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ORIGINAL RESEARCH

Clinical Characteristics, Risk Factors and Prognosis of Carbapenem-Resistant *Pseudomonas aeruginosa* Bloodstream Infections in Cancer Patients: An 8-year Retrospective Study in a Tertiary Cancer Hospital

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Purpose: To ascertain clinical characteristics, risk factors and prognosis of bloodstream infection (BSI) caused by carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) among cancer patients with solid tumors (ST) and hematological malignancies (HM).

Methods: A retrospective study (January 2015 to December 2023) was performed on the health records of cancer patients with *Pseudomonas aeruginosa* (PA) BSI at a tertiary cancer hospital in China. Ninety-two CRPA BSI cases were randomly paired with contemporaneous carbapenem-sensitive *Pseudomonas aeruginosa* (CSPA) BSI cases at a ratio of 1:1. Multivariate logistic regression analysis was performed to identify risk factors associated with the development of CRPA BSI and Cox regression for mortality rates. Survival probability was evaluated using the Kaplan-Meier estimator. Between-group survival differences were analyzed using the Log rank test and Hazard ratios (HR) were calculated to quantify mortality risk disparities.

Results: A total of 361 cancer patients with PA BSI were included, 25.5% (92/361) of which were infected with CRPA. Among the 184 enrolled patients (48 with ST, 136 with HM), the independent risk factors for developing CRPA BSI were platelet counts and recent carbapenem use within 90 days in patients with ST. Presence of multidrug-resistant *P. aeruginosa* (MDRPA) and exposure to carbapenems within 90 days were the risk factors for developing CRPA BSI in patients with HM. The 30-day mortality of CRPA BSI was 37.5% and 35.3% in patients with ST and HM, respectively. Additionally, higher Pitt bacteremia score (PBS) was distinctly associated with increased 30-day mortality in cancer patients suffering from CRPA BSI (HR 1.672, 95% CI 1.309–2.135, $p< 0.001$).

Conclusion: The mortality rates of CRPA BSI are notably high in both patients with ST and HM. The risk factors for CRPA BSI and mortality may guide and optimize the management of CRPA BSI in cancer patients.

Keywords: carbapenem-resistant *Pseudomonas aeruginosa*, bloodstream infection, cancer, solid tumors, risk factor, mortality

Introduction

Infection is a common complication in cancer patients and could occur in various sites, including respiratory tract, urinary tract and bloodstream.[1] Bloodstream infection (BSI) is among the most severe infection types. Cancer patients, especially those experiencing malnutrition, weakened immunity, or undergoing treatments like radiotherapy and chemotherapy, are particularly prone to BSI.[2] According to the data of China Antimicrobial Surveillance Network (CHINET, https://www.chinets.com/Data/GermYear) in 2024, *Pseudomonas aeruginosa* (PA) ranked the third among clinically isolated Gram-negative pathogens from bloodstream and the resistance rates of PA to imipenem and meropenem were 21.3% and 17.3%, respectively. Nevertheless, it is second or third after *Escherichia coli* and *Klebsiella pneumoniae* as a causative agent of BSI in cancer patients.[3–6]

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BSI caused by PA may delay initiation of chemotherapy, prolong hospitalization, increase costs and raise morbidity and mortality.[7,8] Therapeutic options for BSI with PA are limited due to the broad intrinsic and increasing acquired resistance of this bacterium to many antipseudomonal antibiotics.[9] Moreover, BSI caused by carbapenem-resistant *P. aeruginosa* (CRPA) are potentially life-threatening with a higher mortality in cancer patients, such as those with hematologic malignancies (HM) and solid tumors (ST).[10]

Although solid tumors make up the largest proportion of cancers, there are far more studies focused on BSI in patients with HM than those in patients with ST. The incidence of BSI in HM is higher than that in ST.[11] Clinical features of the two groups differ in many aspects. For example, patients with HM are more inclined to suffer from significant immunosuppression and prolonged, severe neutropenia.[12] Conversely, patients with ST are more prone to experiencing damage to normal anatomic barriers, such as those resulting from surgical procedures.[1] Additionally, prospective studies have shown that PA is the primary pathogen responsible for BSI in patients with ST.[13] It is likely that the risk factors and prognosis for BSI in patients with HM and ST will be affected due to the different features. Although several studies have focused on the BSI in these two groups, they have been limited to neutropenic patients.[13,14] Therefore, a knowledge of the clinical features and risk factors of CRPA BSI in overall cancer patients is crucial for infection management and reducing mortality rates.

Thus, an 8-year retrospective study in a tertiary cancer hospital was performed and aimed to delineate clinical characteristics, risk factors and prognosis of CRPA BSI in both patients with HM and ST.

Materials and Methods

Study Design and Data Collection

This study involved cancer patients with PA BSI at the affiliated cancer hospital of Zhengzhou University between January 2015 and December 2023. Eligibility criteria included: (1) inpatients with a malignant tumor with comprehensive clinical data; (2) at least one blood culture positive for CRPA accompanied by clinical signs of infection. A total of 369 patients with PA BSI were identified, with 8 cases excluded due to polymicrobial bacteremia. Carbapenem-sensitive *Pseudomonas aeruginosa* (CSPA) BSI cases were randomly paired with contemporaneous CRPA BSI cases at a ratio of 1:1, forming 92 matched pairs. They were matched for age (± 5 years) and sex. The study flow chart was shown in Supplementary Figure S1. The data obtained from electronic medical records included demographic information, pre-existing health conditions, admissions to the intensive care unit, laboratory examinations, therapeutic interventions, antibiotic exposure in the prior 90 days, use of central venous and indwelling catheters, mechanical ventilation, Pitt bacteremia score (PBS), instances of septic shock, length of hospital stay prior to the diagnosis of BSI, results of antimicrobial susceptibility testing, and the antibiotic treatment regimen administered. The primary result observed was the mortality rate within a 30-day period.

