MDRO was a significant risk for infection by these pathogens, specially by CRE. Overall, rectal swabs had the highest positivity rate compared with other sites, oropharynx swabs were an option for CRPa, and fecal cultures showed low positivity. Although the impact of the strategy on the mortality of patients undergoing HSCT is not clear, routine VRE surveillance should be questioned with regard to patients undergoing auto-HSCT due to the additional cost and little impact on survival rates.

**KEYWORDS** Hematopoietic stem cell transplant infection. Hospital-acquired infection. Multidrug-resistant organisms. Surveillance cultures. Blood stream infection.

### INTRODUCTION

Infections are the major cause of death in patients undergoing hematopoietic stem cell transplants (HSCT)<sup>1</sup>. These patients are at high risk for acquiring health care-associated infections. The use of empiric antibiotics during febrile neutropenia leads to a higher prevalence of multidrug-resistant organisms (MDROs) in this population<sup>2</sup>, in addition to the risk of dissemination within the transplant unit.

A previous study by the Hospital of Clinics of the University of the Sao Paulo Medical School (HC-FMUSP) identified an association between previous gut colonization by MDROs, particularly by gram-negative bacteria, and blood stream infection (BSI) in patients undergoing HSCT<sup>3</sup>.

<sup>1</sup>Pontifícia Universidade Católica de Campinas, Centro de Ciências da Vida, Programa de Pós-Graduação em Ciências da Saúde, Campinas, São Paulo, Brazil

<sup>2</sup>Universidade de São Paulo, Faculdade de Medicina, Departamento de Doenças Infecciosas e Parasitárias, São Paulo, São Paulo, Brazil

<sup>3</sup>Universidade do Rio Verde, Hospital de Doenças Tropicais, Aparecida de Goiânia, Goiás, Brazil

<sup>4</sup>Universidade de São Paulo, Faculdade de Medicina, Instituto de Medicina Tropical de São Paulo, Laboratório de Microbiologia, São Paulo, São Paulo, Brazil

<sup>5</sup>Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Laboratório Central, Divisão de Microbiologia, São Paulo, São Paulo, Brazil

<sup>6</sup>Universidade de São Paulo, Faculdade de Medicina, Departamento de Hematologia e Hemoterapia, São Paulo, São Paulo, Brazil

**Correspondence to:** Elisa Teixeira Mendes Pontifícia Universidade Católica de Campinas, Centro de Ciências da Vida, Programa de Pós-Graduação em Ciências da Saúde, Av. John Boyd Dunlop, s/n, 2º piso, CEP 13087-571, Campinas, SP, Brazil Tel: +55 11 972839006

**E-mail:** [elisatmendes@gmail.com](mailto:elisatmendes@gmail.com)

**Received:** 23 March 2021

**Accepted:** 15 September 2021

Surveillance strategies to detect colonization have been considered important tools for preventing and controlling the spread of MDROs in the hospital setting<sup>4,5</sup>. However, the cost-effectiveness of this strategy in HSCT units and its impact on the patient's outcome is still controversial<sup>6-8</sup>.

The aim of this study was to evaluate the use of routine surveillance cultures to track colonization and infection by the most prevalent MDROs in an HSCT unit, specifically, carbapenem-resistant Enterobacteriaceae (CRE), carbapenem-resistant *Pseudomonas aeruginosa* (CRPa), and vancomycin-resistant enterococci (VRE).

## MATERIALS AND METHODS

Clinical, epidemiological and microbiological data were collected to analyze the surveillance culture strategy in a single HSCT unit. HC-FMUSP is a reference hospital in Sao Paulo, Brazil, with 2,200 beds. The HSCT unit is a 23-bed unit with four beds designated for allogeneic transplants and 18 for autologous transplants. Patients undergoing allogeneic transplants were accommodated in private rooms with high-efficiency particulate air filtration and positive pressure. Patients undergoing autologous transplants, on the other hand, could share a room with another patient.

Antibacterial prophylaxis with levofloxacin was introduced on the first day of stem cell infusion and discontinued when patients recovered from neutropenia or if they developed febrile neutropenia. Another prophylaxis was administered according to guidelines<sup>1</sup>.

