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Blood Stream Infections in Allogeneic Hematopoietic Stem Cell Transplant Recipients: Reemergence of Gram-Negative Rods and Increasing Antibiotic Resistance

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Blood stream infections (BSI) are a well-known cause of morbidity and mortality in hematopoietic stem cell transplant (HSCT) patients. The aim of this study was to analyze etiology and microbial resistance of BSI in patients undergoing allogeneic HSCT in a single center over a 4-year period (2004-2007). There were 168 episodes of BSI in 132 patients (median 10 days after HSCT) and 182 pathogens were isolated. Gram-positive bacteria (GPB) accounted for 57% of 182 isolates. Gram-negative rods (GNR) for 37% and fungi for 6%. All patients received routine fluoroquinolone prophylaxis. There was a significant decrease in GPB/GNR ratio over time, from 2.4 in 2004 to 1 in 2007 ($P = .043$). Among GPB, staphylococci decreased from 37 of 68 (64%) in 2004-2005 to 8 of 35 (23%) in 2006-2007 ($P < .002$). The *Enterococcus faecalis*/*E. faecium* ratio decreased from 4.5 in 2004 to 0.33 in 2007 ($P = .006$), whereas the total number of enterococcal strains per year did not change. The incidence of *Escherichia coli* among GNR increased from 3 of 15 (20%) in 2004 to 13 of 21 (62%) in 2007 ($P = .003$). Fluoroquinolone-resistance was common, both among GPB and GNR (81% and 74%, respectively). Mortality rate at 7 days after BSI was 11% (19 of 168), reaching 39% for *Pseudomonas aeruginosa* BSI (7 of 18). BSI remains a frequent and potentially life-threatening complication of allogeneic HSCT, the causative organism influencing 7- and 30-day mortality rate. BSI etiology may change rapidly, requiring implementation of new empirical-therapy schemes.

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INTRODUCTION

Blood stream infections (BSI) are a well-known cause of morbidity and mortality in hematopoietic stem cell transplant (HSCT) patients, because of prolonged neutropenia, mucosal damage, and extensive use of venous central lines [1]. BSI incidence varies from 22% to 55.8% in all HSCT recipients, and is particularly high during the preengraftment phase [2-5]. However, BSI may also occur late after HSCT, and are related to factors such as graft-versus-host disease (GVHD), indwelling central venous catheters, and relapse of underlying hematologic disease [6-8].

Even though only about 40% of the febrile episodes during neutropenia can be defined as infection, appropriate empirical antibiotic therapy is mandatory in case of fever in severely immunocompromised hosts. To provide the best empirical coverage, knowledge of both general trends in etiology and antibiotic susceptibility is critical. Over the last 20 years, the global epidemiology of HSCT-related infections seemed to reverse its trends. In fact, the ratio between Gram-positive bacteria—the leading cause of bacteremia in neutropenic patients in the 1980s and early 1990s [9-11]—and Gram-negative bacteria in BSI in HSCT patients was reported to be decreased in some centers [4,12]. Moreover, a significant increase in multidrug resistant bacteria, such as Gram-negative rods and vancomycin resistant enterococci, was observed [13-16].

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The aim of this study was to describe epidemiology, clinical characteristics, etiology, and outcome of BSI in allogeneic HSCT recipients and to track changes—if any—of the epidemiology as well as microbial resistance that occurred in the examined time period in a major Italian HSCT center.

MATERIALS AND METHODS

Data Collection

The study is a review of BSI in all patients who underwent allogeneic HSCT at the HSCT Unit of San Martino Hospital in Genoa, Italy, a clinical unit that performs about 85 HSCTs per year. Computerized database of prospectively collected data was searched for all the episodes of BSI occurred between January 1, 2004 and December 31, 2007. Additionally, clinical charts of the patients who developed BSI were reviewed. All the information concerning demographics, underlying disease, transplant procedures, BSI episode, and survival was noted. All BSI that occurred after the beginning of the conditioning regimen were evaluated. Day of infusion of HSCT was considered day 0.