Definitions

CRPA was characterized by resistance to one or more carbapenems, with a minimum inhibitory concentration (MIC) for meropenem or imipenem of ≥ 8 μg/mL.[15] Conversely, CSPA was defined by susceptible to imipenem or meropenem (MIC ≤ 2 μg/mL). Multidrug-resistant *P. aeruginosa* (MDRPA) indicated resistance to at least one agent in three or more antimicrobial classes.[16] One set of agents—imipenem-cilastatin, ciprofloxacin, levofloxacin, ceftazidime, cefepime, aztreonam, meropenem—was ineffective against difficult-to-treat resistant PA (DTRPA).[17] BSI was confirmed by the detection of PA in blood, causing noticeable clinical symptoms. Neutropenia was specified as an absolute neutrophil count (ANC) $< 0.5 \times 10^9$/L. Septic shock was identified by a sustained systolic blood pressure of < 90 mmHg not responsive to fluid resuscitation or necessitating vasopressor support. Exposure to antibiotics was defined as the administration of antibiotics for at least 24 hours within 90 days before the onset of BSI.

Microbiology

Becton Dickinson's automated BACTEC FX system was used to do blood cultures (Sparks, MD, USA). The BD Phoenix™ M-50 instrument with the composite board (NMIC/ID4) was used to identify bacteria and test antimicrobial susceptibility

according to the manufacturer's instructions. Susceptibility testing for imipenem, meropenem, piperacillin, and ceftazidime-avibactam was routinely supplemented using disk diffusion assays. The polymyxin breakpoint was in accordance with the European Union's 2021 drug sensitivity testing requirements (https://www.eucast.org) and other breakpoints were in accordance with the American Society for Clinical Laboratory Standardization M-100 criteria (2021) [18].

Statistical Analysis

Quantitative data were presented as mean ± standard deviation (SD) or median (interquartile range), while qualitative data were reported as frequency and percentage. Continuous variables underwent analysis through the *t*-test or Mann–Whitney *U*-test, whereas categorical variables were evaluated using the Chi-square test or Fisher's exact test. Variables exhibiting a *p*-value of 0.10 or lower in the univariate analysis underwent additional scrutiny in the multivariate analyses. Multivariate logistic regression was utilized to determine the predictors of CRPA BSI development, typically reported using odds ratios (OR) along with 95% confidence intervals (CI). Cox regression was employed to identify the risk factors affecting outcomes, with results presented as hazard ratios (HR) and 95% CI. The Kaplan-Meier method was utilized for the analysis of survival data. Between-group survival differences were analyzed using the Log rank test. All statistical analyses were performed utilizing IBM SPSS software, version 25.0, with a threshold for statistical significance established at *p*-values <0.05.

Results

Epidemiological Trends of PA BSI Over 8 Years in a Tertiary Cancer Hospital

A total of 361 distinct PA isolates from bloodstream culture samples were documented at the affiliated cancer hospital of Zhengzhou University (January 2015 to December 2023). Among these isolates, 92 (25.5%) were CRPA. Of the 361 BSI cases, 111 (30.7%) occurred in patients with ST and 250 (69.3%) in those with HM, indicating that PA BSI was more prevalent in patients with HM. Additionally, the percentage of CRPA surged from 7% in 2015 to 22% by 2017, with high-level isolation rate of CRPA persisting thereafter (Figure 1A).

Antimicrobial Susceptibility of PA Isolates

The antimicrobial susceptibility of 361 PA isolates were presented in Figure 1B. Notably, the highest resistance rate was observed for imipenem, as high as 25.5%, followed by aztreonam (15.5%), meropenem (12.5%) and ceftazidime (11.9%) (Supplementary Table S1). The antimicrobial susceptibility of PA in patients with ST and HM were shown in Supplementary Table S2. A statistically significant difference in resistance rates to ceftazidime was observed between these two patient groups ($p< 0.05$), while no such significance was noted for other antibiotics.

Analysis of the 184 PA isolates (92 CRPA and 92 CSPA) from the eligible CRPA and CSPA BSI episodes revealed varying resistance patterns against several antibiotics (Table 1). Specifically, resistance rates for the 92 CRPA isolates to

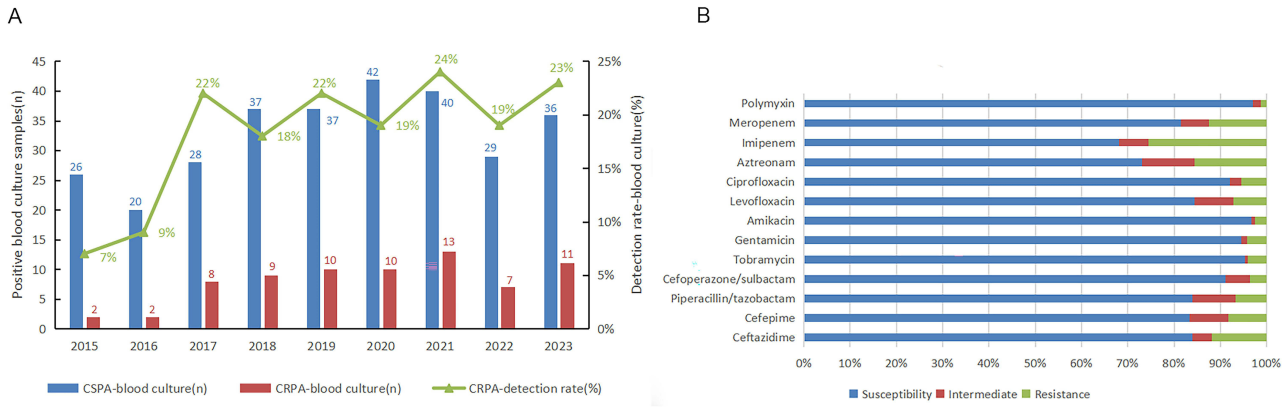

Figure 1 Main axis (left): number of positive samples for carbapenem-resistant *P. aeruginosa* (CRPA) and carbapenem-susceptible *P. aeruginosa* (CSPA) blood culture (n) /year; sub-axis (right): detection rate of CRPA in *P. aeruginosa* (PA) blood culture samples (%)/year (**A**); the antimicrobial susceptibility of 361 *Pseudomonas aeruginosa* isolates (**B**).