Surveillance cultures were collected in the HSCT unit over one year (2012). The most prevalent MDROs in the unit were included in the surveillance culture routine: CRE, CRPa and VRE. Swabs were collected on admission and then weekly until discharge, from multiple sites: axilla, feces, oropharynx and/or rectum. Swabs for CRE and CRPa were incubated overnight in liquid medium and then plated on MacConkey agar with a meropenem disk<sup>3</sup>; VRE samples were incubated in a medium with vancomycin 6 mg/L<sup>9</sup>. Colonization was defined as the presence of at least one positive surveillance culture for one of the studied microorganisms. Identification of resistant bacteria was performed with VITEK 2 (Biomerieux, Marcy-l'Étoile, France). The following clinical and epidemiological data were collected: sex, age, length of stay (LOS) in the HSCT unit, diagnosis, use of antibiotics, infection, BSI and intra-hospital death. Infection was defined according to the Centers for Disease Control and Prevention guidelines<sup>10</sup>.

### Statistical analysis

All data were stored in a database in Excel 97-2004

(Microsoft, Redmond, WA, USA). Then, the surveillance culture positivity was compared for each site and agent. Clinical and epidemiologic data were analyzed according to the colonization status. All statistical analyses were performed using the Epi.Info 7.0 (CDC, Atlanta, GA, USA). The Fisher's exact test or the chi-squared test was used for categorical variables, as appropriate, and Mann-Whitney and log-rank tests were used for continuous variables. The univariate analysis and the multivariate logistic regression analysis were performed (95% confidence interval). We considered a *P* value <0.05 as statistically significant. A Kaplan-Meier curve was generated to compare the survival among patients with and without BSI.

### Ethical considerations

This study was evaluated and approved by the Ethics Committee of the HC-FMUSP, under protocol N° CAAE: 50237715.4.0000.0068.

## RESULTS

We monitored 200 patients undergoing HSCT who underwent the culture surveillance: 82 (41%) had allogeneic transplants and 118 (59%) had autologous transplants; in total, 1,323 samples were collected. The mean age was 45 years, and 107 patients (53.5%) were male. The mortality during hospitalization was 17.7% (Table 1).

**Table 1** - Characteristic of patients who underwent a surveillance culture in the HSCT unit, Hospital of Clinics, Sao Paulo.

Parameter	N (%)
Total number of patients	200 (100)
Mean age (years)	45
Male sex	107 (53.5)
Surveillance samples collected	1,323 (100)
Allo-HSCT	82 (41)
LOS in days. Mean (range)	19.4 (1-66)
LOS in days until MDRO colonization	
Mean (range)	16 (0-55)
CRE	18 (1-55)
CRPa	20 (0-39)
VRE	10.5 (0-40)
LOS in days until MDRO infection	
Mean (range)	23 (0-77)
CRE	26.7 (0-77)
CRPa	21 (0-51)
VRE*	19
Intra-hospital death	43 (17.7)

MDR = Multi-Drug Resistant Organism; Allo = allogeneic; CRE = Carbapenem-Resistant *Enterobacteriaceae*; CRPa = Carbapenem-Resistant *Pseudomonas aeruginosa*; VRE = Vancomycin-Resistant *Enterococci*; LOS = Length of Stay; \*Only one case of VRE infection.

**Table 2** - Data from surveillance cultures collected from patients admitted to the HSCT ward, Hospital of Clinics, Sao Paulo.

Surveillance culture	Total (%)	Positive samples	Positivity by site			
			Axillary (116)	Fecal (1,109)	Rectal (82)	Oropharyngeal (17)
Total samples	1,324 (100)	179 (13.5)	16 (13.8)	140 (12.6)	17 (20.7)	6 (35.3)
CRE (%)	356 (27)	85 (23.8)	62 (20.7)	62 (20.7)	13 (39.4)	5 (45.5)
CRPa (%)	554 (41.8)	41 (7.4)	28 (6.9)	28 (6.9)	1 (2.6)	1 (14.3)
VRE (%)	413 (31.2)	53 (12.8)	50 (12.5)	50 (12.5)	3 (25)	3 (25)

CRE = Carbapenem-Resistant *Enterobacteriaceae*; CRPa = Carbapenem-Resistant *Pseudomonas aeruginosa*; VRE = Vancomycin-Resistant *Enterococci*.