Definitions

All blood cultures were obtained at clinical suspicion of systemic infection, usually fever. BSI was defined as isolation of a bacterial or fungal pathogen from at least 1 blood culture. For coagulase negative staphylococci (CoNS), corynebacteria, and other common skin contaminants, positive results from 2 consecutive blood cultures were required. BSI was considered polymicrobial if 2 or more pathogens were isolated in a single blood culture or in separate blood cultures obtained 48 hours apart. Bacteremia occurring more than 14 days after a previous episode and separated by repeatedly negative blood cultures was considered to be a separate BSI. Pathogens with intermediate susceptibility or resistance were considered as resistant. Gram-negative rods (GNR) were defined as ESBL producers if resistant to aztreonam and third-generation cephalosporins, whereas they were considered multidrug-resistant (MDR) if resistant to at least 2 of the following: ceftazidime, piperacillin/tazobactam, or carbapenems. Neutropenia was defined as an absolute neutrophil count below 0.5×10^9/L. Diagnosis and clinical grading of acute and chronic GVHD (aGVHD, cGVHD) were performed according to established criteria [17,18], and GVHD was considered a significant underlying condition only in case of GVHD grade 2 or more, or chronic extensive GVHD.

Despite the fact that the study was not structured to assess the attributable mortality, overall survival at 7 and 30 days after BSI was noted.

Transplantation Procedures and Management of Infections

Transplantation was performed according to institutional protocols, and the procedures were described elsewhere [19]. Briefly, the most frequent myeloablative conditioning included either total-body irradiation with 990 or 1200 cGy (related HLA-identical donor or others, respectively) and cyclophosphamide (Cy) 120 mg/kg in 2 days or a thiotepa-based regimen (thiotepa 15 mg/kg and Cy 120-150 mg/kg). Reduced-intensity conditioning (RIC) included lower dose thiotepa (10 mg/kg) or fludarabine combined with Cy. Standard GVHD prophylaxis included cyclosporine (CsA) and methotrexate (MTX). Cord blood recipients, instead of MTX, received mycophenoplate mophetil (MMF) 15 mg/kg twice a day from day 1 to 28 after HSCT. Antithymocyte globulin (ATG) (Thymoglobulin, Genzyme, Cambridge, MA), at dosages 6 to 15 mg/kg, was administered to recipients of HSCT others than from related HLA-identical donor.

All patients were cared for in single rooms with positive pressure and high-efficiency particulate air filtration, and received antifungal prophylaxis with fluconazole from the start of conditioning until day 80 after HSCT. They received CMV prophylaxis with foscarnet until day 100 after HSCT. Ciprofloxacin was used as antibacterial prophylaxis from the start of conditioning until neutrophil engraftment. From engraftment until the end of immunosuppressive therapy and immunologic recovery, prophylaxis against *Pneumocystis jiroveci* and herpetic infections were provided, with trimethoprim-sulfamethoxazole (960 mg twice a day, 3 times a week) and acyclovir (400 mg/m^2 twice a day), respectively.

In case of fever (defined as pyrexia of 38°C) or other signs or symptoms of infection, prophylactic antibiotics were stopped and patients were treated with broad-spectrum intravenous antibiotics at the discretion of the attending physicians. Usually, piperacillin/tazobactam was started and an antistaphylococcal agent (usually vancomycin) was added for fever persisting more than 72 h. Antifungal agents, predominantly lipid formulations of amphotericin B, were added in case of persistent fever (>96 h) or suspected fungal infection. Antibiotics were modified according to the susceptibility of all organisms isolated.

Statistical Analysis

P values were calculated with chi-square or Fisher tests. Two-sided *P*s of .05 or less were considered significant. All the statistical analyses were performed with NCSS for Windows and SAS (NCSS 2006, Kaysville, UT).

RESULTS

Patients' Characteristics

During the 4-year observation period, BSI occurred in 132 patients. Median age was 40 years (range: 13 – 64) and 81 (61%) were male. The most common diagnosis was acute leukemia (n = 78, 59%), followed by other lymphoproliferative diseases (n = 18, 14%) such as non-Hodgkin lymphoma (n = 8), Hodgkin disease (n = 5), multiple myeloma (n = 4), and chronic lymphatic leukemia (n = 1). Other underlying conditions included myelofibrosis or chronic myeloid leukemia (n = 13, 10%), myelodysplastic syndrome (n = 12, 9%), acute aplastic anemia and paroxysmal nocturnal hemoglobinuria (n = 7), and other autoimmune diseases (hemophagocytosis, systemic lupus erythematosus, Behçet's disease, 1 patient each). Fifty (38%) patients were classified as phase 1 of underlying disease (first complete remission or inactive disease after the first line of treatment), 36 (27%) were in phase 2 (equal to or greater than second complete remission or inactive disease after more that first line of treatment), whereas 46 (35%) had active disease at HSCT.