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Table 1 Susceptibility to Antibiotics of 184 *Pseudomonas aeruginosa* Isolates

Antibiotics	CRPA (n=92)		CSPA (n=92)		*p*
	MIC Range (μg/mL)	Resistance Rate (%)	MIC Range (μg/mL)	Resistance Rate (%)	
Ceftazidime	1–32	31.5	1–32	9.8	*<0.001*
Cefepime	2–32	26.1	0.5–16	6.5	*<0.001*
Piperacillin/tazobactam	4–128	22.8	4–128	5.4	*<0.001*
Cefoperazone/sulbactam	0.5–64	15.2	4–64	4.3	*0.016*
Tobramycin	1–16	5.4	1–16	4.3	1
Gentamicin	2–16	15.2	2–8	2.2	*0.002*
Amikacin	4–64	10.9	4–16	0	*<0.001*
Levofloxacin	0.5–8	18.5	0.25–8	6.5	*0.019*
Ciprofloxacin	0.25–4	15.2	0.25–4	5.4	*0.034*
Aztreonam	2–64	34.8	4–64	18.5	*0.006*
Imipenem	4–32	100	1–4	0	*<0.001*
Meropenem	0.5–8	57.6	0.25–4	0	*<0.001*
Polymyxin	0.5–8	5.4	0.5–4	2.2	0.442

Note: Italicized text indicates $p < 0.05$.
Abbreviations: CRPA, carbapenem-resistant *Pseudomonas aeruginosa*; CSPA, carbapenem-sensitive *Pseudomonas aeruginosa*; MIC, minimal inhibitory concentration.

imipenem, meropenem, aztreonam, ceftazidime, cefepime and piperacillin-tazobactam were 100%, 57.6%, 34.8%, 31.5%, 26.1%, and 22.8%, respectively. Conversely, the resistance rates to tobramycin and polymyxin stood at a mere 5.4%. Apart from these, resistance to the remaining 11 antibiotics was significantly greater in the CRPA group compared to the CSPA group.

Clinical Characteristics of PA BSI in Cancer Patients

One hundred and eighty-four cancer patients with PA BSI were enrolled in further analysis, comprising 92 with CRPA and 92 with CSPA (Table 2). Of these patients, 115 (62.5%) were male and 69 (37.5%) were female, yielding a median

Table 2 Clinical Characteristics of Patients Infected with CSPA and CRPA

Characteristics	CRPA (n=92)	CSPA (n=92)	Total (n=184)	*p*
Demography				
Age (IQR)	39.2 (23,54)	39.5 (19,57)	39.3 (21,55)	0.488
Male (%)	58 (63%)	57 (62%)	115 (62.5%)	0.879
Ward				
Admission to ICU	19 (21.6%)	5 (5.4%)	24 (13%)	*0.004*
Underlying disease				
Solid malignant tumor	24 (26.1%)	24 (26.1%)	48 (26.1%)	1.000
Hematologic Tumor Type				
ALL	10 (10.9%)	20 (21.7%)	30 (16.3%)	*0.039*
AML	43 (46.7%)	30 (32.6%)	73 (39.6%)	*0.050*
AA	10 (10.9%)	6 (6.5%)	16 (8.7%)	0.295
Others	5 (5.4%)	12 (13.0%)	17 (9.2%)	0.127
Type of resistance				
MDRPA	62 (67.4%)	19 (20.7%)	81 (44.0%)	*<0.001*
DTRPA	11 (12.0%)	0	11 (6.0%)	*0.001*
Treatment				
Surgery	13 (14.1%)	19 (21.6%)	32 (17.4%)	0.243
Chemotherapy	68 (74.0%)	71 (77.2%)	139 (75.5%)	0.607
Radiotherapy	5 (5.4%)	4 (4.3%)	9 (4.9%)	1.000
Glucocorticoid therapy	84 (91.3%)	80 (87.0%)	164 (89.1%)	0.343

(*Continued*)

Table 2 (Continued).

Characteristics	CRPA (n=92)	CSPA (n=92)	Total (n=184)	*p*
Prior invasive procedure				
Mechanical ventilation	12 (13.0%)	1 (1.1%)	13 (7.1%)	*0.004*
CVC	92 (100%)	89 (96.7%)	181 (98.4%)	0.244
Percutaneous catheterization	25 (27.2%)	21 (22.8%)	46 (25%)	0.533
Urinary catheterization	22 (23.9%)	19 (21.6%)	41 (22.3%)	0.595
Source of bacteremia				
Lung	4 (4.3%)	2 (2.2%)	6 (3.3%)	0.678
Skin and soft-tissue	2 (2.2%)	2 (2.2%)	4 (2.2%)	0.613
Biliary tract	4 (4.3%)	8 (8.7%)	12 (6.5%)	0.370
Catheter related	19 (21.6%)	15 (16.3%)	34 (18.5%)	0.447
Intra-abdominal	4 (4.3%)	3 (3.3%)	7 (3.8%)	1.000
Urinary tract	3 (3.3%)	1 (1.1%)	4 (2.2%)	0.613
Unknown	56 (61.9%)	61 (66.3%)	117 (63.6%)	0.444
Exposure to anti-infectives within 90 days				
Polymyxin	6 (6.5%)	0	6 (3.3%)	0.059
Aminoglycosides	9 (9.8%)	3 (3.3%)	12 (6.5%)	0.273
Carbapenems	61 (66.3%)	21 (22.8%)	82 (44.6%)	*<0.001*
Tigecycline	2 (2.2%)	2 (2.2%)	4 (2.2%)	0.613
BLBLIS	18 (19.6%)	25 (27.2%)	43 (23.4%)	0.289
The condition after BSI				
MOF	3 (3.3%)	0	3 (1.63%)	0.123
Septic shock	12 (13.0%)	12 (13.0%)	24 (13.0%)	1.000
Mechanical ventilation	12 (13.0%)	2 (2.2%)	14 (7.6%)	*0.012*
Hospital stay before BSI [a]	23.89±20.08	18.08±11.44	20.98±16.53	*0.002*
Total length of hospital stay (IQR)	40 (24,56.75)	33 (21,40.25)	37 (23,43.75)	0.120
Laboratory examinations				
Neutrophilic granulocyte (10^9/L) [a]	2.62±4.94	2.03±4.23	2.32±4.54	0.470
Hemoglobin (g/L) [a]	82.31±17.2	80.84±20.97	81.57±19.11	0.670
Platelet (10^9/L) [a]	45.42±59.56	68.45±100.22	56.94±82.92	0.120
CRP (mg/L) [a]	163.59±91.85	121.92±76.47	147.73±87.03	*0.013*
PCT (ng/mL) [a]	4.48±8.98	5.47±11.56	4.92±10.13	0.670
Agranulocytosis	49 (53.3%)	43 (46.7%)	92 (50.0%)	0.376
PBS (IQR)	3 (1,4)	1 (0,1)	2 (0,2)	*0.001*
ALT (U/L) [a]	31.08±47.32	30.02±32.61	30.8±40.52	0.940
AST (U/L) [a]	34.1±55.1	27.31±31.52	30.73±40.92	0.404
ALB (g/L) [a]	33.49±6.33	33.46±5.65	33.47±5.98	0.980
TBIL (μmol/L) [a]	38.65±58.1	22.86±36.69	30.82±49.12	0.080
Mortality (n, %)				
All-cause death at 7 d	13 (14.1%)	2 (2.2%)	15 (8.15%)	*0.007*
All-cause death at 14 d	24 (26.1%)	3 (3.3%)	27 (14.7%)	*<0.001*
All-cause death at 30 d	33 (35.9%)	6 (6.5%)	39 (21.2%)	*<0.001*

