ORIGINAL ARTICLE

Outcome of bloodstream infections among spinal cord injury patients and impact of multidrug-resistant organisms

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Study design: Retrospective cohort study.

Objectives: Our study aimed to describe the outcome of bloodstream infection (BSI) in spinal cord injury (SCI) patients and their associated risk factors for severity and mortality.

Setting: A French University Hospital.

Methods: We conducted a retrospective cohort study of all BSIs occurring in hospitalized SCI patients. We analyzed their outcome and risk factors especially the impact of multidrug-resistant organisms (MDROs).

Results: Overall, 318 BSIs occurring among 256 patients were included in the analysis. Mean age was 50.8 years and gender ratio (M/F) was 2.70, with a mean injury duration of 11.6 years. Severity and 30-day mortality of BSI episodes were, respectively, 43.4% and 7.9%. BSI severity was significantly more frequent when caused by respiratory tract infections (RTIs) (odds ratio (OR)=1.38; 95% confidence interval (CI): 1.13–1.44) and significantly lower when caused by urinary tract infections (UTIs) (OR=0.47; 95% CI: 0.28–0.76). BSI mortality was significantly higher when caused by RTIs (OR=3.08; 95% CI: 1.05–8.99), catheter-related bloodstream infections (OR=3.54; 95% CI: 1.36–9.18) or *Pseudomonas aeruginosa* infections (OR=3.79; 95% CI: 1.14–12.55). MDROs were responsible for 41.2% of all BSI. They have no impact on severity and mortality, whichever be the primary site of infection. In multivariate analysis, mortality was higher when BSI episodes were due to RTIs (OR=3.26; 95% CI: 1.29–8.22) and *Pseudomonas aeruginosa* infections (OR=3.53; 95% CI: 1.06–11.70), or when associated with immunosuppressive therapy (OR=2.57; 95% CI: 1.14–5.78) or initial severity signs (OR=1.68; 95% CI: 1.01–2.81).

Conclusion: BSI occurring in SCI population were often severe but mortality remained low. MDROs were frequent but not associated with severity or mortality of BSI episodes. Risk factors associated with mortality were initial severe presentation, RTI, immunosuppressive therapy and BSI due to *Pseudomonas aeruginosa*.

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INTRODUCTION

Nearly 250 000 inhabitants are affected with spinal cord injury (SCI) in the United States, with an annual incidence of 11 000.¹ In Europe, SCI incidence varies between 10.4 and 29.4 per million inhabitants.

Infections are the main cause of death in SCI patients, especially bloodstream infections (BSIs).^{2–8}

Colonizing multidrug-resistant organisms (MDROs) are frequent in the SCI population.^{7,9–13} In the general population, hospital-acquired infections and MDRO infections are associated with increased mortality and increased cost.⁷ In the SCI population, such infections have been shown to increase the number of hospitalizations and the length of stay.¹⁴

The outcome of BSI in SCI has been little studied. Bhatt *et al.* noticed a hypotension in 5 out of 29 cases (17.1%), although mortality in this population ranges from 1.7 to 29% according to different reports.^{4,15–17}

In particular, the outcome of BSI due to MDROs in this population is unknown. In a previous retrospective study on BSI epidemiology in SCI population over 16 years, we concluded that the prevalence of MDROs, which was high, remained stable over the years. Also, it was not significantly different regarding age, gender, type and duration of SCI, primary site of infection or bacteria species involved.⁹

From this large cohort, we studied the severity and mortality of BSI according to the primary site of infection and according to the drug resistance characteristics of the microorganisms involved.

MATERIAL AND METHODS

Settings and design

We performed a retrospective cohort study. We identified all patients hospitalized at our teaching Hospital (R. Poincaré, Garches, France), from 1 July 1998 to 31 October 2013, with an international classification disease 10th version (ICD-10). It included paraplegia or quadriplegia, and positive blood cultures for bacteria.

