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Bacteria and Bacterial Diseases

Predictors of mortality and therapeutic efficacy in carbapenem-resistant *Acinetobacter baumannii* bacteremia

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SUMMARY

Objectives: Bacteremia caused by carbapenem-resistant Acinetobacter baumannii (CRAB) is associated with high morbidity and mortality. The primary objective was to identify clinical and therapeutic factors associated with 14- and 30-day mortality following infection onset.
Methods: This was a prospective, observational, multicenter study conducted across 52 Italian centers. Over an 18-month period, adult hospitalized patients with CRAB bacteremia were enrolled.
Results: Among 398 patients with CRAB bacteremia, sources were mainly CVC-related or primary, with 14- and 30-day mortality rates of 22% and 27% respectively. Cox regression analysis identified male sex (p=0.006), and chronic kidney disease (p=0.016) as independent predictors of 14-day mortality, while colistin-containing regimen (p=0.014), and cefiderocol-containing-regimen ($p < 0.001$) were associated with 14-day survival; male sex (p=0.027), septic shock (p=0.018), previous colonization by A. baumannii ($p < 0.001$), and tigecycline-containing regimen (p=0.021) were independent predictors of 30-day mortality, while cefiderocol-containing-regimen ($p < 0.001$) was associated with 30-day survival. Propensity score matching revealed that cefiderocol was significantly associated with 14-day survival

and clinical success. The combination of cefiderocol plus Fosfomycin was also significantly associated with clinical success.
Conclusion: Our findings highlight key clinical and therapeutic determinants of mortality and survival in patients with CRAB bacteraemia, providing valuable insights for improving the management of this challenging infection.

Introduction

According to the World Health Organization, carbapenem-resistant *Acinetobacter baumannii* (CRAB) is one of the most critical and high-priority nosocomial pathogens worldwide, due to its extensive resistance profile and high associated morbidity and mortality rates.[1–3]

Infections caused by multidrug-resistant CRAB are associated with morbidity and mortality rates up to four times higher than those of other multidrug-resistant (MDR) pathogens.[4,5] Specifically, bacteremia due to CRAB is associated with mortality rates as high as 60%.[6,7] Recent data from the ALARICO study in Italy further emphasize the excess mortality linked to CRAB bacteremia compared to other Gram-negative pathogens.[8] These findings are alarming for clinicians, given the limited therapeutic options available for managing such infections. Resistance to many antibiotics such as penicillins, cephalosporins, trimethoprim/sulfamethoxazole, fluoroquinolones, aminoglycosides, carbapenems, and colistin make these infections difficult-to-treat.[9]

New molecules, like cefiderocol, used as mono or combination-therapy with a synergistic effect were recently available and are active against this pathogen.[10–12] Clinical trials have demonstrated that cefiderocol is as effective as best available therapy including colistin for treating severe Gram-negative infections, including ventilator-associated pneumonia (VAP) and bacteremia. These findings have also been corroborated by real-world data.[13,14] In addition, many other drugs that have demonstrated synergism in vitro but also clinical effectiveness such as fosfomycin and ampicillin/sulbactam are still being evaluated.[15–18] Nonetheless, despite these therapeutic advancements, the reasons behind the persistently high mortality rates in patients with CRAB bloodstream infections remain poorly understood.

The ITACA study was designed to identify predictors of 14- and 30-day mortality and to assess the effectiveness of different therapeutic regimens in a large prospective cohort of patients with CRAB bacteremia across Italy.

Materials and methods

Study design and patient selection

This was an observational, prospective, multicenter study that included hospitalized patients with bloodstream infections caused by CRAB from March 2023 to September 2024 in 52 hospitals in 14 different Italian Regions.

Patients were eligible for the study if: 1) aged ≥18 years, 2) had blood cultures (collected at the onset of infection symptoms) positive from CRAB in the absence of other isolates related to the development of infection (monomicrobial BSI), 3) presented concomitant signs and symptoms related to CRAB infection, and 4) were treated for at least 24 h from the onset of infection.

Blood cultures were collected at the onset of infection symptoms.

Patients were excluded if they died within 24 h from the onset of infection or had other concomitant infections.

The study was conducted according to the principles stated in the Declaration of Helsinki and has been approved by local ethics committees. Collected data were anonymized and informed consent was obtained when possible.

Procedures

Each center received a case report form (CRF). Patients were assigned to a sequential number, and their data were retrieved from medical records during hospitalization. Subsequently, each case was uploaded into an online platform (REDCap) anonymously with the name of the participating center and a sequential number. The data were then reviewed by the principal investigator from coordinating center. Data discrepancies, outliers and missing data were discussed with the investigators at each site after the study period, at the data cleaning step.

The following data were examined: demographic data; comorbid conditions; clinical and laboratory findings; microbiological data including the colonization at the time of admission by *A. baumannii*, the day of blood culture positivity, the origin of bacteremia by CRAB, the antibiotic susceptibility pattern for each microbiological isolate and the duration of blood culture positivity; were collected information about the hospital ward and length of stay; treatments and procedures (e.g., non-invasive ventilation [NIV], mechanical ventilation, continuous renal replacement therapy [CRRT], extracorporeal membrane oxygenation [ECMO]) performed during admission; antibiotic regimens used for CRAB infection, including dosage, formulation and duration of antibiotic therapy; sequential assessment of organ failure (SOFA) at the time of infection; 14- and 30-day mortality.

Definition of clinical failure, other definitions, and microbiological identification according with protocol are reported in Supplementary material.

Outcomes

The primary outcome was all-causes 30-day mortality following the development of CRAB bacteremia.

Secondary outcomes included all-cause mortality at 14 days and the clinical effectiveness of targeted antibiotic regimens.