We performed 554 (41.8%) surveillance cultures for CRPa, 413 (31.2%) for VRE and 356 (27%) for CRE. Surveillance cultures had an overall positivity of 13.5% (179), and the oropharyngeal and rectal swabs showed the highest rates (35.5% and 20.7% positivity, respectively) (Table 2). Fecal samples displayed only 12.6% of positivity, and the positivity of CRE was twice as high in rectal cultures.

Infection due to MDROs occurred in 52 (21.5%) patients; among them, 45 (86.5%) had bacteremia, and 12 (23%) had a positive surveillance culture before the infection.

Table 3 describes the characteristics of infections according to the type of HSCT, with 38% occurring in allogeneic HSCT. CRE infections were more common in autologous HSCT (75%), whereas CRPa was more common in allogeneic (66%) HSCT.

**Table 3** - Clinical and epidemiological characteristics of MDR infection cases in HSCT patients.

	Total N (%)	Allo (%)	Auto (%)
Total	52 (100)	20 (38)	32 (62)
Age mean (years)	41	42	39
Male sex	40	15 (75)	25 (78)
CRE	24	6 (25)	18 (75)
CRPa	27	18 (66)	9 (34)
VRE	1	1 (100)	0
LOS in days. Mean (range)	28.4 (4-66)	27.7 (6-66)	2.3 (4-63)
Hospital Death	22	12 (55)	10 (45)

HSCT = Allo: Allogeneic HSCT, Auto = Autologous HSCT; MDR = Multi-Drug Resistant Organism; CRE = Carbapenem-Resistant *Enterobacteriaceae*; CRPa = Carbapenem-Resistant *Pseudomonas aeruginosa*; VRE = Vancomycin-Resistant *Enterococci*; LOS = Length of Stay; \*Only one case of VRE infection.

The average time between MDRO colonization and infection was 21.4 days for CRE and only 14.1 days for CRPa infections (Table 1). The average LOS for MDRO colonization and infection was 16 and 23 days, respectively.

Infection and colonization by VRE occurred earlier compared with other MDROs; however, having VRE was not a risk factor for MDRO infection or death.

Being colonized by any MDRO ( $P = 0.002$ ), CRE ( $P < 0.001$ ) or CRPa ( $P = 0.027$ ) was associated with a higher risk of infection in the bivariate analysis, and only the colonization by CRE ( $P = 0.009$ ) remained significant in the multivariate analysis. Risk of death was significantly higher among patients with MDRO infections, including CRE and CRPa in the bivariate analysis ( $P < 0.001$ ), whereas in the multivariate analysis, only CRPa infections ( $P = 0.028$ ) remained significant (Tables 4 and 5). CRE and CRPa infections were more significant among patients colonized with CRE and CRPa ( $P = 0.004$  and  $P = 0.002$ , respectively) (Table 4). Chance of survival was significantly lower among patients with BSI, as demonstrated in the Kaplan-Meier curve ( $P = 0.012$ ), as well as among those infected with CRPa (0.0053) (Figure 1).

## DISCUSSION

This study evaluated the practice of MDRO surveillance cultures in an HSCT unit for one year; the prevalence of colonized patients was 13.5%. The variety of MDRO species and their prevalence varies widely in the literature, ranging from extremely low (4.2%-16%) in Germany<sup>11</sup> and higher rates among centers that evaluate only patients undergoing allogeneic HSCT, such as Poland (57.7%) and India (53.8%)<sup>4,11-14</sup>. This variation is due to many factors, such as local epidemiology, prophylaxis protocols, HSCT type, among others<sup>5-8</sup>.

The average LOS before colonization with VRE was 10 days, half the time compared with CRPa colonization. The LOS before MDRO infection averaged 23 days. Heidenreich *et al.*<sup>11</sup> diagnosed 27% of cases of MDRO colonization in the first 100 days after transplantation, with a predominance of CRPa (26.9%).