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Table 1 Definition of MDR depending on the micro-organism

Micro-organisms	MDR strains are intermediate or resistant to
<i>Pseudomonas aeruginosa</i>	At least three of the following group of antibiotics: <ul style="list-style-type: none"> • Piperacillin/tazobactam or Ticarcillin/clavulanate • Ceftazidime or Cefepime • Carbapenems (Imipenem, Meropenem) • Aminoglycosides (Gentamicin, Tobramycin, Amikacin) • Fluoroquinolones (Ciprofloxacin)
Enterobacteria (<i>Escherichia coli</i> and the KES bacterial group (<i>Klebsiella</i> , <i>Enterobacter</i> , <i>Serratia</i>))	At least one of the following class of antibiotics: <ul style="list-style-type: none"> • Third-generation cephalosporins • Carbapenems • Aminoglycosides • Fluoroquinolones
<i>Enterococcus</i>	Glycopeptide or presence of β -lactamase
Non-enterococcal <i>Streptococcus</i>	Penicillin
<i>Staphylococcus aureus</i>	Methicillin (MRSA)
MRCNS	Both: <ul style="list-style-type: none"> • Rifampicin • Fluoroquinolones
<i>Stenotrophomonas maltophilia</i>	Always considered as MDR bacteria

Abbreviations: MDR, multidrug resistance; MRCNS, methicillin-resistant coagulase-negative *Staphylococcus*; MRSA, methicillin-resistant *Staphylococcus aureus*.

Then, we reviewed medical charts and excluded any code mistakes. The microbiological data, as well as demographic characteristics, risk factors and outcomes were recovered from the local computerized medical entry and medical charts.

Because of its retrospective design, no ethical advice and written consent from patients were needed for this study.

Definitions

Case definition. BSI case was defined as the association of the following:

- At least one positive blood culture. For common skin contaminants (e.g., coagulase-negative *Staphylococci* diptheroids and so on), at least two different sets of blood cultures were required.
- A prescription of a systemic antibiotic treatment to treat the BSI.

Polymicrobial BSI was defined as having more than one organism found in the same BSI episode.

Microbiological definitions. During the study, different identification methods were used. Until May 2011, Gram-negative bacilli, except for *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia*, were phenotypically identified by the API 20E biochemical identification system (BioMérieux, Lyon, France). *P. aeruginosa* and *S. maltophilia* were identified by the API 20 NE biochemical identification system (BioMérieux). The identification of *Staphylococci* was based on the coagulase test (Bio-Rad, Paris, France), and the identification of *Enterococci* was based on the use of tellurite and bile esculin agar media (BD Diagnostics, Sparks, NV, USA). After May 2011, all isolates were identified by mass spectrometry (Bruker, Bremen, Germany).

Anti-microbial susceptibility was tested using the agar disk diffusion method (Bio-Rad) or an automated broth microdilution method (Phoenix, BD Diagnostics, Oxford, UK), with susceptibility breakpoints defined by the French Committee for Anti-microbial Susceptibility Testing.

MDRO status was confirmed after antibiotic susceptibility reviewing and comparison with the definitions described in Table 1.

Confirmation of extended-spectrum β -lactamase activity was determined according to the National Committee for Clinical Laboratory Standards.^{10,11}

Extended-spectrum β -lactamases are enzymes produced by bacteria (also known as penicillinase) that provide multiresistance to β -lactam antibiotics such as penicillins and cephalosporins.

Primary site of infection. Primary site of infection was defined clinically by the physician in charge (reported in medical chart), or bacteriologically (same bacterial identification as in the blood culture). Primary sites were categorized as follows: urinary tract infection (UTI), pressure sore, catheter-related BSI, osteoarticular infection (OAI), respiratory tract infection (RTI), others (including skin and soft tissue infection and intra-abdominal infection) and unknown when no primary site had been identified.

Severity. Severity was defined as the requirement of at least one of the following criteria: volume expansion, assisted (mechanical) ventilation, vasopressor requirement and intensive care unit admission during the episode.