Notes: [a] mean ± standard deviation; italicized text indicates $p < 0.05$.

Abbreviations: CRPA, carbapenem-resistant *Pseudomonas aeruginosa*; CSPA, carbapenem-sensitive *P. aeruginosa*; IQR, interquartile range; ICU, intensive care unit; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; AA, aplastic anemia; MDRPA, multidrug-resistant *P. aeruginosa*; DTRPA, difficult-to-treat resistant *P. aeruginosa*; CVC, central venous catheter; BLBLIS, β-lactam/β-lactamase inhibitor combinations, including piperacillin-tazobactam and cefoperazone-sulbactam; BSI, bloodstream infection; MOF, multiple organ failure; CRP, C-reactive protein; PCT, procalcitonin; PBS, Pitt bacteremia score; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; TBIL, total bilirubin.

age of 39.3 years. Except for unknown origin of infection, catheter-related infection (18.5%) was the most common infection source followed by biliary tract (6.5%), intra-abdominal (3.8%), lung (3.3%), urinary tract (2.2%), and skin and soft tissue infections (2.2%), with no significant variance observed between the groups. Furthermore, the occurrence of MDRPA and extensively DTRPA was significantly more frequent in the CRPA group (67.4% vs 20.7%, $p<0.001$; 12% vs 0%, $p=0.001$).

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One hundred and eighty-four enrolled cases of PA BSI contained 136 patients with HM and 48 with ST (Table 3). ST patients were more inclined to undergo surgical treatments (60%), percutaneous (71%) and urinary catheterization (52%), and display elevated levels of aspartate aminotransferase (AST) and TBIL. Ninety percent of patients with HM received

Table 3 Clinical Characteristics of PA BSI in Patients with HM and ST

Characteristics	ST (n=48)	HM (n=136)	*p*
Demography			
Age (IQR)	58 (49, 64)	33 (16, 48)	*<0.001*
Male (%)	30 (63%)	86 (63%)	0.956
Ward			
ICU	9 (18%)	15 (11%)	0.252
Type of resistance			
MDRPA	24 (50%)	57 (42%)	0.456
DTRPA	0	11 (8%)	0.116
Treatment			
Surgery	29 (60%)	3 (2%)	*<0.001*
Chemotherapy	16 (33%)	123 (90%)	*<0.001*
Radiotherapy	5 (10%)	4 (3%)	0.363
Glucocorticoid therapy	40 (83%)	124 (92%)	0.270
Prior invasive procedure			
Mechanical ventilation	4 (8%)	9 (7%)	0.888
CVC	48 (100%)	133 (98%)	1.000
Percutaneous catheterization	34 (71%)	12 (9%)	*<0.001*
Urinary catheterization	25 (52%)	16 (12%)	*<0.001*
Source of bacteremia			
Lung	2 (4%)	4 (3%)	1.000
Skin and soft-tissue	2 (4%)	2 (2%)	0.678
Biliary tract	11 (23%)	1 (1%)	*<0.001*
Catheter related	5 (10%)	29 (21%)	0.094
Intra-abdominal	7(15%)	0	*0.007*
Urinary tract	2 (4%)	2 (1%)	0.599
Exposure to anti-infectives within 90 days			
Polymyxin	2 (4%)	4 (3%)	1.000
Aminoglycosides	0	12 (9%)	0.085
Carbapenems	14 (30%)	68 (50%)	0.032
Tigecycline	0	4 (3%)	0.549
BLBLIS	13 (27%)	30 (22%)	0.462
The condition after BSI			
MOF	1 (2%)	2 (2%)	0.451
Septic shock	0	24 (18%)	*0.006*
Mechanical ventilation	3 (6%)	11 (8%)	1.000
Hospital stay before BSI [a]	19.16±16.77	21.62±16.49	0.470
Total length of hospital stay (IQR)	40 (24, 56.75)	33 (21, 40.25)	0.391
Laboratory examinations			
Neutrophilic granulocyte (10^9/L) [a]	7.72±5.83	0.45±1.60	*<0.001*
Hemoglobin (g/L) [a]	97.25±16.97	76.12±16.71	*<0.001*
Platelet (10^9/L) [a]	163.06±102.82	20.02±18.77	*<0.001*
CRP (mg/L) [a]	118.90±60.43	148.95±90.64	0.083
PCT (ng/mL) [a]	15.23±29.28	4.01±7.34	0.162
Agranulocytosis	0	92 (68%)	*0.001*
PBS (IQR)	1 (0, 1.75)	1 (0, 2)	0.578

(*Continued*)

Table 3 (Continued).