Statistical analysis

Continuous variables were reported as median and interquartile range (IQRs, 25%–75%) or mean with standard deviation (±SD) according to normal distribution. The normality of distributions was evaluated using the Kolmogorov-Smirnov test. To detect significant differences between groups, we used Chi-square tests or Fisher's exact tests for categorical variables, and the 2-tailed Student's *t*-test or Mann-Whitney *U* test for continuous variables, when appropriate. In a multivariate analysis of survival, the Cox regression model adjusted for confounding factors including sex and age was tested using a proportional hazards model analysis with backward stepwise selection and $p < 0.05$ for all variables, to identify factors independently associated with 30-day survival and determine the effects of all clinical and therapeutic variables on 30-day survival. Adjusted hazard ratios (HR) and 95% confidence intervals (CIs) were reported. Kaplan–Meier curves were used to determine in-hospital survival in patients treated with the antibiotic regimens. Survival curves for time-to-event variables, constructed using Kaplan–Meier estimates, were based on all available data and were compared using the log-rank test. Wald confidence intervals and tests for HR were computed based on the estimated standard errors. Possible confounding factors

Table 1
Univariate analysis of survivors vs. non-survivors at 30 days.

Variables	Survivors n=291	Non survivors n=107	p-value
Anamnestic characteristics			
Age, years (mean)	60.87 ± 9.17	61.15 ± 6.04	0.879
Male, sex	94 (32.3%)	46 (43.5%)	0.058
Previous surgery (30 days)	148 (50.9%)	50 (46.7)	0.498
> 2 Comorbidities	198 (68%)	84 (78.5%)	**0.047**
Charlos Comorbidity Index, mean (± SD)	5.35 (± 3.8)	6.15(± 3.04)	0.401
Heart failure	177 (60.8%)	67 (62.6%)	0.817
Chronic kidney disease	52 (17.9%)	28 (26.2%)	0.090
Diabetes	98 (33.7%)	32 (29.9%)	0.547
Dyalisis	21 (7.2%)	3 (2.8%)	0.152
Cirrhosis	31 (10.7%)	15 (14%)	0.378
COPD	64 (22%)	36 (33.6%)	**0.019**
Immunosuppressive therapy	38 (21.1%)	30 (36.3%)	**0.010**
Neurologic disease	92 (32.7%)	35 (32.7%)	1.000
Vasculitis	18 (6.2%)	14 (13.1%)	**0.036**
Solid neoplasm	43 (14.8%)	15 (14.3%)	1.000
Hematological neoplasm	15 (5.2%)	4 (3.8%)	0.791
Previous CRAB colonization or infection (60 days)	40 (13.7%)	28 (26.2%)	**0.006**
Previous antibiotic therapy (30 days)	165 (56.7%)	76 (71.0%)	**0.011**
Previous steroid therapy (30 days)	19 (6.5%)	17 (15.9%)	**0.006**
COVID 19	20 (6.9%)	13 (12.1%)	0.102
Clinical characteristics at time of infection			
APACHE, mean (± SD)	36.17 (± 8.13)	39.84 (± 8.29)	0.491
SAPS II, mean (± SD)	31.07 (± 19.45)	41.88 (± 2.57)	**0.006**
SOFA, mean (± SD)	5.14 (± 3.10)	7.00(± 3.65)	**< 0.001**
QSOFA, mean (± SD)	1.41(± 0.94)	1.89 (± 1.12)	0.406
Fever	199 (68.4%)	71 (66.4%)	0.718
Septic shock	94 (32.3%)	53 (49.5%)	**0.002**
ECMO	4 (1.4%)	3 (2.8%)	0.392
CRRT	25 (8.6%)	15 (14.0%)	0.132
Multisite colonization	41 (14.1%)	16 (15.0%)	0.872
Origin of bacteremia			
Primary bacteremia	65 (22.3%)	42 (39.3%)	**0.001**
CVC-related bacteremia	81 (27.8%)	33 (30.8%)	0.617
HAP	52 (17.9%)	16 (15%)	0.550
VAP	67 (23.0%)	23 (21.5%)	0.788
Intra-abdominal infection	13 (4.5%)	5 (4.7%)	1.000
Urinary tract infection	23 (7.9%)	2 (1.9%)	**0.034**
Multisite	30 (10.3%)	12 (11.2%)	0.854
Laboratory findings			
CRP, mean gm/l (± SD)	23.7 (± 33.7)	71.7 (± 90.57)	0.395
PCT, mean ng/ml(± SD) reduction of PCT values less than 50%	12.3 (± 39.1)	11.33 (± 25.15)	0.805
Lactates serum, mean mmol/l (± SD)	2.39 (± 3.04)	3.72 (± 6.05)	0.051
Therapeutic regimens			
Inappropriate empirical therapy	202 (69.4%)	77 (72%)	0.711
Tigecycline in targeted therapy	26 (8.9%)	17 (15.9%)	0.067
Fosfomycin in targeted therapy	39 (13.4%)	15 (14%)	0.870
Colistin in targeted therapy	46 (15.8%)	23 (21.5%)	0.183
Cefiderocol in targeted therapy	158 (54.3%)	53 (49.5%)	0.429
Ampicillin/Sulbactam in targeted therapy	53 (18.2%)	29 (27.1%)	0.068
Time to targeted therapy, mean days (± SD)	3.5 (± 1.7)	3.7 (± 1.9)	0.782
Clinical characteristics at 72 h after the start of therapy			
Adequate source-control of infection	175 (60.1%)	53 (49.5%)	0.067
Negative follow-up blood culture	133 (75.1%)	41 (65.1%)	0.140
Fever	41 (14.1%)	26 (24.3%)	**0.023**
Respiratory improvement	207 (71.1%)	37 (34.9%)	**< 0.001**
PCT < 50%	180 (61.9%)	42 (39.3%)	**< 0.001**

COPD, chronic obstructive pulmonary disease; CVC, central venous catheter; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; HAP, hospital-acquired pneumonia; VAP, ventilator-associated pneumonia; SOFA, sequential organ failure assessment; PCT, procalcitonin; APACHE, Acute Physiologic Assessment and Chronic Health Evaluation; SAPS, Simplified Acute Physiology Score; SOFA, sequential organ failure assessment; qSOFA, quick sequential organ failure assessment; CRP, C-reactive protein; PCT, procalcitonin.

and interactions were weighted during analysis. Statistical significance was established at ≤0.05. All reported P-values are 2-tailed. The results obtained were analyzed using commercially available statistical software package (SPSS, version 20.0; SPSS Inc, Chicago, Illinois).