Mortality. Mortality was defined as death of the patient within 30 days following BSI episode.¹²

Immunosuppressive therapy. Immunosuppressive therapy was defined as corticotherapy, chemotherapy or immunosuppressive treatment such as cyclophosphamide, azathioprine and cyclosporine.

Statistical analysis

All continuous variables were presented as mean (m) and standard deviation (s.d.), and the categorical variables were presented as frequencies.

Correlations between risk factors and characteristics of BSI in patients with SCI and outcome (mortality and severity) were determined by Student's *t*-test for continuous variables and the Pearson's χ^2 test for categorical variables.

Multivariate analyses were performed to assess the relationship between all associated risks that had a *P*-value ≤ 0.2 . The Hosmer–Lemeshow statistic was calculated to assess the model's goodness of fit. Odds ratio (OR) was calculated from the multivariate analyses to quantify association with severity and mortality with a confidence interval (CI) of 95%. An OR > 1 was considered to be associated with severity or mortality.

All reported probability values (*P*-values) were based on two-sided tests, and a *P*-value < 0.05 was considered statistically significant.

All analyses were performed using the SPSS 17.0 software (SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 396 positive blood cultures were detected among 317 patients; 78 episodes (61 patients) were excluded because the microorganism involved was considered a contaminant. Overall, we included 318 episodes of BSI occurring among 256 patients. Table 2 shows the global sociodemographic and clinical characteristics of the study population.

The median age of the cohort was 50.8 ± 17.0 years and the gender ratio (M/F) was 2.70. The mean duration of spinal cord injury was 11.6 years (Table 2).

Primary site of infection was identified in 91% of BSI. They were mainly UTI (34.0%) and pressure sore (25.2%), then catheter-related BSIs (11.3%) and RTI (8.5%) (Table 2).

There were 351 microorganisms identified in all 318 BSI episodes; 31 episodes (9.7%) were polymicrobial.

The most frequent pathogens identified were *Enterobacteriaceae* in 44.3% of cases ($n = 141$). They were followed by *Staphylococcus aureus* ($n = 84$; 26.4%), *Pseudomonas aeruginosa* ($n = 22$; 6.9%), *Streptococcus* spp. ($n = 32$; 10.1%) and *Enterococcus* spp. ($n = 16$; 5%) (Table 2).

MDROs were involved in 41.2% of BSI and were distributed as follows: 53.4% of *Enterobacteriaceae* (*Escherichia coli* ($n = 26$), *Klebsiella* spp. ($n = 13$), *Proteus* spp. ($n = 7$), *Enterobacter* spp. ($n = 5$), *Morganella* spp. ($n = 3$), *Citrobacter* spp. ($n = 3$), *Providencia* spp. ($n = 2$) and *Serratia* spp. ($n = 1$)), 32.8% of *Staphylococcus aureus* (methicillin-resistant) and 6.1% of *Pseudomonas aeruginosa*.

Median anti-microbial treatment duration varied from 12 to 15 days, except for OAI with a median duration of 45 days (Table 3).

Empiric treatments were microbiologically effective in 78% of the cases.

UTI were mostly treated by parenteral third-generation cephalosporins associated with aminoglycosides. Pressure sore, RTI and catheter-related BSIs were mostly treated by glycolipopeptides associated with aminoglycosides. OAIs were predominantly treated by penicillin and aminoglycosides (Table 4).

Treatment durations according to bacterial species are presented in Supplementary Appendix 1. More than 60% of the patients received combination therapy, especially when treating *Pseudomonas aeruginosa* infections, even if it did not involve MDR strains (Supplementary Appendix 2). The most prescribed associations were β -lactam with aminoglycosides regarding *Pseudomonas aeruginosa* and Enterobacteria infections (Supplementary Appendix 3).