Characteristics	ST (n=48)	HM (n=136)	*p*
ALT (U/L) [a]	45.71±56.59	25.78±32.33	0.071
AST (U/L) [a]	45.32±53.72	25.82±40.70	*0.036*
ALB (g/L) [a]	31.74±5.73	34.06±5.97	0.061
TBIL (μmol/L) [a]	56.58±83.45	22.14±25.22	*0.031*

Notes: [a] mean ± standard deviation; italicized text indicates $p < 0.05$.
Abbreviations: PA, *Pseudomonas aeruginosa*; BSI, bloodstream infection; ST, solid tumors; HM, hematological malignancies; IQR, interquartile range; ICU, intensive care unit; MDRPA, multidrug-resistant *P. aeruginosa*; DTRPA, difficult-to-treat resistant *P. aeruginosa*; CVC, central venous catheter; BLBLIS, β-lactam/β-lactamase inhibitor combinations, including piperacillin-tazobactam and cefoperazone-sulbactam; MOF, multiple organ failure; CRP, C-reactive protein; PCT, procalcitonin; PBS, Pitt bacteremia score; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; TBIL, total bilirubin.

chemotherapy, 50% were treated with carbapenems, and 68% had severe neutropenia. Additionally, they were typically younger, more likely experience septic shock, associated with reduced neutrophil, hemoglobin, and platelet counts.

Risk Factors of CRPA BSI Development

Univariate analysis of 92 matched pairs of patients with CRPA and CSPA BSI demonstrated that CRPA patients tended to have longer pre-infection hospitalization, more frequent ICU admissions, a greater need for mechanical ventilation, and higher CRP and PBS levels compared to CSPA patients. And they were more prone to develop MDRPA and DTRPA BSI. Significant variance was noted in the exposure to antibiotics within 90 days prior to BSI, particularly with carbapenems (66.3% vs 22.8%, $p<0.001$) (Table 2). A multivariate logistic regression analysis of 92 matched pairs of CRPA and CSPA BSI patients highlighted PBS (OR 1.373, 95% CI 1.094–1.724), prior carbapenem exposure within 90 days of BSI (OR 7.27, 95% CI 2.625–20.135), and MDRPA (OR 4.88, 95% CI 1.757–13.555) as distinct independent risk factors for the emergence of CRPA BSI in cancer patients (Table 4).

We further performed subgroup analysis comparing CRPA and CSPA separately in ST and HM patients (Table 5). Comparative univariate analysis between patients with ST indicated that platelet count, exposure to carbapenems, and 30-day mortality rate were statistically significant between the CRPA and CSPA groups. In patients with HM, those with CRPA BSI tended to experience more frequently admitted to the ICU, require mechanical ventilation therapy, and

Table 4 Predictors of CRPA BSI Development Based on Multivariate Analysis

Variables	OR (95% CI)	*p*
CRPA BSI in cancer patients (n=184)		
PBS	1.373 (1.094–1.724)	*0.006*
Exposure to carbapenems within 90 days	7.27 (2.625–20.135)	*<0.001*
MDRPA	4.88 (1.757–13.555)	*0.002*
CRPA BSI in patients with ST (n=48)		
Platelet	0.989 (0.978–1)	*0.048*
Exposure to carbapenems within 90 days	15.2 (1.315–175.642)	*0.029*
CRPA BSI in patients with HM (n=136)		
Exposure to carbapenems within 90 days	7.647 (2.306–25.361)	*0.001*
MDRPA	7.038 (2.017–24.558)	*0.002*

Note: Italicized text indicates $p < 0.05$.
Abbreviations: CRPA, carbapenem-resistant *P. aeruginosa*; BSI, bloodstream infection; PBS, Pitt bacteremia score; MDRPA, multidrug-resistant P. *aeruginosa*; ST, solid tumors; HM, hematological malignancies.

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Table 5 Clinical Characteristics of ST and HM Patients Stratified by CRPA and CSPA Groups

Characteristics	ST			HM		
	CRPA (n=24)	CSPA (n=24)	*p*	CRPA (n=68)	CSPA (n=68)	*p*
Admission to ICU	7 (29.2%)	2 (8.3%)	0.139	12 (17.6%)	3 (4.4%)	*0.014*
MDRPA	15 (62.5%)	9 (37.5%)	0.083	47 (69.1%)	10 (14.7%)	*<0.001*
DTRPA	0	0		11 (16.2%)	0	*0.001*
Exposure to carbapenems within 90 days	12 (50%)	2 (8.3%)	*0.005*	49 (72.1%)	19 (27.9%)	*<0.001*
The condition after BSI						
Mechanical ventilation	3 (12.5%)	0	0.233	9 (13.2%)	2 (2.9%)	*0.028*
Hospital stay before BSI [a]	22.44±17.39	15.88±16.00	0.276	24.39±21.09	18.85±9.47	0.109
CRP (mg/L) [a]	115.11±66.38	125.40±52.91	0.731	175.92±93.09	121.36±80.04	*0.004*
PBS (IQR)	1 (0, 2.5)	1 (0, 1.75)	0.163	1 (1,4)	1 (0,1.25)	*0.004*
Platelet (10^9/L) [a]	119.5±73.457	206.63±111.371	*0.014*	19.65±19.509	20.39±18.197	0.851
Mortality						
All-cause death at 7 d	2 (8.3%)	0	0.47	11 (16.2%)	2 (2.9%)	*0.009*
All-cause death at 14 d	6 (25.0%)	1 (4.2%)	0.102	18 (26.5%)	2 (2.9%)	*<0.001*
All-cause death at 30 d	9 (37.5%)	1 (4.2%)	0.004	24 (35.3%)	5 (7.4%)	*<0.001*