All the patients received allogeneic HSCT at our institution, 49 (37%) from related HLA-identical donor, 41 (31%) from matched unrelated, 19 (14%) from mismatched related donor, 13 (10%) from cord blood, and 10 (8%) from mismatched unrelated donor.

Of those who developed BSI, 120 were transplanted during the observation period and 12 received HSCT before January 1, 2004.

Incidence and Timing of BSI

All BSI episodes observed during the study period were included in the study, even if patients had actually been transplanted earlier. The total number of patients who developed at least 1 episode of BSI during the study period was 132; 103 (78%) of them had a single episode, 24 (18%) had 2 episodes, and 5 (4%) had more than 2 episodes. The total number of BSI episodes was 168, with isolation of 182 pathogens. To obtain information about the incidence of BSI, we calculated that out of 343 patients who received HSCT during the study period, 116 (34%) developed at least 1 episode of BSI.

Median time of BSI was day +10, ranging from −8 to 4876. Seventeen (10%) episodes occurred before HSCT, 101 (60%) within 30 days after HSCT and 50 (30%) more than 30 days after HSCT. Considering solely those patients (n = 108) who had sepsis after HSCT, time to BSI was 12 days (range: 1-4876).

Etiology of BSI

Among 168 episodes, 91 (54.2%) were caused by Gram-positive bacteria (GPB), 54 (32.1%) by GNR, and 9 (5.4%) by fungi. In addition, there were 14 (8.3%) polymicrobial BSI with 24 isolated pathogens: 12 GPB, 14 GNR, and 2 *Candida*.

Out of 182 pathogens isolated, 57% were GPB, 37% were GNR, and 6% were fungi (11 *Candida* species). Detailed etiology is outlined in Table 1.

There was a significant change in the etiology of BSI during the study period. As shown in Figure 1, during the first 2 years GPB isolates were more frequent than GNR; since 2006, this difference was no longer present. Whereas the overall number of GNR per year remained stable, GPB isolates decreased, with a consequent relative percent GNR increase from 28% in 2004 to 48% in 2007 (Figure 1). The GPB/GNR ratio decreased significantly from 2.4 in 2004 to 1 in 2007 ($P = .043$); and from 2 in years 2004-2005 to 1 in years 2006-2007 ($P = .029$).

Among 103 GPB, the most frequent were *Staphylococcus* species (44%), *Enterococcus* species (39%) and *Streptococcus viridans* (11%). The number of isolated staphylococci decreased sharply during the observation period, from 54% (37 of 68) in 2004-2005 to 23% (8 of 35) in 2006-2007 ($P = .002$). The number of enterococcal isolates per year remained stable, but *Enterococcus faecium* replaced *Enterococcus faecalis* as the predominant species, with *E. faecalis* to *E. faecium* ratio decreasing from 4.5 in 2004 to 0.3 in 2007, $P = .006$ (Figure 2).

Escherichia coli and *Pseudomonas aeruginosa* were the most frequently isolated GNR (37% and 26% of GNR, respectively). The prevalence of *E. coli* among GNR increased, from 20% in 2004 (3 of 15) to 62% in 2007 (12 of 21), $P = .026$.

Among 11 Candida BSI, *Candida krusei* was the most frequent species (36%). Seven fungal BSI occurred during neutropenia (4 before engraftment and 3 during secondary neutropenia), 3 during GVHD and 1 episode of *C. parapsilosis* BSI was related to indwelling central venous catheter.

Out of 168 BSI episodes, 129 (77%) occurred during neutropenia, 21 (12%) during GVHD, and 18 (11%) under other conditions. Of 21 BSI that were GVHD related, 14 (67%) were caused by GNR, 4 (19%) by GPD, and 3 (14%) by *Candida*. Detailed etiology of single pathogen bacterial BSI during neutropenia, GVHD and other periods is shown in Figure 3.