Table 2 Sociodemographic, clinical and microbiological characteristics of BSI in spinal cord injury population (N= 318)

Population	N = 318
Age (mean $\pm$ s.d.)	50.8 $\pm$ 17.0
Gender, male (N; %)	232 (73)
Paraplegic (N; %)	191 (60.1)
Tetraplegic (N; %)	122 (38.4)
Primary site of infection (N; %)	
UTI	108 (34.0)
Pressure ulcer	80 (25.2)
Catheter-related bloodstream infection	36 (11.3)
RTI	27 (8.5)
OAI	19 (6.0)
Other	20 (6.3)
Bacteria species (N; %)	
<i>Staphylococcus aureus</i>	84 (26.4)
Coagulase-negative Staphylococci	20 (6.3)
<i>Escherichia coli</i>	70 (22.0)
<i>Pseudomonas aeruginosa</i>	22 (6.9)
<i>Proteus</i> spp.	16 (5.0)
<i>Klebsiella</i> spp.	24 (7.5)
<i>Acinetobacter</i> spp.	5 (1.6)
<i>Enterobacter</i> spp.	9 (2.8)
<i>Morganella</i> spp.	6 (1.9)
<i>Providencia</i> spp.	2 (0.6)
<i>Stenothrophomonas</i> spp.	1 (0.3)
Anaerobes	28 (8.8)
<i>Streptococcus</i> spp.	32 (10.1)
<i>Enterococcus</i> spp.	16 (5.0)
Others (<i>Citrobacter</i> , <i>Serratia</i>)	12 (3.8)
Existing signs of severity	138 (43.4)
Severity types	
ICU admission	111 (34.9)
Volume repletion (volemia expansion)	79 (24.8)
Assisted ventilation (mechanical ventilation)	63 (19.8)
Vasopressors requirements	50 (15.7)
Mortality (<30 days)	25 (7.9)

Abbreviations: BSI, bloodstream infection; ICU, intensive care unit; m, mean; N, number of BSI episodes; OAI, osteoarticular infection; RTI, respiratory tract infection; UTI, urinary tract infection.

At initial presentation, 43.4% of BSI episodes were considered severe, corresponding mostly to intensive care unit admission and volume expansion (Table 2).

Regarding the primary site of infection, UTI and OAI were associated with less frequent severity (respectively, OR=0.47; 95% CI: 0.28–0.76; $P=0.002$; OR=0.13; 95% CI: 0.03–0.61; $P=0.003$), contrary to RTI (OR=1.38; 95% CI: 1.13–1.44; $P<10^{-4}$) (Table 5).

The mortality rate was 7.9% (Table 2). Studying the relationship between mortality and primary site of infection, UTI was significantly associated with less mortality (OR=0.15; 95% CI: 0.03–0.66; $P=0.004$). On the contrary, RTI (OR=3.08; 95% CI: 1.05–8.99; $P=0.031$) and catheter-related BSIs (OR=3.54; 95% CI: 1.36–9.18; $P=0.006$) were associated with a higher mortality (Table 5).

Considering BSI severity and mortality, we performed several analyses comparing these outcomes according to bacterial species (Table 6). BSI due to *Pseudomonas aeruginosa* was significantly associated with a higher mortality (OR=3.79; 95% CI: 1.14–12.55).

Also, there was no significant difference in severity presentation or mortality while comparing MDRO and non-MDRO groups (respectively, $P=0.981$ and $P=0.306$).

In multivariate analysis (Table 7), the following factors were independently associated with a higher mortality: immunosuppressive

Table 3 Antibiotic treatment duration among spinal cord injury patients with BSI, according to primary site of infection (N= 279)