Propensity score matching (PSM) analyses were conducted for each antibiotic or antibiotic combination as targeted therapy. Propensity scores were estimated using logistic regression models including covariates selected based on previous literature, biological plausibility, and the number of observed events. These covariates comprised cardiovascular disease, diabetes mellitus, chronic kidney disease, chronic corticosteroid therapy, septic shock, presence of multiple comorbidities, and CRRT. In cases of model instability due to quasi-complete separation, selected covariates were excluded.

Patients were matched 1:1 using nearest-neighbor matching with a caliper of 0.05. The average treatment effect (ATE) was calculated for each outcome (14-day mortality, 30-day mortality, and clinical failure). A negative ATE was considered indicative of a protective association. Covariate balance and common support were assessed for all models.

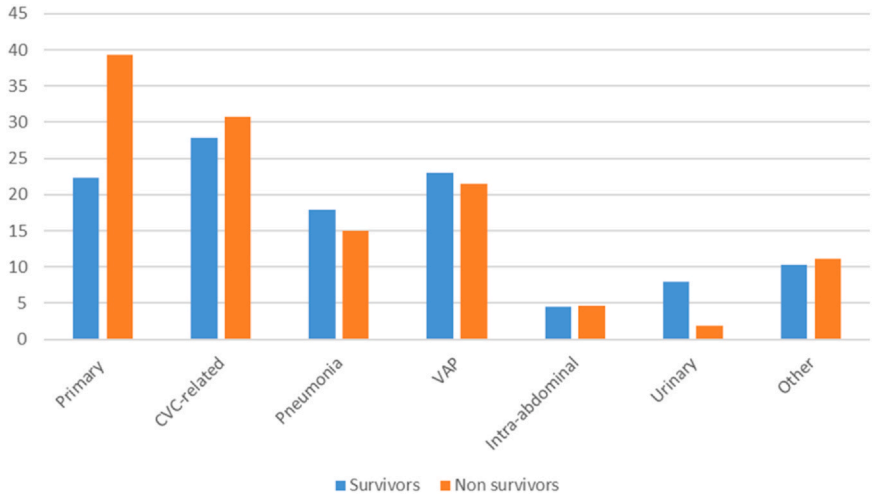

Fig. 1. Survivors vs. non-survivors at 30 days, source of bacteremia. *primary bacteremia: p < 0.001. CVC, central venous catheter; VAP, ventilator associated pneumonia.

Table 2
Cox regression analysis about risk factors associated with 14- and 30-day mortality.

Variables	HR	95%CI lower	95%CI upper	p-value
14-day mortality				
Male sex	1.98	1.21	3.23	**0.006**
Chronic kidney disease	1.75	1.18	3.12	**0.016**
Colistin-containing regimen	0.35	0.15	0.81	**0.014**
Cefiderocol-containing regimen	0.27	0.15	0.48	**< 0.001**
30-day mortality				
Male sex	1.54	1.05	2.26	**0.027**
Septic shock	1.61	1.09	2.4	**0.018**
Previous *Acinetobacter* colonization	2.356	1.726	4.34	**< 0.001**
Tigecycline-containing regimen	2.08	1.11	3.87	**0.021**
Cefiderocol-containing regimen	0.34	0.22	0.53	**< 0.001**

COPD, chronic obstructive pulmonary disease; PCT, procalcitonin.

See supplementary material for additional information.

Results

A total of 398 patients from 52 centers were enrolled during the study period. Of these, 258 (64.9%) were female. The mean age was 60 years (±9.17), and the mean Charlson Comorbidity Index was 5 (±3.8). Previous CRAB colonization or infection was reported in 68 patients (17%), while 241 (60%) had received prior antibiotic therapy. Septic shock occurred in 147 patients (36%); vasopressors were used in 108 (27%), and 7 patients (1%) underwent ECMO.

The source of bacteremia was CVC-related in 28.6% (n=114) of patients, primary in 26.8% (n=107), ventilator-associated pneumonia in 22.6% (n=90), secondary to hospital-acquired (non-VAP) pneumonia in 17% (n=68). The most frequently administered agents were cefiderocol used in 211/398 (53%) of patients, ampicillin/sulbactam in 82/398 (20.6%), colistin in 69/398 (17.3%), tigecycline in 43/398 (10.8%), fosfomycin in 54/398 (13.5%) and meropenem in 65/398 (16.3%).

Overall, 107 patients (26.8%) died within 30 days of infection onset, and 89 (22.3%) died within 14 days.

Table 1 reports the univariate analysis of variables associated with 30-day mortality. Compared to survivors, non-survivors more frequently had ≥2 comorbidities (78.5% vs. 27.3%, p=0.047), prior CRAB colonization or infection (26.2% vs. 13.7%, p=0.006), and prior antibiotic therapy (71% vs. 56.7%, p=0.011). Primary bacteremia was significantly more common in non-survivors (39.3% vs. 22.3%, p=0.001), while urinary tract infection was more frequently the source in survivors (7.9% vs. 1.9%, p=0.034). At 72 h after the initiation of active therapy, non-survivors more often had persistent fever (24.3% vs. 14.1%, p=0.023); in contrast, survivors more frequently showed respiratory improvement (71.1% vs. 34.9%, p < 0.001) and a reduction in procalcitonin (PCT) values by ≥50% (61.9% vs. 39.3%, p < 0.001).

Fig. 1 shows the source of bacteremia in survivors compared to non-survivors at 30-day.

Table 2 presents the Cox regression analysis of factors independently associated with 14- and 30-day mortality. Male sex (HR 1.98, 95%CI 1.21–3.23, p=0.006), and chronic kidney disease (HR 1.75, 95%CI 1.18–3.12, p=0.016) resulted as independent predictors of 14-day mortality, while colistin-containing regimen (HR 0.35, 95%CI 0.15–0.81, p=0.014), and cefiderocol-containing-regimen (HR 0.27, 95%CI 0.15–0.48, p < 0.001) were associated with 14-day survival; male sex (HR 1.54, 95%CI 1.05–2.26, p=0.027), septic shock (1.61, 95%CI 1.09–2.4, p=0.018), previous colonization by *A. baumannii* (HR 2.356, 95%CI 1.726–4.34, p < 0.001), and tigecycline-containing regimen (HR 2.08, 95%CI 1.11–3.87, p=0.021) were independent predictors of 30-day mortality, while cefiderocol-containing-regimen (HR 0.34, 95%CI 0.22–0.53, p < 0.001) was associated with 30-day survival.