Antibiotic Resistance

All 41 CoNS and 3 of 4 *Staphylococcus aureus* isolates were resistant to oxacillin. Moreover, 64% (7 of 11) of isolates of *Streptococcus viridans* isolates resulted in resistant to penicillin. There was a major shift in antimicrobial resistance among enterococci. Resistance to ampicillin increased from 43% (7 of 20) in 2004-2005 to 70% (14 of 20) in 2006-2007, $P = .027$ (Figure 4).

Table 1. Etiology of 168 Blood Stream Infections with 182 Pathogens Isolated between 01/01/04 and 31/12/07 in 132 Allogeneic Stem Cell Transplant Recipients

	Number, (%)				
Organism	2004	2005	2006	2007	Total, 182
Gram positive	36 (68%)	32 (58%)	14 (47%)	21 (48%)	103 (57%)
Staphylococcus	19	18	4	4	45
Coagulase negative	18	17	2	4	41
Staphylococcus aureus	1	1	2	0	4
Enterococcus	11	9	7	13	40
Enterococcus faecalis	9	6	3	3	21
Enterococcus faecium	2	2	4	9	17
Others	0	1*	0	1†	2
Viridans streptococci	4	4	2	1	11
Corynebacterium	2	1	0	2	5
Others	0	0	1‡	1§	2
Gram negative	15 (28%)	18 (33%)	14 (47%)	21 (48%)	68 (37%)
Escherichia coli	3	5	4	13	25
Pseudomonas aeruginosa	6	3	4	5	18
Klebsiella pneumoniae	2	0	3	2	7
Enterobacter	2	4	0	1	7
Stenotrophomonas maltophilia	1	2	2	0	5
Burkholderia cepacia	0	2	1	0	3
Others	1¶	2^	0	0	3
Candida	2 (4%)	5 (9%)	2 (7%)	2 (5%)	11 (6%)
krusei	2	1	1	0	4
albicans	0	2	0	0	2
parapsilosis	0	0	1	1	2
species	0	2	0	0	2
glabrata	0	0	0	1	1

*_Enterococcus_ species.
†_Enterococcus avium._
‡_Rothia mucillaginosa._
§_Streptococcus pneumoniae._
¶_Pseudomonas_ species.
^_Pseudomonas_ species and _Acinetobacter_ species.

Among 18 isolates of *Pseudomonas aeruginosa*, 9 (50%) were resistant to third- generation cefalosporin (namely, ceftazidime), 3 (16%) were resistant to piperacillin/tazobactam, and 8 (44%) to carbapenems; 2 strains were resistant to all antimicrobials except for colistin. Among others, GNR rods, 18% (7 of 25) of *E. coli*, 86% (6/7) of *K. pneumoniae*, and 57% (4 of 7) of *Enterobacter* species were ESBL producers. *E. coli* was resistant to ceftazidime in 28%, to piperacillin/tazobactam in 24%, and no resistant strains to carbapenems were found. The rate of ESBL-producing bacteria remained stable during each year of the study,

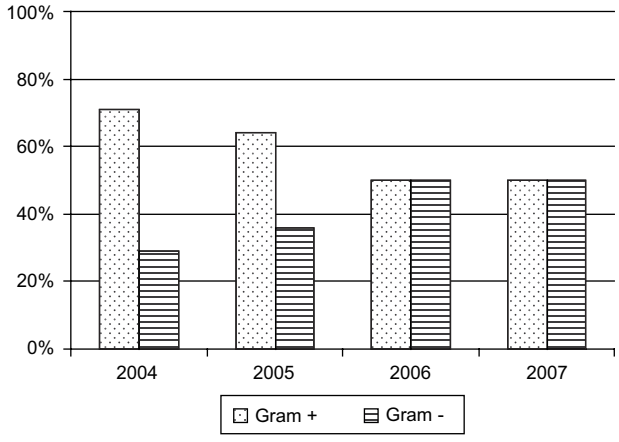

Figure 1. Percentage of Gram-positive and Gram-negative bacteria isolated from blood stream infections over the 4-year period. The Gram-positive to Gram-negative bacteria ratio decreased significantly: from 2.4 in 2004 to 1 in 2007, $P = .043$; and from 2 in years 2004-2005 to 1 in 2006-2007, $P = .029$.