	Total treatment duration (days)	Combined anti-microbial therapy duration (days)	Mono anti-microbial therapy duration (days)
Urinary tract infection (N = 95)			
Mean $\pm$ s.d.	18.70 $\pm$ 11.14	6.97 $\pm$ 9.99	11.74 $\pm$ 10.72
Median	15	3	10
Pressure ulcer (N = 69)			
Mean $\pm$ s.d.	23.94 $\pm$ 23.74	18.65 $\pm$ 24.98	5.46 $\pm$ 9.64
Median	15	10	
Respiratory tract infection (N = 25)			
Mean $\pm$ s.d.	12.16 $\pm$ 5.44	4.64 $\pm$ 5.84	7.52 $\pm$ 6.00
Median	12	3	9
Catheter-related bloodstream infection (N = 34)			
Mean $\pm$ s.d.	15.76 $\pm$ 11.90	9.06 $\pm$ 11.58	6.65 $\pm$ 8.53
Median	14	3.5	5.5
Osteoarticular infection (N = 16)			
Mean $\pm$ s.d.	62.69 $\pm$ 42.39	59.75 $\pm$ 41.98	2.94 $\pm$ 11.23
Median	45	45	
Digestive infection (N = 8)			
Mean $\pm$ s.d.	14.50 $\pm$ 12.54	6.25 $\pm$ 9.05	8.25 $\pm$ 10.96
Median	10.5	2	3.5
Other (N = 11)			
Mean $\pm$ s.d.	22.27 $\pm$ 11.79	15.45 $\pm$ 15.00	6.82 $\pm$ 8.00
Median	21	13	3
Unknown (N = 21)			
Mean $\pm$ s.d.	17.05 $\pm$ 11.37	8.75 $\pm$ 9.34	10.50 $\pm$ 13.18
Median	14	7.5	5

Abbreviations: BSI, bloodstream infection; N, number of BSI episodes.

Table 4 Types of anti-microbial therapies of BSIs in spinal cord injury patients according to primary site of infection (N=279)

	Penicillin	Piperacillin and tazobactam	Parenteral third-generation cephalosporin	Amino glycoside	Quinolone	Carbapenem	Rifampicin	Glycolipo peptide	Parenteral sodium colistimethate	Parenteral fosfomycin
<i>Urinary tract infection (N = 95)</i>										
1st line (N=95)	13	9	48	51	15	22	1	9	0	3
2nd line (N=46)	11	2	16	4	11	5	3	2	1	0
3rd line (N=15)	7	0	0	1	3	1	1	0	0	0
<i>Pressure ulcer (N = 69)</i>										
1st line (N=69)	20	14	12	31	4	12	5	25	0	2
2nd line (N=33)	9	4	2	14	6	9	7	9	1	1
3rd line (N=7)	1	0	1	0	2	0	2	0	0	0
<i>Respiratory tract infection (N = 25)</i>										
1st line (N=25)	9	2	4	13	1	4	1	10	1	0
2nd line (N=11)	7	0	1	1	2	1	0	1	0	1
3rd line (N=0)										
<i>Catheter-related bloodstream infection (N = 34)</i>										
1st line (N=34)	3	3	7	15	4	5	3	23	1	1
2nd line (N=12)	3	1	6	2	3	0	2	6	0	1
3rd line (N=1)	1	0	0	0	0	0	1	0	0	0
<i>Osteoarticular infection (N = 16)</i>										
1st line (N=16)	8	1	1	7	4	1	6	6	0	0
2nd line (N=10)	3	1	1	2	5	1	6	2	0	1
3rd line (N=8)	1	0	0	0	4	0	5	0	0	0
<i>Digestive infection (N = 8)</i>										
1st line (N=8)	1	0	5	4	0	1	1	2	0	0
2nd line (N=4)	1	1	1	0	2	0	0	0	0	0
3rd line (N=1)	1	0	0	0	0	0	0	0	0	0
<i>Other (N = 11)</i>										
1st line (N=11)	1	2	0	6	3	1	2	5	0	0
2nd line (N=5)	1	0	1	0	2	1	2	1	0	0
3rd line (N=2)	0	0	0	0	0	0	2	0	0	0
<i>Unknown (N = 21)</i>										
1st line (N=21)	4	2	7	13	3	4	0	6	0	0
2nd line (N=14)	3	2	4	4	2	0	0	4	0	0
3rd line (N=4)	0	0	0	0	3	0	1	0	0	0