Notes: [a] mean ± standard deviation; italicized text indicates $p < 0.05$.
Abbreviations: ST, solid tumors; HM, hematological malignancies; CRPA, carbapenem-resistant *P. aeruginosa*; CSPA, carbapenem-sensitive *P. aeruginosa*; ICU, intensive care unit; MDRPA, multidrug-resistant *P. aeruginosa*; DTRPA, difficult-to-treat resistant *P. aeruginosa*; BSI, bloodstream infection; CRP, C-reactive protein; PBS, Pitt bacteremia score; IQR, interquartile range.

demonstrate higher levels of CRP and PBS. Moreover, among patients with HM, those with CRPA BSI were more likely to have prior exposure to carbapenems and develop MDRPA and DTRPA. Multivariate logistic regression analysis revealed that platelet counts (OR 0.989, 95% CI 0.978–1) and recent exposure to carbapenems (OR 15.2, 95% CI 1.315–175.642) were distinct independent risk factors for the emergence of CRPA BSI in patients with ST. Prior carbapenem exposure within 90 days of BSI (OR 7.647, 95% CI 2.306–25.361), and MDRPA (OR 7.038, 95% CI 2.017–24.558) independently emerged as risk factors for CRPA BSI development in patients with HM (Table 4).

Clinical Outcomes of PA BSI

Among the 184 cancer patients with PA BSI, 39 (21.2%) died over a 30-day observation period (Table 2), including 30 infected with MDRPA. Noteworthy differences in the crude mortality rates at 7 days, 14 days and 30 days post-infection were documented between the CRPA and CSPA groups, registering at 14.1% vs 2.2% ($p = 0.007$), 26.1% vs 3.3% ($p< 0.001$), and 35.9% vs 6.5% ($p< 0.001$), respectively (Table 2). Survival rates within 30 days were significantly lower for patients with

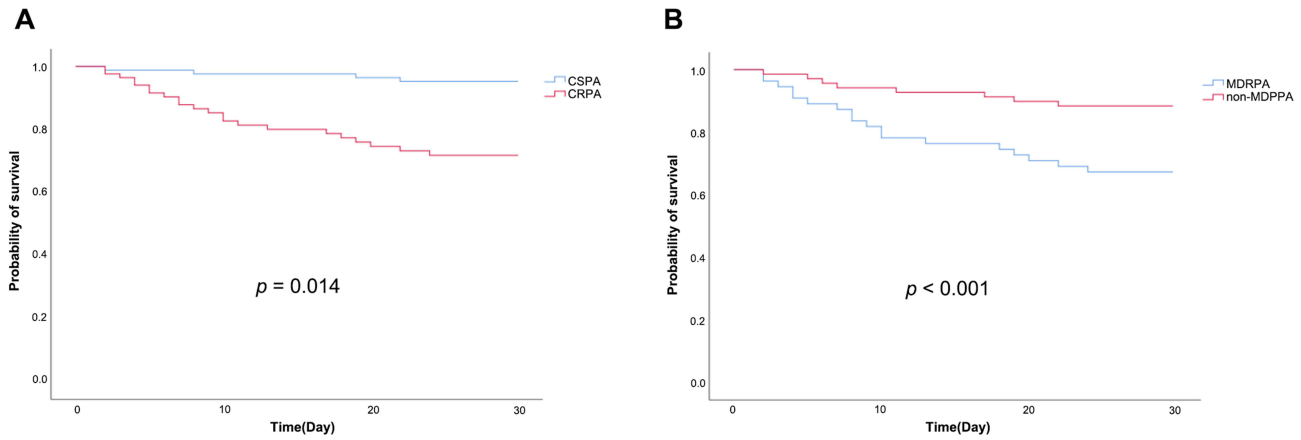

Figure 2 Kaplan–Meier curves of survival rates within 30 days for 184 *P. aeruginosa* bloodstream infection (PA BSI) patients caused by carbapenem-resistant *P. aeruginosa* (CRPA) and carbapenem-susceptible *P. aeruginosa* (CSPA) (**A**); with multidrug-resistant (MDR) type and non-MDR type (**B**).

CRPA BSI compared to those with CSPA BSI (p = 0.014, Log rank test; Figure 2A). Additionally, the survival rates for patients with MDRPA BSI were notably lower than for those without MDRPA (p< 0.001; Figure 2B).

The 30-day mortality rate of CRPA BSI was 37.5% in patients with ST and 35.3% in those with HM (Table 5). In both ST and HM patients groups, only the 30-day mortality of CRPA BSI demonstrated statistically significant differences compared to that of CSPA BSI.

Risk Factors for 30-Day Mortality in CRPA BSI Patients

Univariate Cox regression analysis for patients deceased within 30 days revealed higher levels of PCT, diminished ALB, increased PBS, along with frequent ICU admissions and mechanical ventilation requirements (Table 6). There was no evident link between tumor types and the 30-day mortality rate.