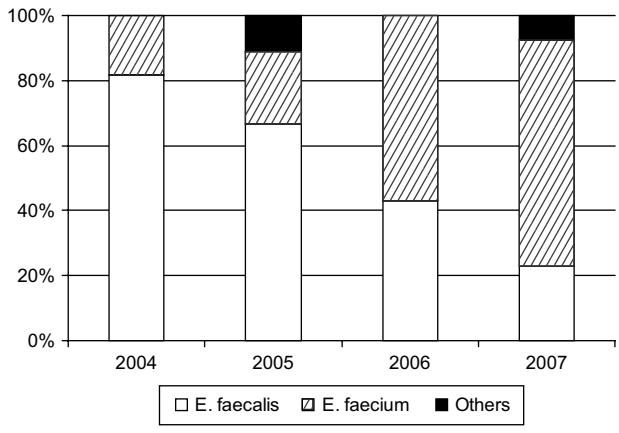

Figure 2. Etiology change among *Enterococcus* species throughout the study period, percent values of number of isolates. The number of isolates remained stable, but *E. faecium* replaced *E. faecalis* as the predominant species with *E. faecalis* to *E. faecium* ratio decreasing from 4.5 in 2004 to 0.3 in 2007, $P = .006$.

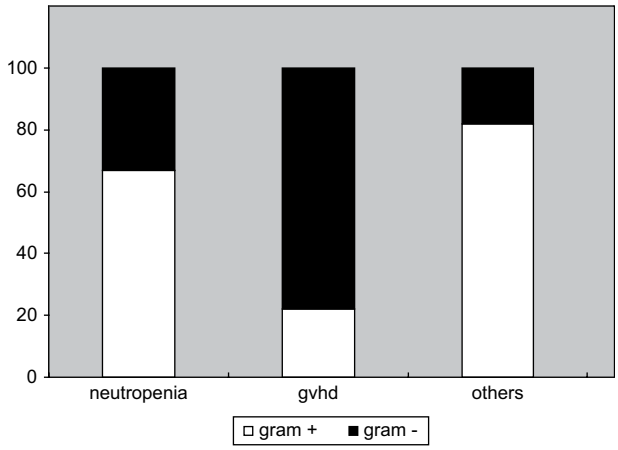

Figure 3. Different etiology of single bacterial blood stream infections (BSI) during neutropenia (129 BSI), graft-versus-host-disease (GVHD) (21 BSI) and other periods (18 BSI). Note: Neutropenia: staphylococci 25%, Enterococci 28%, other Gram-positive 14%, *E.coli* 14%, *P. aeruginosa* 9%, other Gram-negative 10%; GVHD: 11%, 11%, 0%, 17%, 33%, 28%; other periods: 56%, 13%, 13%, 6%, 6%, 6%, respectively.

being 43% (3 of 7), 44% (4 of 9), 71% (5 of 7), and 31% (5 of 16) during each year of the study. Overall prevalence of ESBL producing *E. coli*, *K. pneumoniae*, and *Enterobacter* was 44% (17 of 39). Even though GNR BSI rate increased significantly in our center, the incidence of MDR remained stable. Detailed antimicrobial sensitivity of GNR is presented in Table 2.

Fluoroquinolone (FQ) resistance was frequent, with only 19% of GPB and 26% of GNR being susceptible to FQ (no data for 4 isolates of *Streptococcus viridans*). Among GNR, resistance to fluoroquinolones increased during the 4 years of the study, although the difference was not statistically significant (60%, 72%, 71%, and 86%. respectively).

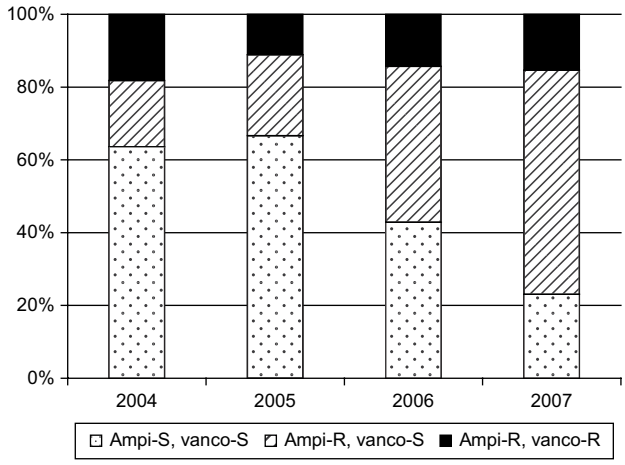

Figure 4. Resistance changes among *Enterococcocus* species throughout the study period; percent values of number of isolates. Ampicillin-susceptible (Ampi-S) isolates decreased in 2006-2007 compared to 2004-2005, $P = .027$. Ampicillin and vancomycin resistant (Ampi-R, vanco-R) strains remained stable.