Table 3 reports the univariate analysis of variables associated with 14-day mortality. Compared to non-survivors, survivors were more frequently treated with cefiderocol-containing regimens (58.9% vs. 32.6%, p < 0.001), underwent adequate source control within 72 h (62.8% vs. 38.2%, p < 0.001), had a first negative follow-up blood culture (75.3% vs. 4.0%, p=0.008), showed respiratory improvement (73.7% vs. 19.1%, p < 0.001), and experienced a reduction in procalcitonin (PCT) values ≥50% (66.7% vs. 18%, p < 0.001).

In Table 4 are reported therapeutic regimens associated with 14-, 30-day mortality and clinical failure after propensity score matching. At 14 days and for clinical failure cefiderocol was associated with survival (p < 0.001) and clinical success (p < 0.001), respectively. A therapeutic regimen containing cefiderocol plus fosfomycin was significantly associated with clinical success (p=0.024).

Finally, The Fig. 2 shows Kaplan–Meier curves about 30-day mortality in patients treated or not treated with cefiderocol (p < 0.001).

In supplementary material are reported: S-Table 1 about covariates balancing before and after propensity score matching (cefiderocol-treated vs. not-treated); S-Table 2 about covariates balancing before and after propensity score matching (cefiderocol plus fosfomycin treated vs. not-treated); S-Tables 3–7 about covariate balance

Table 3
Univariate analysis of survivors vs. non-survivors at 14 days.

Variables	Survivors n=309	Non survivors n=89	p-value
Anamnestic characteristics			
Age, years (mean ± SD)	61.17 ± 8.17	60.95 ± 6.44	0.914
Male, sex	99 (32%)	41 (46.1%)	**0.017**
Previous surgery (30 days)	165 (53.4%)	33 (37.1%)	**0.008**
> 2 Comorbidities	204 (66%)	78 (87.6%)	**< 0.001**
Charlos Comorbidity Index, mean (± SD)	7.14 (± 2.07)	5.95 (± 2.59)	0.454
Heart failure	179 (57.9%)	65 (73%)	**0.010**
Chronic kidney disease	47 (15.2%)	33 (37.1%)	**< 0.001**
Diabetes	102 (33%)	28 (31.5%)	0.898
Dyalisis	17 (5.5%)	7 (7.9%)	0.448
Cirrhosis	33 (10.7%)	13 (14.6%)	0.346
COPD	70 (22.7%)	30 (33.7%)	**0.038**
Immunosuppressive therapy	51 (24.6%)	17 (30.9%)	0.388
Neurologic disease	100(33%)	27 (31.8%)	0.896
Vasculitis	20 (6.5%)	12 (13.5%)	**0.045**
Solid neoplasm	43 (14%)	15 (17.2%)	0.493
Hematological neoplasm	16 (5.2%)	3 (3.4%)	0.776
Previous CRAB colonization or infection (60 days)	57 (18.4%)	11 (12.4%)	0.203
Previous antibiotic therapy (30 days)	184 (59.5%)	57 (64%)	0.463
Previous steroid therapy (30 days)	21 (6.8%)	15 (16.9%)	**0.006**
COVID 19	28 (9.1%)	5 (5.6%)	0.385
Clinical characteristics at time of infection			
APACHE, mean (± SD)	38.91 (± 8.11)	33.46 (± 8.25)	0.361
SAPS II, mean (± SD)	32.37 (± 9.77)	43.55 (± 3.73)	**0.012**
SOFA, mean (± SD)	5.13 (± 3.18)	7.40 (± 3.37)	**< 0.001**
QSOFA, mean (± SD)	1.77 (± 1.40)	(2.16 ± 1.27)	0.502
Fever	207 (67%)	63 (70.8%)	0.523
Septic shock	102 (33%)	45 (50.6%)	**0.004**
ECMO	6 (1.9%)	1 (1.1%)	1.000
CRRT	28 (9.1%)	12 (13.5%)	0.232
Multisite colonization	50 (16.2%)	7 (7.9%)	0.058
Origin of bacteremia			
Primary bacteremia	76 (24.6%)	31 (34.8%)	0.059
CVC-related bacteremia	97 (31.4%)	17 (19.1%)	**0.024**
HAP	57 (18.4%)	11 (12.3%)	0.078
VAP	70 (22.7%)	20 (22.5%)	1.000
Intra-abdominal infection	15 (4.9%)	3 (3.4%)	0.774
Urinary tract infection	24 (7.8%)	1 (1.1%)	**0.023**
Multisite	34 (11%)	8 (9.0%)	0.697
Laboratory findings			
CRP, mean gm/l (± SD)	22.6 (± 27.0)	25.26 (± 95.75)	0.455
PCT, mean ng/ml (± SD)	12.76 (± 39.53)	9.69 (± 23.15)	0.485
Lactates serum, mean mmol/l (± SD)	2.50 (± 4.11)	3.49 (± 4.33)	0.150
Therapeutic regimens			
Empirical therapy	211 (68.3%)	68 (76.4%)	0.150
Tigecycline in targeted therapy	32 (10.4%)	11 (12.4%)	0.566
Fosfomycin in targeted therapy	44 (14.2%)	10 (11.2%)	0.598
Colistin in targeted therapy	57 (18.4%)	12 (13.5%)	0.341
Cefiderocol in targeted therapy	182 (58.9%)	29 (32.6%)	**< 0.001**
Ampicillin/Sulbactam in targeted therapy	70 (22.7%)	12 (13.5%)	0.074
Time to targeted therapy, mean days (± SD)	3.6 (± 1.8)	3.6 (± 1.4)	0.992
Clinical characteristics at 72 h after the start of therapy			
Adequate source-control of infection	194 (62.8%)	34 (38.2%)	**< 0.001**
Negative follow-up blood culture	162 (75.3%)	12 (48.0%)	**0.008**
Fever	37 (12%)	30 (33.7%)	**< 0.001**
Respiratory improvement	227 (73.7%)	17 (19.1%)	**< 0.001**
PCT < 50%	206 (66.7%)	16 (18%)	**< 0.001**