Abbreviations: BSI, bloodstream infection; N, number of BSI episodes.

therapy (OR 2.57; 95% CI: 1.14–5.78; $P=0.022$), RTI (OR 3.26; 95% CI: 1.29–8.22; $P=0.012$), BSI due to *Pseudomonas aeruginosa* (OR=3.53; 95% CI: 1.06–11.70; $P=0.039$) and presence of initial severity sign (OR 1.68; 95% CI: 1.01–2.81; $P=0.045$).

DISCUSSION

Despite the frequency of BSI episodes in SCI population, only few studies have reported their outcome. In our study, BSIs were often severe (43.4%), but the mortality rate remained low (7.9%). Moreover, severity was higher when BSI was due to RTI, and mortality rate was higher when BSI was caused by RTI, catheter-related BSIs or *Pseudomonas aeruginosa*. On the contrary, BSI seemed less severe and with a better outcome when the primary site was a UTI or an OAI. Also, being infected with MDROs had no impact on the severity or the mortality of the episode. A higher mortality in this population was

independently associated with RTI, *Pseudomonas aeruginosa* infections, immunosuppressive therapy and initial severity signs.

Our study's population was a chronic SCI population with similar characteristics than previous data from literature.^{3,15–17}

The median age of our study population was inferior to median age of general population suffering from BSI found in the literature.¹³

We reported a high proportion of episodes with severe presentation, mostly due to intensive care unit admission, volemic expansion, mechanical ventilation and vasopressor requirement. This high rate of severe cases has not yet been reported. However, really few studies are available on this topic. Only Bhatt *et al.*¹⁶ in their study described hypotension in 5 out of 29 cases (17.1%). This could be due to the difficulty to diagnose sepsis in SCI patients and the delay before hospitalization.

In the general population, the usual mortality rate in BSI varies from 30% to 50%.^{14,18} In SCI population, according to several reports,

Table 5 Severity and mortality rates of BSI in patients with spinal cord injury, according to primary sites of infection (N = 318)

Primary site of infection	Existing signs of severity (N = 138)			Mortality (N = 25)		
	N (%) ^a	P-value	OR (95% CI)	N (%)	P-value	OR (95% CI)
Urinary tract infection (N = 108)	34 (31.5)	0.002	0.47 (0.28–0.76)	2 (1.9)	0.004	0.15 (0.03–0.66)
Pressure ulcer (N = 80)	30 (37.5)	0.198	0.71 (0.42–1.19)	4 (5.0)	0.272	0.54 (0.18–1.63)
Catheter-related BSI (N = 36)	20 (55.6)	0.127	1.71 (0.85–3.45)	7 (19.4)	0.006	3.54 (1.36–9.18)
Respiratory tract infection (N = 27)	27 (100)	0.000	1.38 (1.13–1.44)	5 (18.5)	0.031	3.08 (1.05–8.99)
Osteoarticular infection (N = 19)	2 (10.5)	0.003	0.13 (0.03–0.61)	0 (0.0)	0.189	1.91 (0.88–2.94)
Others (N = 20)	12 (60.0)	0.122	2.02 (0.80–5.09)	3 (15.0)	0.220	2.21 (0.60–8.13)
Unknown (N = 28)	13 (46.4)	0.624	1.21 (0.55–2.68)	4 (14.3)	0.186	2.13 (0.67–6.72)

Abbreviations: BSI, bloodstream infection; CI, confidence interval; N, number of BSI episodes; OR, odds ratio.