Outcome

The crude mortality rate at 7 and 30 days after each BSI episode was 11.3% (19 of 168) and 20.2% (34 of 168), respectively. Analyzing mortality according to BSI etiology, 7-day mortality rate was 7% (6 of 91) in case of single GPB BSI, 17% (9 of 54) for single GNR BSI, 22% (2 of 9) for Candida BSI, and 14% for polymicrobial BSI (2 of 14); 30-day mortality rate was 18% (16 of 91), 24% (13 of 54), 22% (2 of 9), and 21% (3 of 14), respectively. *Pseudomonas aeruginosa* (7 of 18, 39%) was the pathogen with the highest associated 7-day mortality rate, followed by *Candida* (2 of 9, 22%), *Klebsiella pneumoniae* (1 of 6, 17%), and polymicrobial infection (2 of 14, 14%) ($P = .011$). Results of mortality rates at 7 and 30 days after BSI are shown in Table 3.

DISCUSSION

This study reports a 34% rate of BSI occurring in HSCT recipients, either before or after BMT procedure. We observed—as is already shown in other centers—a high incidence of BSI in allogeneic HSCT, particularly during the preengraftment phase. However, we also showed that a consistent number of BSI occurred late after HSCT, concomitantly with clinical conditions such as secondary (recurrent) neutropenia and/or GVHD.

In our center, BSI etiology changed, with a significant decrease of the Gram-positive/Gram-negative bacteria ratio, in line with recent reports analyzing similar patient populations [4,12,20]. This shift occurred progressively during the 4 years of the study, appearing, therefore, as a real change in microbial ecology and not only an incidental and transitory phenomenon. In addition, when comparing our study with a previous one carried out in our center [19], the number of GNR as BSI agents increased from 27 in years 1998-2002 to 68 in years 2004-2007.

The high proportion of CoNS during the first 2 years of our study is unlikely to be expression of contamination rather than true bacteremia, because rigorous definition criteria of BSI were applied throughout the study, in accordance with other investigators [2,6,21]. The sharp decrease of CoNS BSI in the last 2 years of our observation is difficult to explain. In HSCT patients, the sources of most BSI are usually the skin, the oral mucosa, or the gastrointestinal (GI) tract. Although the aim of the current study was not finding the BSI source, it is likely that the oral mucosa or the GI tract replaced the skin as a portal of entry, given the parallel increase of *E. coli* and other GNR. Further prospective studies are warranted to better investigate the reasons for this shift.

The development of resistance to antimicrobial agents remains an important concern in the

Table 2. Antibiotic Susceptibility in 68 Gram-Negative Isolates Responsible for 66 Episodes of Blood Stream Infections

	Number (%)					
Organism (Number)	FQ—R	Third-Generation Cephalosporin—R	Pip/taz—R	Carbapenem—R	ESBL Producers	MDR
Total (68)	50 (74%)	30 (44%)	18 (26%)	17 (25%)	17 (44%)	24 (35%)
Escherichia coli (25)	23 (92%)	7 (28%)	6 (24%)	0	7 (28%)	3 (12%)
Pseudomonas aeruginosa (18)	13 (72%)	9 (50%)	3 (16%)	8 (44%)	—	10 (55%)
Klebsiella pneumoniae (7)	6 (86%)	6 (86%)	4 (57%)	1 (14%)	6 (86%)	5 (71%)
Enterobacter (7)	5 (71%)	4 (57%)	1 (14%)	1 (14%)	4 (57%)	1 (14%)
Stenotrophomonas maltophilia (5)	4 (80%)	5 (100%)	5 (100%)	5 (100%)	—	5 (100%)
Burkholderia cepacia (3)	0	0	0	3 (100%)	—	1 (33%)
Others* (3)	0	0	0	0	—	0

ESBL indicates extended spectrum beta-lactamase; FQ, fluoroquinolone; MDR, multidrug resistant; Pip/taz, piperacillin-tazobactam; R, resistant.
*Two Pseudomonas species; 1 Acinetobacter species.