COPD, chronic obstructive pulmonary disease; CVC, central venous catheter; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; HAP, hospital-acquired pneumonia VAP, ventilator-associated pneumonia; SOFA, sequential organ failure assessment; PCT, procalcitonin; APACHE, Acute Physiologic Assessment and Chronic Health Evaluation; SAPS, Simplified Acute Physiology Score; SOFA, sequential organ failure assessment; qSOFA, quick sequential organ failure assessment; CRP, C-reactive protein; PCT, procalcitonin.

before and after propensity score matching for respectively cefiderocol, colistin, ampicillin/sulbactam, fosfomycin and cefiderocol plus fosfomycin-based regimen. S-Table 8 about Propensity score–matched comparison between cefiderocol monotherapy and cefiderocol plus fosfomycin (restricted to cefiderocol-treated patients). S-Fig. 1 about participating centers and number of enrolled patients; S-Fig. 2 about the therapeutic regimens used among survivors and non-survivors at 30 days; S-Fig. 3 about sources of infection among survivors and non-survivors at 14 days; S-Fig. 4 about the therapeutic regimens among survivors and non-survivors at 14 days.

Discussion

To our knowledge, this is the largest, prospective, multicenter cohort of patients with BSI caused by CRAB. Of importance, at Cox regression analysis we identified that male sex and chronic kidney

Table 4
Therapeutic regimens associated with 14-, 30-day mortality and clinical failure after propensity score matching.

Variables	ATE	95%CI lower	95%CI upper	p-value
14-day mortality				
Cefiderocol	−0.1509	−0.2197	−0.0441	**<0.001**
Colistin	−0.0875	−0.2119	0.0619	0.251
Ampicillin-sulbactam	−0.0744	−0.1124	0.0357	0.117
Fosfomycin	−0.0276	−0.1415	0.0873	0.683
Cefiderocol plus fosfomycin	−0.078	−0.261	0.117	0.418
30-day mortality				
Cefiderocol	−0.0424	−0.1515	0.0567	0.324
Colistin	0.0452	−0.0531	0.1627	0.423
Ampicillin-sulbactam	0.0988	−0.0267	0.2643	0.241
Fosfomycin	−0.0437	−0.1852	0.0995	0.554
Cefiderocol plus fosfomycin	−0.004	−0.216	0.211	0.463
Clinical failure				
Cefiderocol	−0.2158	−0.2948	−0.1497	**<0.001**
Colistin	0.1018	−0.0664	0.1499	0.335
Ampicillin-sulbactam	−0.0632	−0.1662	0.0359	0.129
Fosfomycin	−0.0503	−0.2196	0.1139	0.560
Cefiderocol plus fosfomycin	−0.163	−0.343	−0.746	**0.024**

ATE, average treatment effect; CI, confidence interval.

disease resulted as independent predictors of 14-day mortality, while colistin-containing regimen, and cefiderocol-containing-regimen were associated with 14-day survival; moreover, male sex, septic shock, previous colonization by *A. baumannii*, and tigecycline-containing regimen were independent predictors of 30-day mortality, while cefiderocol-containing-regimen was associated with 30-day survival.

Of note, therapeutic regimens containing cefiderocol and the combination of cefiderocol plus fosfomycin (after testing all possible antibiotic combination used in our cohort) were associated with clinical success following propensity score matching; specifically, we observed that at 14 days cefiderocol was associated with survival ($p < 0.001$) and clinical success ($p < 0.001$), respectively. A therapeutic regimen containing cefiderocol plus fosfomycin was significantly associated with clinical success (p=0.024).

Data from this study highlight some important points that should be discussed. Mortality in patients with CRAB bacteremia is influenced by multiple factors such as patient-, infection-, and treatment-related factors.[19,20]

Firstly, anamnestic factors like male sex and chronic kidney disease together with severity of clinical condition expressed by septic shock, and the CRAB colonization at time of infection were factors independently associated with an unfavorable outcome.[19]

The role of colonization may reflect a higher bacterial load and a greater likelihood of bacterial translocation across mucosal barriers. Furthermore, colonization could also indicate more widespread environmental contamination, increasing the risk of cross-contamination between colonized sites. This suggests that colonization may be not only a marker of disease severity but also a predictor of poor prognosis.[20] Interestingly, the presence of colonization may also reflect more complex underlying pathophysiological processes, including impaired host defenses and prolonged exposure to invasive procedures or broad-spectrum antibiotics. Future studies could focus on interventions targeting patients with colonization to reduce the risk of infection, also BSI, such as enhanced decolonization protocols or more frequent microbiological screening during their ICU stay.

Of importance, CRAB bloodstream infections, causing septic shock, remain a peculiar hospital-acquired infection, related to high mortality rates in many studies.[9] CRAB bloodstream infections represent a major clinical concern. They frequently originate from central venous catheters, which serve as direct access points, though alternative sources such as the lungs may also be implicated. As our findings confirm, clinical manifestations vary, from mild symptoms to severe septic shock with organ failure. Infection severity is commonly shaped by the patient's baseline condition and existing comorbidities.