Table 6 Mortality Risk Factors in CRPA BSI Patients

Variables	Non-Survivor	Survivor	Univariate Analysis		Multivariate Analysis	
	(n=33)	(n=59)	HR (95% CI)	*p*	HR (95% CI)	*p*
Demographic						
Male (%)	19 (58%)	38 (64%)	1.23 (0.525–2.879)	0.633		
Age [a]	41.68±21.45	37.8±16.79	1.011 (0.987–1.036)	0.356		
Underlying disease						
ST	9 (27%)	15 (25%)	1.012 (0.396–2.587)	0.980		
Hematologic Tumor Type						
ALL	3 (9%)	7 (12%)	0.759 (0.177–3.25)	0.711		
AML	18 (55%)	25 (42%)	1.547 (0.668–3.583)	0.308		
AA	3 (9%)	7 (12%)	0.752 (0.176–3.218)	0.701		
Type of resistance						
MDRTA	25 (76%)	37 (63%)	0.569 (0.21–1.541)	0.267		
DTRPA	3 (9%)	8 (14%)	0.748 (0.175–3.202)	0.695		
Admission to ICU	15 (45%)	4 (7%)	6 (2.542–14.163)	*<0.001*		
Hospital stay before BSI [a]	24.59±22.16	23.5±19.13	1.001 (0.981–1.022)	0.921		
Total length of hospital stay [a]	31.09±26.27	45.2±28.79	0.977 (0.954–1.001)	0.057		
The condition after BSI						
MOF	3 (9%)	0	6.201 (1.377–27.917)	*0.017*		
Septic shock	12 (36%)	0	2.656 (0.975–7.234)	0.056		
Mechanical ventilation	11 (33%)	1 (2%)	5.791 (2.304–14.554)	*<0.001*		
Treatment						
Surgery	6 (18%)	7 (12%)	0.63 (0.343–1.156)	0.136		
Glucocorticoid therapy	31 (94%)	53 (90%)	2.261 (0.304–16.821)	0.426		
Chemotherapy	22 (67%)	46 (78%)	0.678 (0.276–1.664)	0.396		
Radiotherapy	2 (6%)	3 (5%)	0.823 (0.111–6.126)	0.850		
Laboratory examinations						
Neutrophilic granulocyte (10^9/L) [a]	3.22±5.39	2.28±4.71	1.024 (0.949–1.104)	0.545		
Hemoglobin (g/L) [a]	85.27±14.01	80.68±18.69	1.009 (0.986–1.033)	0.429		
Platelet (10^9/L) [a]	31.95±35.95	52.82±68.52	0.994 (0.984–1.004)	0.215		
CRP (mg/L) [a]	170.65±91.79	158.38±91.68	1.002 (0.997–1.007)	0.411		
Agranulocytosis	17 (51%)	32 (54%)	1.149 (0.498–2.651)	0.745		
PBS (IQR)	5 (2.75, 10.25)	1 (0, 1)	1.518 (1.335–1.726)	*<0.001*	1.672 (1.309–2.135)	*<0.001*
PCT (ng/mL) [a]	12.88±24.04	1.69±1.81	1.018 (1.002–1.034)	*0.026*		
ALT (U/L) [a]	49.23±72.55	21.1±19.49	1.005 (1–1.011)	0.063		
AST (U/L) [a]	56.82±84.89	21.6±20.38	1.006 (1.001–1.011)	*0.021*		
ALB (g/L) [a]	31.38±7.90	34.64±5.01	0.925 (0.859–0.996)	*0.038*		
TBIL (umol/L) [a]	48.29±50.30	33.35±61.93	1.002 (0.997–1.008)	0.398		
Antibiotics usage after infection						
Quinolones	9 (15%)	5 (15%)	1.214 (0.411–3.589)	0.725		
Aminoglycosides	15 (25%)	6 (18%)	0.673 (0.199–2.276)	0.524		

(*Continued*)

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Table 6 (Continued).

Variables	Non-Survivor	Survivor	Univariate Analysis		Multivariate Analysis	
	(n=33)	(n=59)	HR (95% CI)	*p*	HR (95% CI)	*p*
BLBLIS	25 (42%)	8 (24%)	0.449 (0.165–1.218)	0.116		
Carbapenems	14 (42%)	42 (72%)	0.338 (0.144–0.794)	*0.013*		
Polymyxin B	13 (22%)	6 (18%)	0.747 (0.253–2.207)	0.597		
Ceftazidime Avibactam	0	4 (7%)	0.045 (0–117.534)	0.440		

Notes: [a] mean ± standard deviation; italicized text indicates $p < 0.05$.

Abbreviations: CRPA, carbapenem-resistant *Pseudomonas aeruginosa*; BSI, bloodstream infection; ST, solid tumors; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; AA, aplastic anemia; MDRPA, multidrug-resistant *P. aeruginosa*; DTRPA, difficult-to-treat resistant *P. aeruginosa*; ICU, intensive care unit; MOF, multiple organ failure; CRP, C-reactive protein; PBS, Pitt bacteremia score; IQR, interquartile range; PCT, procalcitonin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; TBIL, total bilirubin; BLBLIS, β-lactam/β-lactamase inhibitor combinations, including piperacillin-tazobactam and cefoperazone-sulbactam.

The multivariate analysis revealed that higher PBS (HR 1.672, 95% CI 1.309–2.135, $p< 0.001$) served as an independent risk factor associated with 30-day mortality. The analysis of the receiver operating characteristic (ROC) curve determined that a PBS threshold of 2.5 served as a reliable predictor of mortality in patients with cancer suffering from CRPA BSI. The area beneath the curve was measured at 0.893 (95% CI 0.798–0.988, $p< 0.001$; Figure 3), exhibiting a sensitivity of 77.3% and a specificity of 95.0%. Kaplan-Meier curve analysis showed that PBS≥2.5 was associated with higher mortality ($p<0.001$; Figure 4).

Discussion

The antimicrobial resistance of PA, especially CRPA, poses a significant challenge in the realm of clinical infection control. Data from CHINET (https://www.chinets.com/Data/GermYear) have shown that resistance levels of PA to antibiotics such as imipenem and meropenem have fluctuated between 17.3% and 30.7%. For cancer patients, whose immune system may be compromised by extensive use of radiotherapy, chemotherapy, or hormones, the risk of severe infections like BSI is significantly heightened.[2] It is, therefore, vital to pinpoint risk elements for CRPA BSI in this demographic. However, most previous studies have focused solely on BSI in neutropenic HM patients, with limited

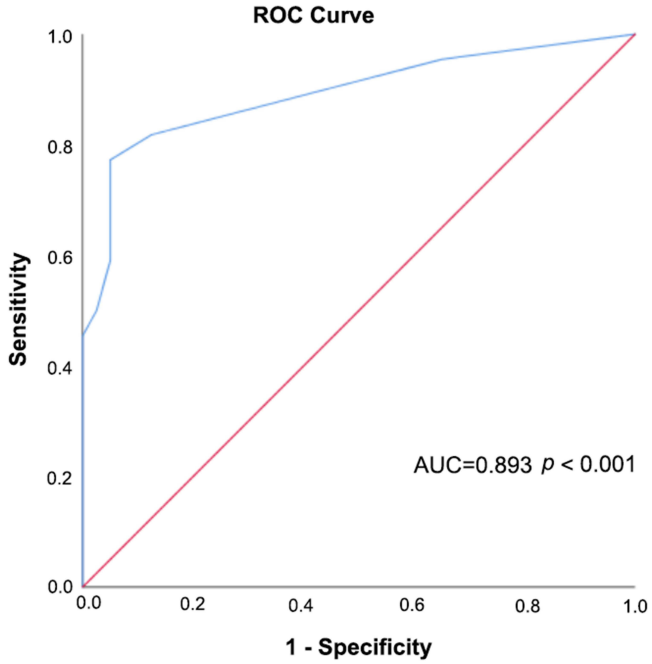

Figure 3 ROC curve of PBS score.