In our cohort, a previous colonization by MDROs was a significant risk factor for infections by the same pathogen, especially in those colonized by CRE. A study conducted

**Table 4** - Risk factors for death and infection. Total data and results stratified by each agent in a bivariate analysis, in a HSCT ward, Hospital of Clinics, Sao Paulo.

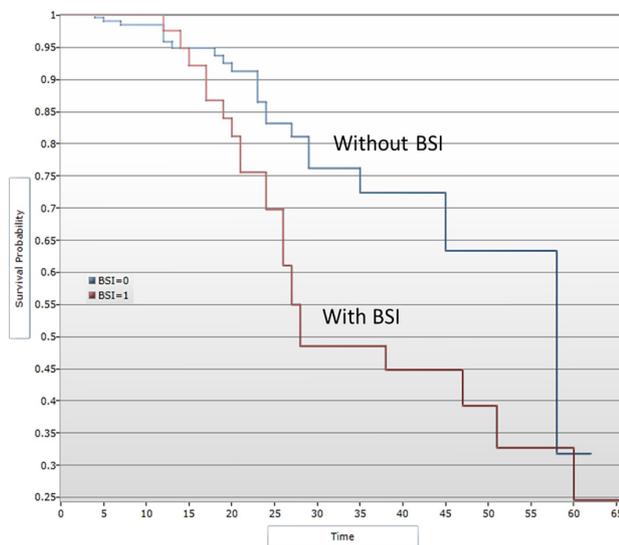
Death						
Risk factor	Deaths/patients with risk factor (%)	Deaths/patients without risk factor (%)	OR	CI (95%)		P
Colonization by:						
Any MDRO	20/94 (21.28)	22/145 (15.17)	1.08	0.95	1.22	0.22
CRE	12/50 (24)	30/189 (15.87)	1.11	0.94	1.31	0.18
CRPa	5/31 (16.13)	37/208 (17.79)	0.98	0.83	1.16	0.82
VRE	7/47 (14.89)	35/192 (18.23)	0.96	0.84	1.10	0.59
Infection by:						
Any MDRO	22/44 (50)	21/196 (10.71)	1.79	1.32	2.41	< 0.001
CRE	10/21 (47.62)	33/219 (15.07)	1.62	1.07	2.44	< 0.001
CRPa	16/26 (61.54)	27/214 (12.62)	2.27	1.39	3.70	< 0.001
VRE	1/1 (100)	42/239 (17.57)	Undef.	Undef.	Undef.	0.18
Infection						
Risk factor	Infections/patients with risk factor (%)	Infections /patients without risk factor (%)	OR	CI (95%)		P
Colonization by:						
Any MDRO	26/94 (27.66%)	17/145 (11.72%)	1.22	1.06	1.40	0.002
CRE	19/50 (38%)	24/189 (12.70%)	1.41	1.13	1.76	< 0.001
CRPa	10/31 (32.26%)	33/208 (15.87%)	1.24	0.97	1.59	0.027
VRE	12/47 (25.53%)	31/192 (16.15%)	1.13	0.94	1.35	0.133
Infection by Carbapenem-Resistant <i>Enterobacteriaceae</i>						
Risk factor	Infection CRE/patients with risk factor (%)	Infection CRE/patients without risk factor(%)	OR	CI (95%)		P
Colonization by:						
Any MDRO	13/94 (13.83%)	8/145 (5.52%)	1.10	1.002	1.20	0.027
CRE	10/50 (20%)	11/189 (5.82%)	1.18	1.02	1.36	0.004
CRPa	2/31 (6.45%)	19/208 (9.13%)	0.97	0.88	1.07	1.00
VRE	5/47 (10.64%)	16/192 (8.33%)	1.03	0.92	1.14	0.57
Infection by Carbapenem-Resistant <i>Pseudomonas aeruginosa</i>						
Risk factor	Infections CRPa/patients with risk factor (%)	Infections CRPa/patients without risk factor (%)	OR	CI (95%)		P
Colonization by:						
Any MDRO	15/94 (15.96%)	10/145 (6.90%)	1.11	1.004	1.22	0.025
CRE	11/50 (22%)	14/189 (7.41%)	1.19	1.02	1.38	0.003
CRPa	9/31 (29.03%)	16/208 (7.69%)	1.30	1.03	1.63	0.002
VRE	7/47 (14.89%)	18/192 (9.38%)	1.06	0.94	1.21	0.29
Infection by Vancomycin-Resistant <i>Enterococci</i>						
Risk factor	InfectionsVRE/patients with risk factor (%)	InfectionsVRE/patients without risk factor (%)	OR	CI (95%)		P
Colonization by:						
Any MDRO	1/94 (1.06%)	0/145 (0%)	1.01	0.99	1.03	0.39
CRE	0/50 (0%)	1/189 (0.53%)	0.99	0.98	1.00	1.00
CRPa	1/31 (3.23%)	0/208 (0%)	1.03	0.97	1.10	0.13
VRE	1/47 (2.13%)	0/192 (0%)	1.02	0.98	1.07	0.19