^aPercentage within primary site of infection.**Table 6 Outcome (severity and mortality) of BSIs in spinal cord injury patients according to micro-organisms**

Microorganisms	Severity			Mortality		
	N (%) ^a	OR (95% CI)	P-value	N (%) ^a	OR (95% CI)	P-value
<i>Enterobacteriaceae</i> (N = 98)	37 (37.8)	0.71 (0.43–1.16)	0.176	5 (5.1)	0.53 (0.19–1.47)	0.222
<i>Staphylococcus aureus</i> (N = 78)	41 (52.6)	1.63 (0.97–2.73)	0.060	6 (7.7)	0.96 (0.37–2.52)	0.949
Streptococci and Enterococci (N = 31)	12 (38.7)	0.80 (0.37–1.72)	0.579	3 (9.7)	1.29 (0.36–4.58)	0.693
<i>Pseudomonas aeruginosa</i> (N = 18)	11 (61.1)	2.14 (0.80–5.67)	0.118	4 (22.2)	3.79 (1.14–12.55)	0.020
AmpC-producing <i>Enterobacteriaceae</i> (N = 18)	10 (55.6)	1.68 (0.64–4.37)	0.284	3 (16.7)	2.52 (0.68–9.39)	0.153
Coagulase-negative Staphylococci (N = 17)	5 (29.4)	0.52 (0.18–2.53)	0.232	0 (0.0)	—	0.216
Anaerobes (N = 19)	10 (52.6)	1.48 (0.58–3.75)	0.402	0 (0.0)	—	0.189
Others (N = 10)	3 (30.0)	0.54 (0.13–2.16)	0.385	0 (0.0)	—	0.348
Polymicrobial (N = 29)	9 (31.0)	0.55 (0.24–1.26)	0.159	3 (10.3)	1.40 (0.39–4.99)	0.602

Abbreviations: BSI, bloodstream infection; CI, confidence interval; N, number of BSI episodes; OR, odds ratio.

^aPercentage within bacterial species.**Table 7 Multivariate analysis of the factors associated with mortality in spinal cord injury patients (N = 318)**

Factors	Adjusted OR (95% CI)	P-value
Immunosuppressive treatment	2.57 (1.14–5.78)	0.022
Respiratory tract infection	3.26 (1.29–8.22)	0.012
Bloodstream infection due to <i>Pseudomonas aeruginosa</i>	3.53 (1.06–11.70)	0.039
Presence of initial severity sign	1.68 (1.01–2.81)	0.045

Abbreviations: CI, confidence interval; OR, odds ratio.

it varies from 1.7% to 29%.^{4,15–17} The low rate of mortality in this specific population could be explained by the young age of the patients compared with the general population.

Outcome depending on the primary site of infection

When focusing on the primary site of infection, UTI was associated with a significant lower mortality rate, contrary to RTI and catheter-related BSIs. This is consistent with the literature: RTI is well known to have a high mortality rate in SCI population^{3,7} and UTI to be less fatal than others infections.^{3,17}

Indeed, DeVivo *et al.*¹⁹ have shown that pneumonia is the most common cause of death after SCI in all age groups. Severe bacterial pneumonias are often accompanied with bacteremia in this population, especially in patients undergoing mechanical ventilation.

However, the high mortality rate associated with catheter-related BSIs could be due to their occurrence mostly in intensive care unit.

Therefore, it could be a marker of fatal prognosis rather than an independent risk factor.

Outcome depending on bacteria species involved

Considering bacterial species, the only significant association was mortality and *Pseudomonas aeruginosa* species. *Pseudomonas aeruginosa* is frequently associated with higher mortality up to 21% and could be due to difficult treatment strategy.²⁰

Indeed, few therapeutic options exist for treating BSI due to *Pseudomonas aeruginosa*. A specific antipseudomonal β -lactam is needed such as ceftazidime or ureidopenicillin (ceftriaxone and cefotaxime are not effective). Moreover, a dual effective therapy is usually required.²¹

Outcome depending on the presence of MDROs

There is an increasing incidence of infections due to MDROs in the general population, especially due to *Enterobacteriaceae* and particularly extended-spectrum β -lactamase and carbapenemase producers.²² In our previous study, we found no significant increase of MDROs in SCI population.⁹