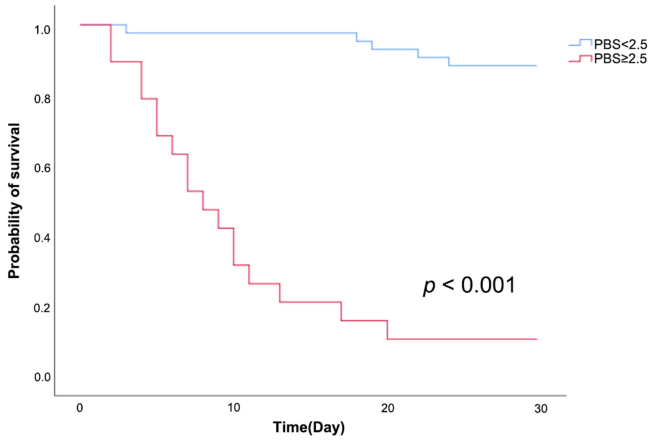

Figure 4 Kaplan–Meier curves of survival rates within 30 days for 92 carbapenem-resistant *P. aeruginosa* bloodstream infection (CRPA BSI) patients with different PBS scores.

research evaluating the risk factors for BSI in cancer patients (ST and HM) without neutropenia. Therefore, we conducted a retrospective study to describe the clinical characteristics and identify the risk factors of CRPA BSI in both ST and HM patients, regardless of their neutropenia status.

Most BSI episodes among patients with ST occurred in those without neutropenia, aligning with our observations that the site of primary or metastatic tumors frequently acts as the portal for BSI.[8] Patients with HM experienced higher rates of BSI, likely attributable to more severe immunosuppression from intensive chemotherapy, sustained neutropenia, and prevalent chemotherapy-induced mucositis, all of which predispose them to aggressive bacterial invasions.[13]

Our findings affirmed that carbapenem use within 90 days preceding the onset of BSI was one of the independent predictors for CRPA BSI in overall cancer patients, as well as in both ST and HM subgroups. In this analysis, 66.3% of cancer patients with CRPA had previously been treated with carbapenems. These results were in line with research by Shi et al and Lee et al,[19,20] suggesting that prior exposure to carbapenems may promote the development of resistance through mechanisms such as the loss of outer membrane porins or the production of metallo β-lactamases, thereby fostering bacterial resistance or multidrug resistance.

Platelet count was identified as a risk factor for CSPA BSI in patients with ST. In patients with ST, the platelet count was significantly lower in the CRPA group compared to the CSPA group. Platelets interact directly or indirectly with diverse microbial pathogens, internalize microorganisms, and confer critical host defense functions, potentially enhancing pathogen clearance from the bloodstream.[21–23] Thrombocytopenia is increasingly recognized as an important independent correlate of infection-related morbidity and mortality.[24] In cancer patients, thrombocytopenia serves as an independent predictor of increased morbidity and mortality due to bacterial infections.[25] In another cohort study, thrombocytopenia was identified as an independent risk factor for bacterial infections in 12% of pediatric patients.[26] Yoshida et al employed multivariable analysis to demonstrate that reduced platelet counts independently predicted severe bacteremia in healthcare settings.[23]

Evidence from multiple studies indicated that resistance to carbapenems escalated the mortality rates of PA BSI.[27–30] Consistent with previous studies, the CRPA group exhibited significantly higher mortality rates than the CSPA group at 7-, 14-, and 30-days post-infection. The emergence of MDRPA introduced significant challenges in clinical pharmacology, often associated with adverse outcomes for patients.[31] The severity of the host's condition, inappropriate antibiotic treatment, and increased virulence of PA may all contribute to adverse outcomes.[32–34] In our study, the survival rates for patients with MDRPA BSI were notably lower than for those without MDRPA. In patients with ST and HM, the 30-day mortality rates of CRPA BSI were 37.5% and 35.3%, respectively, demonstrating statistically significant differences compared to that of CSPA BSI. Nevertheless, no substantial difference in 30-day mortality rates was observed between ST and HM patients, possibly due to the sparse occurrence of PA BSI and limited inclusion of patients.

PBS is routinely employed to evaluate infectious diseases, serving as a prognostic marker for severity and mortality risk among PA BSI patients.[35] Scores range from 0 to 14, with values of 4 or above generally indicating severe illness

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and a higher mortality risk.[36,37] Our research supported this scale, identifying an elevated PBS as an independent risk factor for 30-day mortality, consistent with previous studies.[38,39] Analysis using the ROC curve demonstrated that a PBS threshold of 2.5 effectively predicted mortality from CRPA BSI in cancer patients, with a sensitivity of 77.3% and a specificity of 95.0%.

Admittedly, this study was conducted in a specialized oncology hospital, which may restrict the generalizability of the results to other clinical environments or patient groups. Moreover, limitations in data capture and unmeasured confounders are inevitable to retrospective studies.

Conclusion

The mortality rates of CRPA BSI are notably high in both patients with ST and HM. Elevated PBS was a significant predictor of 30-day mortality in cases of CRPA BSI. The risk factors for CRPA BSI and mortality may guide and optimize the management of CRPA BSI in cancer patients.

Ethics Approval

Patient consent was waived due to the retrospective nature of the study and patient data was confidential. The study was conducted in accordance with the Declaration of Helsinki. Ethics approval for this study was submitted and approved by the Ethics Committee of the Affiliated Cancer Hospital of Zhengzhou University, China (NO: 2024-KY-0124).

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Disclosure

The authors report no conflicts of interest in this work.

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