Undef. = Undefined; CI = Confidence Interval; MDRO = Multi-Drug Resistant Organism (CRE, CRPa or VRE); CRE = Carbapenem-Resistant *Enterobacteriaceae*; CRPa = Carbapenem-Resistant *Pseudomonas aeruginosa*; VRE = Vancomycin-Resistant *Enterococci*.

**Table 5** - Variables associated with infection in a multiple logistic regression, BTM unit, Hospital of Clinics, Sao Paulo.

Colonization by:	Infection		
	OR	CI (95%)	P
CRE	4.54	1.46 - 14.13	<b>0.009</b>
CRPa	1.91	0.68 - 5.35	0.220
VRE	1.77	0.60 - 5.23	0.304
Any MDRO	0.71	0.18 - 2.89	0.636

OR = Odds Ratio; CI = Confidence Interval; MDRO = Multi-Drug Resistant Organism (CRE, CRPa or VRE); CRE = Carbapenem-Resistant *Enterobacteriaceae*; CRPa = Carbapenem-Resistant *Pseudomonas aeruginosa*; VRE = Vancomycin-Resistant *Enterococci*.

**Figure 1** - Survival analysis by the Kaplan Meier curve in patients undergoing HSCT with and without BSI, Hospital of Clinics, Sao Paulo.

in our center (HC-FMUSP), in 2014 and 2015, reported that previous colonization by MDROs was associated with BSI ( $P < 0.001$ ), and that 20% of patients colonized by gram-negative MDROs developed BSI by the same agent<sup>9</sup>. Other studies have also found that being colonized by an MDRO is a risk factor for BSI by the same pathogen<sup>13,15,16</sup>. Strategies for the selective decolonization (SDD) of the gastrointestinal tract in this context have been evaluated, and a single-center study demonstrated the cost-effectiveness of SDD in patients colonized with CRE in intensive care units<sup>17</sup>. However, a systematic review in 2019 still classified the evidence of decolonization as being limited, and did not recommend this intervention as a routine. Moreover, studies on immunocompromised patients are still extremely scarce in the literature<sup>18</sup>.

Although colonization is associated with a higher risk of infection, the impact of this strategy on the mortality of

patients undergoing HSCT is not clear. We observed that infection by any MDRO, CRE or CRPa was associated with the risk of death. Several studies have associated MDRO colonization with a higher risk of death, however, this was not observed in our population. Sadowska-Klasa *et al.*<sup>4</sup> and Bilinski *et al.*<sup>7</sup> evaluated patients undergoing allogeneic HSCT and, in both studies, MDRO colonization had an impact on overall 1-year survival. In a multicenter study carried out in Italy, being colonized by resistant gram-negative bacteria significantly reduced survival rates. In addition, in this study, colonization by CRE and CRPa increased the risk of infection with these pathogens ( $P < 0.001$ )<sup>19</sup>. The relative high rate of autologous HSCT in our series (59%) may explain some differences in our results in comparison with the literature. These patients were less immunocompromised than those undergoing allogeneic HSCT, therefore they had a lower probability of infectious complications. In addition, there was a high prevalence of VRE colonization in our study, which was the only MDRO that did not affect the risk of infection. VRE is generally less virulent than gram-negative bacilli, and this high prevalence possibly reduced the impact of MDRO colonization on our mortality rate<sup>12</sup>.