As a matter of fact, a cefiderocol-containing regimen was a predictor of early survival (14 days) in this cohort, while the antibiotic combination cefiderocol plus fosfomycin was associated with clinical success. Our findings are consistent with previous studies that showed as cefiderocol may be effective in the treatment of serious Gram-negative infections.[13,14,21–23] Despite the concern about the occurrence of resistance to cefiderocol among CRAB isolates, it represents a therapeutic option from CRAB infections.[24] In a randomized clinical trial, cefiderocol was found to be effective as best available therapy, including colistin, for the treatment of serious Gram-negative infections with limited therapeutic options, including ventilator-associated pneumonia (VAP) and bacteremia, despite more deaths occurring in the cefiderocol-treated group.[25] In another retrospective cohort study, cefiderocol was associated with lower 30-day mortality compared with colistin therapy for the treatment of CRAB bacteremia.[26] This effectiveness of cefiderocol against CRAB could be explained by his unique mechanism of action which allows to overcome carbapenemase-mediated resistance, by binding to ferric iron and being actively transported into bacterial cells through the iron siderophore transport system.[27] Of importance, recently Paterson et al. showed that among patients with a hospital-acquired or health-care-associated Gram-negative bacteremia, cefiderocol resulted in non-inferior 14-day mortality

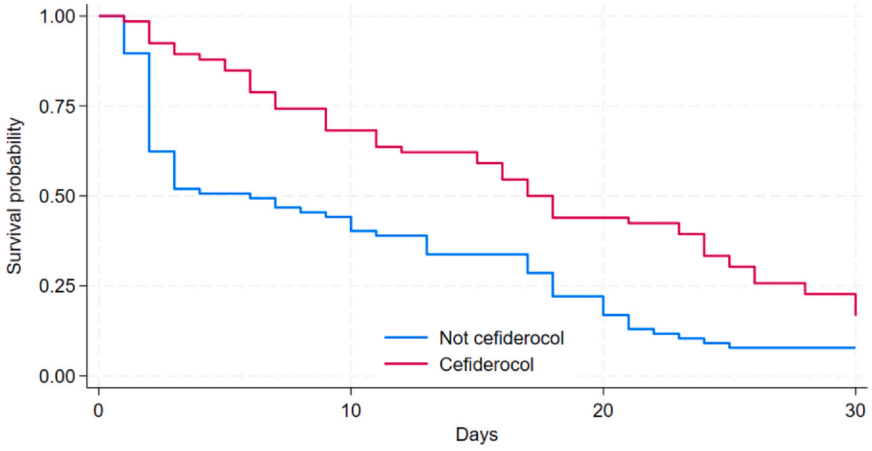

Fig. 2. Kaplan–Meier curves about 30-day mortality in patients treated or not treated with cefiderocol. *p < 0.001.

compared with standard of care suggesting that cefiderocol is efficacious in patients with health-care-associated Gram-negative bloodstream infection.[2]

Different antibiotic combinations have been studied for the treatment of severe infections caused by CRAB, suggesting the advantage of various combinations based on high in vitro synergy rates. Out of these, a therapeutic combination including colistin as backbone is considered one of the most important options for treatment of CRAB infections also in guidelines from Europe.[28,29] It should be noted that studies assessing monotherapy efficacy (primarily colistin) versus combination therapies for *Acinetobacter baumannii* have examined various severe infections, including ventilator-associated pneumonia, though these were not consistently linked to bacteremia.[30,31] However, these findings should be further explored in trials focusing on antibiotic treatments of CRAB infections.

Of note, the ITACA study also highlights the role of cefiderocol in the first days from diagnosis of infection. While the use of cefiderocol significantly improves survival in the first 2 weeks from infection onset, this advantage seems to reduce when considering patient outcomes over a 30-day period. This suggests that antibiotic therapy might not be enough to counteract all the factors that contribute to mortality in these critically ill patients over a longer time. However, it is important to underline in our cohort the mortality rates were 22.3% (89/398) and 26.8% (107/398) at 14 days and 30 days, lower if compared to recent data.[32]

The present study has several strengths. Firstly, the study is of a prospective, multicenter nature. Secondly, the study included a substantial number of patients with CRAB bacteremia. Thirdly, a rigorous methodology was employed to assess the primary and secondary outcomes.

Furthermore, the ITACA study offers valuable insights that can guide clinical practice. The findings support the consideration of an early effective treatment, including cefiderocol, as a promising option for treating CRAB bacteremia, particularly for achieving early clinical improvement. However, it is crucial for clinicians to recognize the many factors that can influence a patient's outcome and to take these into account when making treatment decisions. The study underscores the importance of controlling infection, preventing CRAB spread, and maintaining surveillance of antibiotic resistance and colonization.

Our study also has some limitations. Firstly, the observational design of the study. Secondly, data were collected by numerous clinicians across different centers, which introduces the possibility of inconsistencies in how data was recorded and interpreted. Furthermore, the number of patients enrolled varied between centers. Thirdly, there's also the potential for confounding bias, where unmeasured factors might affect both the choice of treatment and patient outcomes. The patients showed high variablity in clinical presentation, with varying levels of illness and different underlying health issues, which could limit how broadly the findings can be applied. This may limit the generalizability of the findings to other settings. Moreover, the study did not include a detailed analysis of the specific mechanisms by which *A. baumannii* develops resistance to antibiotics. Finally, ampicillin-sulbactam (recommended in ESCMID guidelines and IDSA guidance) was used, also in combination, with different dose (standard or high dose) and in few cases compared to patients treated with cefiderocol, considering to the main recommendations from italian guidelines about CRAB treatment.[33]

These limitations emphasize the need for additional research to confirm the results of the ITACA study and to address the questions that remain unanswered. Future research might include randomized controlled trials to more definitively establish the effectiveness of cefiderocol and other antibiotics, studies to determine the best strategies for treatment (including the optimal duration and combinations of antibiotics), investigations into personalized treatment approaches that consider individual patient characteristics and the specific resistance profile of the infecting bacteria, and detailed analyses of resistance mechanisms to aid in the development of new therapies.

In conclusion, the ITACA study contributes significantly to our understanding of the complex dynamics between patient characteristics, the specifics of the infection, and treatment choices in cases of CRAB bacteremia, highlighting the need to implement research with appropriate study designs to confirm the findings of this work. Cefiderocol, also in association with fosfomycin, demonstrates promise as an effective therapeutic option; however, further research is essential to optimize treatment strategies and improve patient outcomes in CRAB bacteremia.

Author contributions

A.R., S.P.G., and F.S. conceived, designed, wrote and revised the study. L.S., M.B., and G.B.Z performed and revised statistical analysis. A.V., G.C., F.A., C.M.M., A.O., E.V.R., G.C., A.C., M.I., G.N., F.D.G., A.S. A.M, B.C., G.T., M.F., V.G., C.I., G.P., A.C., S.C., L.M., F.S.S., N.B., M.L., F.G.D.R., A.M., A.C., M.T., L.F.S., C.P., P.B., R.M., B.T., N.C., V.S., M.M., O.S., A.M., F.B., R.S., C.M., M.B. collected data and reviewed the manuscript for intellectual content. All authors reviewed and approved the final manuscript.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jinf.2026.106742.