Infections due to MDROs could be associated with an increased mortality. As shown by Kang *et al.*,²³ during BSI due to *Enterobacter* species in non-SCI population, the 30-day mortality rate was significantly higher when a broad-spectrum cephalosporin-resistant *Enterobacter* was involved (3.7% vs 18.6%; $P = 0.021$).²³ Moreover, Deal *et al.*²⁴ identified resistance to second- or third-generation cephalosporins and to trimethoprim-sulfamethoxazole as independent risk factors for mortality during BSI caused by *Enterobacter* species or

Citrobacter freundii (respectively, adjusted OR = 5.16; 95% CI: 2.66–10.0; $P=0.013$ and OR = 5.44; 95% CI: 2.53–11.7; $P=0.027$). At last, Chang *et al.*²⁵ during *Enterobacter aerogenes* bacteremia found that resistance to extended-spectrum cephalosporins was an independent risk factor for mortality (OR = 9.21; 95% CI: 1.02–83.04; $P=0.048$).

However, other reports state that MDROs could have no impact on mortality, as suggested by Kim *et al.*²⁶ They found no difference in BSI caused by resistant or susceptible to extended-spectrum cephalosporins *Citrobacter freundii* (19.4% vs 25.6%; $P=0.45$).

Overall, the impact of MDROs during BSI is uncertain. In our study, no impact of MDRO on severity and/or mortality was noted. The main factor could be the adequacy of the initial anti-microbial therapy that has shown its major effect.²⁷ In our center, we are aware of the high prevalence of MDROs in SCI patients and local guidelines recommend an empirical use of broad-spectrum anti-microbial treatment for this population in case of severe sepsis. This attitude could explain the absence of impact of MDROs during BSI among SCI population in our study.

Moreover, some authors suggest that immunity of SCI population is stronger against bacterial aggression because of their recurrent infections that could explain both the low mortality rate (despite the high severity rate) and the absence of impact of MDROs.^{16,17,28} These data should reassure physicians about the favorable prognosis of BSI because of MDROs occurring in disabled population, and reinforce their use of invasive therapeutics.

Outcome depending on independent factors

Finally, the only independent factors associated with 30-day mortality were RTI, immunosuppressive therapy and initial severity. In this situation, handling of such patients should be quickly optimized with prompt intensive care management and broad-spectrum anti-microbial therapy. In a retrospective study on 123 BSIs occurring in 63 SCI patients (mean age 59 ± 2 years), Wall *et al.*³ reported hypoalbuminemia as the strongest independent predictor for mortality.³ This factor is linked to the initial severity of the episode or to the underlying poor conditions of patients.

The bias and weakness of our study are due to its monocentric and retrospective design. However, it is one of the largest cohorts of patients in relation to this topic to the best of our knowledge.

Therefore, these retrospective results need to be confirmed by future prospective studies. The definition of MDROs could be discussed, but there is no standard definition of anti-microbial resistance, especially for *P. aeruginosa* and other Gram-negative bacilli. Thus, we used a classification proposed by different authors.^{10,11,29–32}

In our study, MDROs have no impact on severity or mortality, whichever be the primary site of infection.

The only factors associated with higher mortality were RTI (OR = 3.26; 95% CI: 1.29–8.22), BSI due to *Pseudomonas aeruginosa* (OR = 3.53; 95% CI: 1.06–11.70), immunosuppressive therapy (OR = 2.57; 95% CI: 1.14–5.78) or initial severity signs (OR = 1.68; 95% CI: 1.01–2.81).

Despite the difficulties in medical management encountered with such population, mortality remained lower than that in the general population, even in critical situations, which were common. It might be due to the young age of the patients.

Thus, SCI population even with MDROs BSI has a good prognosis when managed by an expert team.

DATA ARCHIVING

There were no data to deposit.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Supplementary Information accompanies this paper on the Spinal Cord website (<http://www.nature.com/sc>)