A study conducted at the Mayo Clinic with a 10-year series evaluated the influence of colonization by VRE on the prognosis of patients undergoing allogeneic HSCT due to acute myeloid leukemia. In a multivariate analysis, colonization by VRE was an independent risk factor for VRE infection, but did not influence any other post-transplant outcome, including death<sup>8</sup>. In agreement with our findings, Heidenreich *et al.*<sup>11</sup> also found a similar risk of death regardless of the status of colonization by MDROs, even though CRE was the main colonizer in their study population<sup>11</sup>.

In this study, the collection site varied according to the pathogen tested (Table 2). Our data corroborate the fact that rectal swabs were more sensitive than fecal cultures<sup>20,21</sup>, especially regarding VRE and CRE. Despite this, rectal swabs should be used with care in patients undergoing HSCT to prevent skin or mucosal injuries during severe neutropenia. In this scenario, an oropharyngeal swab may be an alternative because it presented a high positivity for CRE and VRE. The use of VRE surveillance should be questioned in patients undergoing autologous transplantations because it generates additional costs and has little impact on the survival and the development of bloodstream infections.

The present study has some limitations such as the fact that it was carried out in a single center, and was retrospective. However, it provides important reflections on the practice of screening for MDROs in patients undergoing HSCTs. Being colonized by an MDRO does not seem to

interfere with the post-HSCT survival, especially the VRE colonization in patients who have undergone autologous HSCTs.

## CONCLUSION

In conclusion, despite the fragile evidence related to prognosis and mortality, from our point of view, performing MDRO surveillance cultures in patients undergoing HSCTs is an important tool in the context of hospital infection control, and it can be implemented in the context of high endemicity of MDROs, especially of gram-negative bacteria. Knowledge of the colonizing microbiota of an immunocompromised population is important to propose pathogen-specific control measures as a precaution in this type of patient with regard to prophylactic and empirical antibiotic therapy.

## ACKNOWLEDGMENTS

We thank our HSCT patients.