hospitalized neutropenic patients, mostly because MDR infections are known to be associated with increased mortality and costs [22,23]. In fact, GNR bacteremia has always been considered an ominous sign, because of its high mortality rate. Furthermore, GNR antimicrobial resistance could hamper an effective empirical treatment. We found an MDR incidence of 35%, for the whole GNR population as well as for individual pathogens, such as *P. aeruginosa*, *E. coli*, and *K. pneumoniae*. This MDR incidence was higher than that found in an European study focused on GNR bacteremia [24], possibly because of the peculiar clinical characteristics of the study patients, repeatedly and heavily treated with broad-spectrum antibiotics in other centers before being admitted in our unit. However, the increase of MDR GNR as a cause of BSI is very worrisome, because of the lack of new agents active on GNR, particularly *Pseudomonas*.

Considering the widespread FQ prophylaxis, it is not surprising that FQ resistance was frequent, with less than one-fifth of GPB and one-third of GNR being susceptible to FQ. Therefore, given the high incidence of FQ-resistance in our patients, the implementation of prophylactic protocols should be carefully evaluated.

Table 3. Seven- *and 30-Day Crude Mortality Rate Divided by Bacterial Strain in 168 Episodes of Blood Stream Infection in Recipients of allogeneic Hematopoietic Stem Cell Transplant*

Bacterial Strain, Number of Patients	7-Day Mortality, Number (%)	30-Day Mortality, Number (%)
Total		
Staphylococci, 39	2 (5)	4 (10)
Enterococci, 35	4 (11)	8 (23)
Streptococcus viridans, 7	0 (0)	3 (43)
Other Gram-positive bacteria, 10	0 (0)	1 (10)*
Pseudomonas aeruginosa, 18	7 (39)	8 (44)
Escherichia coli, 20	0 (0)	1 (5)
Klebsiella pneumoniae, 6	1 (17)	1 (14)
Other Gram-negative bacteria, 12	1 (8)	3 (25)†
Candida, 9	2 (22)	2 (22)
Polymicrobial, 14	2 (14)	3 (21)

**Corynebacterium* species.
†Two Burkholderia cepacia, 1 Stenotrophomonas maltophilia.

Enterococci remained an important threat in our patients, with constantly high prevalence of these bacteria since 1998 [19]. However, a major shift in species, and consequently in antimicrobial resistance, was observed from 2004 to 2007. *E. faecium*, constantly resistant to ampicillin and in 24% of isolates resistant to vancomycin (VRE), replaced *E. faecalis* as the most frequent species. The empirical use of vancomycin is controversial, and probably not indicated. Nevertheless, in our center it remains common practice. For the time being, the incidence of VRE bacteremia remained stable but as suggested by other reports, its incidence will probably rise [13,15,16].

Although the study was not designed to assess the mortality attributable to BSI, some comments on short-term survival can be made. The 7-day mortality in the whole cohort was as high as 11%, with different rates depending on the causal pathogen. In fact , similarly to results of other studies [3,4,25], *P. aeruginosa* and *Candida* were associated to the highest mortality rate. Even though mortality rate was the lowest in case of Gram-positive BSI, it still reached 7%. Considering that, unlike in other studies [3], viridans *Streptococci* accounted for very low mortality rate, overall Gram-positive fatality rate is because of enterococci and staphylococci. However, despite important changes in BSI etiology and antimicrobial resistance, the 30-day mortality did not increase when compared to the 1998-2001 study (20% and 26%, respectively), probably because the 30-day mortality is a variable depending more on the underlying disease than the infectious event.

There are some limitations to this study. As with many other studies, the current 1 is retrospective in nature. In a population of allogeneic HSCT recipient, the attributable mortality is often difficult to establish. In fact, several coexisting patoneologies (GVHD, relapse, infection, bleeding disorders), may be not only the direct cause of death but also may reciprocally overlap. Therefore, we chose to analyze only short-term survival after BSI, although some pathogens may not be responsible for the high post-BSI mortality, and the sepsis per se might be a sign of poor clinical conditions [13].

In summary, BSI is a frequent and potentially life-threatening complication of HSCT.

The type of causative organism influenced mortality early after BSI. BSI etiology may change rapidly, requiring implementation of new empirical-therapy schemes. Therefore, regularly performed epidemiologic surveillance is mandatory.

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