References

1. Sati H, Carrara E, Savoldi A, Hansen P, Garlasco J, Campagnaro E, et al. WHO Bacterial Priority Pathogens List Advisory Group. *The WHO Bacterial Priority Pathogens List 2024: a prioritisation study to guide research, development, and public health strategies against antimicrobial resistance. Lancet Infect Dis* 2025;**25**:1033–43. https://doi.org/10.1016/S1473-3099(25)00118-5
2. Paterson DL, Sulaiman H, Liu PY, Chatfield MD, Yilmaz M, Salmuna ZN, et al. GAME CHANGER Trial Investigators. *Cefiderocol versus standard therapy for hospital-acquired and health-care-associated Gram-negative bacterial bloodstream infection (the GAME CHANGER trial): an open-label, parallel-group, randomised trial. Lancet Infect Dis* 2026;**26**:148–59. https://doi.org/10.1016/S1473-3099(25)00469-4
3. Ibrahim S, Al-Saryi N, Al-Kadmy IMS, Aziz SN. *Multidrug-resistant Acinetobacter baumannii as an emerging concern in hospitals. Mol Biol Rep* 2021;**48**:6987–98. https://doi.org/10.1007/s11033-021-06690-6
4. Bartal C, Rolston KVI, Nesher L. *Carbapenem-resistant Acinetobacter baumannii: colonization, infection and current treatment options. Infect Dis Ther* 2022;**11**:683–94. https://doi.org/10.1007/s40121-022-00597-w
5. Serapide F, Quirino A, Scaglione V, Morrone HL, Longhini F, Bruni A, et al. *Is the pendulum of antimicrobial drug resistance swinging back after COVID-19. Microorganisms* 2022;**10**:957. https://doi.org/10.3390/microorganisms10050957
6. Thacharodi A, Vithlani A, Hassan S, Alqahtani A, Pugazhendhi A. *Carbapenem-resistant Acinetobacter baumannii raises global alarm for new antibiotic regimens. iScience* 2024;**27**:111367. https://doi.org/10.1016/j.isci.2024.111367