## REFERENCES

1. Tomblyn M, Chiller T, Einsele H, Gress R, Sepkowitz K, Storek J, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant.* 2009;15:1143-238.
2. Averbuch D, Tridello G, Hoek J, Mikulska M, Akan H, Yanëz L, et al. Antimicrobial resistance in gram-negative rods causing bacteremia in hematopoietic stem cell transplant recipients: intercontinental prospective study of the Infectious Diseases Working Party of the European Bone Marrow Transplantation Group. *Clin Infect Dis.* 2017;65:1819-28.
3. Ferreira AM, Moreira F, Guimaraes T, Spadão F, Ramos JF, Batista MV, et al. Epidemiology, risk factors and outcomes of multi-drug-resistant bloodstream infections in hematopoietic stem cell transplant recipients: importance of previous gut colonization. *J Hosp Infect.* 2018;100:83-91.
4. Sadowska-Klasa A, Piekarska A, Prejzner W, Bieniaszewska M, Hellmann A. Colonization with multidrug-resistant bacteria increases the risk of complications and a fatal outcome after allogeneic hematopoietic cell transplantation. *Ann Hematol.* 2018;97:509-17.
5. Patriarca F, Cigana C, Massimo D, Lazzarotto D, Geromin A, Isola M, et al. Risk factors and outcomes of infections by multidrug-resistant gram-negative bacteria in patients undergoing hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant.* 2017;23:333-9.
6. Forcina A, Lorentino F, Marasco V, Oltolini C, Marcatti M, Greco R, et al. Clinical impact of pretransplant multidrug-resistant gram-negative colonization in autologous and allogeneic hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant.* 2018;24:1476-82.
7. Bilinski J, Robak K, Peric Z, Marchel H, Karakulska-Prystupiuik E, Halaburda K, et al. Impact of gut colonization by antibiotic-resistant bacteria on the outcomes of allogeneic hematopoietic stem cell transplantation: a retrospective, single-center study. *Biol Blood Marrow Transplant.* 2016;22:1087-93.
8. Hefazi M, Damlaj M, Alkhateeb HB, Partain DK, Patel R, Razonable RR, et al. Vancomycin-resistant *Enterococcus* colonization and bloodstream infection: prevalence, risk factors, and the impact on early outcomes after allogeneic hematopoietic cell transplantation in patients with acute myeloid leukemia. *Transpl Infect Dis.* 2016;18:913-20.
9. Lisboa LF, Miranda BG, Vieira MB, Dulley FL, Fonseca GG, Guimarães T, et al. Empiric use of linezolid in febrile hematology and hematopoietic stem cell transplantation patients colonized with vancomycin-resistant *Enterococcus* spp. *Int J Infect Dis.* 2015;33:171-6.
10. Bouza E, Burillo A, Gumbre M. Managing intravascular catheter-related infections in heart transplant patients: how far can we apply IDSA guidelines for immunocompromised patients? *Curr Opin Infect Dis.* 2011;24:302-8.
11. Heidenreich D, Kreil S, Jawhar M, Müller N, Nolte F, Becker KP, et al. Course of colonization by multidrug-resistant organisms after allogeneic hematopoietic cell transplantation. *Ann Hematol.* 2018;97:2501-8.
12. Scheich S, Reinheimer C, Brandt C, Wichelhaus TA, Hogardt M, Kempf VA, et al. Clinical impact of colonization with multidrug-resistant organisms on outcome after autologous stem cell transplantation: a retrospective single-center study. *Biol Blood Marrow Transplant.* 2017;23:1455-62.
13. Korula A, Perumalla S, Devasia AJ, Abubacker FN, Lakshmi KM, Abraham A, et al. Drug-resistant organisms are common in fecal surveillance cultures, predict bacteremia and correlate with poorer outcomes in patients undergoing allogeneic stem cell transplants. *Transpl Infect Dis.* 2020;22:e13273.
14. Baier C, Beck M, Panagiota V, Lueck C, Kharazipour D, Hintze SC, et al. Infection control management and surveillance of carbapenem-resistant Gram-negative bacteria in hematopoietic stem cell recipients. *Antimicrob Resist Infect Control.* 2019;8:160.
15. Neshler L, Rolston KV, Shah DP, Tarrand JT, Mulanovich V, Ariza-Heredia EJ, et al. Fecal colonization and infection with *Pseudomonas aeruginosa* in recipients of allogeneic hematopoietic stem cell transplantation. *Transpl Infect Dis.* 2015;17:33-8.
16. Demiraslan H, Cevahir F, Berk E, Metan M, Cetin M, Alp E, et al. Is surveillance for colonization of carbapenem-resistant gram-negative bacteria important in adult bone marrow transplantation units? *Am J Infect Control.* 2017;45:735-39.

17. You JH, Li HK, Ip M. Surveillance-guided selective digestive decontamination of carbapenem-resistant Enterobacteriaceae in the intensive care unit: a cost-effectiveness analysis. *Am J Infect Control*. 2018;46:291-6.
18. Tacconelli E, Mazzaferri F, de Smet AM, Bragantini D, Eggimann P, Huttner BD, et al. ESCMID-EUCIC clinical guidelines on decolonization of multidrug-resistant Gram-negative bacteria carriers. *Clin Microbiol Infect*. 2019;25:807-17.
19. Aschbacher R, Pagani L, Migliavacca R, Pagani L. Recommendations for the surveillance of multidrug-resistant bacteria in Italian long-term care facilities by the GLISTer working group of the Italian Association of Clinical Microbiologists (AMCLI). *Antimicrob Resist Infect Control*. 2020;9:106.
20. Prado GV, Marchi AP, Moreno LZ, Rizek C, Amigo U, Moreno AM, et al. Virulence and resistance pattern of a novel sequence type of linezolid-resistant *Enterococcus faecium* identified by whole-genome sequencing. *J Glob Antimicrob Resist*. 2016;6:27-31.
21. Yan L, Sun J, Xu X, Huang S. Epidemiology and risk factors of rectal colonization of carbapenemase-producing Enterobacteriaceae among high-risk patients from ICU and HSCT wards in a university hospital. *Antimicrob Resist Infect Control*. 2020;9:155.