7. Russo A, Olivadese V, Trecarichi EM, Torti C. *Bacterial ventilator-associated pneumonia in COVID-19 patients: data from the second and third waves of the pandemic. J Clin Med* 2022;**11**:2279. https://doi.org/10.3390/jcm11092279
8. Falcone M, Tiseo G, Carbonara S, Marino A, Di Caprio G, Carretta A, et al. Advancing knowLedge on Antimicrobial Resistant Infections Collaboration Network (ALARICO Network). *Mortality attributable to bloodstream infections caused by different carbapenem-resistant gram-negative bacilli: results from a nationwide study in Italy (ALARICO Network). Clin Infect Dis* 2023;**76**:2059–69. https://doi.org/10.1093/cid/ciad100
9. Russo A, Serapide F. *The multifaceted landscape of healthcare-associated infections caused by carbapenem-resistant Acinetobacter baumannii. Microorganisms* 2025;**13**:829. https://doi.org/10.3390/microorganisms13040829
10. Russo A, Bruni A, Gullì S, Borrazzo C, Quirino A, Lionello R, et al. *Efficacy of cefiderocol- vs colistin-containing regimen for treatment of bacteraemic ventilator-associated pneumonia caused by carbapenem-resistant Acinetobacter baumannii in patients with COVID-19. Int J Antimicrob Agents* 2023;**62**:106825. https://doi.org/10.1016/j.ijantimicag.2023.106825
11. Oliva A, Ceccarelli G, De Angelis M, Sacco F, Miele MC, Mastroianni CM, et al. *Cefiderocol for compassionate use in the treatment of complicated infections caused by extensively and pan-resistant Acinetobacter baumannii. J Glob Antimicrob Resist* 2020;**23**:292–6. https://doi.org/10.1016/j.jgar.2020.09.019
12. Mohd Sazlly Lim S, Sime FB, Roberts JA. *Multidrug-resistant Acinetobacter baumannii infections: current evidence on treatment options and the role of pharmacokinetics/pharmacodynamics in dose optimisation. Int J Antimicrob Agents* 2019;**53**:726–45. https://doi.org/10.1016/j.ijantimicag.2019.02.016
13. Falcone M, Tiseo G, Leonildi A, Della Sala L, Vecchione A, Barnini S, et al. *Cefiderocol- compared to colistin-based regimens for the treatment of severe infections caused by carbapenem-resistant Acinetobacter baumannii. Antimicrob Agents Chemother* 2022;**66**:e0214221. https://doi.org/10.1128/aac.02142-21
14. Falcone M, Tiseo G, Nicastro M, Leonildi A, Vecchione A, Casella C, et al. *Cefiderocol as rescue therapy for Acinetobacter baumannii and other carbapenem-resistant gram-negative infections in intensive care unit patients. Clin Infect Dis* 2021;**72**:2021–4. https://doi.org/10.1093/cid/ciaa1410
15. Antonello RM, Principe L, Maraolo AE, Viaggi V, Pol R, Fabbiani M, et al. *Fosfomycin as partner drug for systemic infection management. A systematic review of its synergistic properties from in vitro and in vivo studies. Antibiotics (Basel)* 2020;**9**:500. https://doi.org/10.3390/antibiotics9080500
16. Russo A, Bassetti M, Bellelli V, Bianchi L, Marincola Cattaneo F, Mazzocchetti S, et al. *Efficacy of a fosfomycin-containing regimen for treatment of severe pneumonia caused by multidrug-resistant Acinetobacter baumannii: a prospective, observational study. Infect Dis Ther* 2021;**10**:187–200. https://doi.org/10.1007/s40121-020-00357-8
17. Mohd Sazlly Lim S, Heffernan AJ, Roberts JA, Sime FB. *Semi-mechanistic PK/PD modelling of fosfomycin and sulbactam combination against carbapenem-resistant Acinetobacter baumannii. Antimicrob Agents Chemother* 2023;**65**:e02472–20. https://doi.org/10.1128/AAC.02472-20
18. Spernovasilis N, Ishak A, Tsioutis C, Alon-Ellenbogen D, Agouridis AP, Mazonakis N. *Sulbactam for carbapenem-resistant Acinetobacter baumannii infections: a literature review. JAC Antimicrob Resist* 2025;**7**:dlaf055. https://doi.org/10.1093/jacamr/dlaf055
19. Ahn JY, Ahn SM, Kim JH, Jeong SJ, Ku NS, Choi JY, et al. *Clinical characteristics and associated factors for mortality in patients with carbapenem-resistant enterobacteriaceae bloodstream infection. Microorganisms* 2023;**11**:1121. https://doi.org/10.3390/microorganisms11051121
20. Russo A, Serapide F, Alessandri F, Gullì SP, Bruni A, Longhini F, et al. *Risk factors for the development of hospital-acquired pneumonia in patients with carbapenem-resistant Acinetobacter baumannii respiratory colonization and the role of multisite colonization: a multicenter retrospective study. Eur J Clin Microbiol Infect Dis* 2025;**44**:1667–76. https://doi.org/10.1007/s10096-025-05137-1
21. Magrini E, Rando E, Liguoro B, Salvati F, Del Vecchio P, Fantoni M, et al. *Risk factors associated with bloodstream infections caused by Acinetobacter baumannii in hospital settings: a systematic review and meta-nalysis. CMI Commun* 2025;**2**(1):105060. https://doi.org/10.1016/j.cmicom.2025.105060
22. Torre-Cisneros J, Almirante B, Martos CF, Rascado P, Lletí MS, Sánchez-García M, et al. *Effectiveness and safety of cefiderocol treatment in patients with Gram-negative bacterial infections in Spain in the early access programme: results of the PERSEUS study. Eur J Clin Microbiol Infect Dis* 2025;**44**:1375–90. https://doi.org/10.1007/s10096-025-05108-6
23. Soueges S, Faure E, Parize P, Lanternier-Dessap F, Lecuyer H, Huynh A, et al. *Real-world multicentre study of cefiderocol treatment of immunocompromised patients with infections caused by multidrug-resistant Gram-negative bacteria: CEFI-ID.* G2I (Groupe Immunodepression et Infections) network. *J Infect* 2025;**90**:106376. https://doi.org/10.1016/j.jinf.2024.106376
24. Tiseo G, Giordano C, Leonildi A, Riccardi N, Galfo V, Limongi F, et al. *Salvage therapy with sulbactam/durlobactam against cefiderocol-resistant Acinetobacter baumannii in a critically ill burn patient: clinical challenges and molecular characterization. JAC Antimicrob Resist* 2023;**5**:dlad078. https://doi.org/10.1093/jacamr/dlad078
25. Bassetti M, Echols R, Matsunaga Y, Ariyasu M, Doi Y, Ferrer R, et al. *Efficacy and safety of cefiderocol or best available therapy for the treatment of serious infections caused by carbapenem-resistant Gram-negative bacteria (CREDIBLE-CR): a randomised, open-label, multicentre, pathogen-focused, descriptive, phase 3 trial. Lancet Infect Dis* 2021;**21**:226–40. https://doi.org/10.1016/S1473-3099(20)30796-9
26. Bavaro DF, Papagni R, Belati A, Diella L, De Luca A, Brindicci G, et al. *Cefiderocol versus colistin for the treatment of carbapenem-resistant Acinetobacter baumannii complex bloodstream infections: a retrospective, propensity-score adjusted, monocentric cohort study. Infect Dis Ther* 2023;**12**:2147–63. https://doi.org/10.1007/s40121-023-00854-6
27. Serapide F, Guastalegname M, Gullì SP, Lionello R, Bruni A, Garofalo E, et al. *Antibiotic treatment of carbapenem-resistant Acinetobacter baumannii infections in view of the newly developed β-lactams: a narrative review of the existing evidence. Antibiotics (Basel)* 2024;**13**:506. https://doi.org/10.3390/antibiotics13060506
28. Tamma PD, Heil EL, Justo JA, Mathers AJ, Satlin MJ, Bonomo RA. *Infectious Diseases Society of America 2024 guidance on the treatment of antimicrobial-resistant Gram-negative infections. Clin Infect Dis* 2024:ciae403. https://doi.org/10.1093/cid/ciae403
29. Paul M, Carrara E, Retamar P, Tängdén T, Bitterman R, Bonomo RA, et al. *European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines for the treatment of infections caused by multidrug-resistant Gram-negative bacilli (endorsed by European society of intensive care medicine. Clin Microbiol Infect* 2022;**28**:521–47. https://doi.org/10.1016/j.cmi.2021.11.025
30. Paul M, Daikos GL, Durante-Mangoni E, Yahav D, Carmeli Y, Benattar YD, et al. *Colistin alone versus colistin plus meropenem for treatment of severe infections caused by carbapenem-resistant Gram-negative bacteria: an open-label, randomised controlled trial. Lancet Infect Dis* 2018;**18**:391–400. https://doi.org/10.1016/S1473-3099(18)30099-9
31. Kaye KS, Marchaim D, Thamlikitkul V, Carmeli Y, Chiu CH, Daikos G, et al. *Colistin monotherapy versus combination therapy for carbapenem-resistant organisms. NEJM Evid* 2023;**2**. https://doi.org/10.1056/evidoa2200131
32. Huralska M, Pogue JM, Rybak M, Abdul-Mutakabbir JC, Stamper K, Marchaim D, et al. *The impact of synergistic therapy between colistin and meropenem on outcomes of people with pneumonia or bloodstream infection due to carbapenem-resistant Gram-negative pathogens. Clin Infect Dis* 2026;**82**:391–8. https://doi.org/10.1093/cid/ciaf398
33. Tiseo G, Brigante G, Giacobbe DR, Maraolo AE, Gona F, Falcone M, et al. *Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM). Int J Antimicrob Agents* 2022;**60**:106611. https://doi.org/10.1016/j.ijantimicag.2022.106611