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Risk factors for early mortality in patients with carbapenem-resistant *Acinetobacter baumannii* bacteremia

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Abstract

BACKGROUND

Although many deaths due to carbapenem-resistant *Acinetobacter baumannii* (CRAB) bacteremia occur within a few days after the onset of bacteremia, risk factors for early mortality (EM) have not been deeply investigated. We aimed to determine the risk factors for EM and the difference between risk factors associated with EM and late mortality (LM) in CRAB bacteremia.

METHODS

Clinical information on all patients with CRAB bacteremia in 10 hospitals during a 1-year period was collected. Among the cases with mortality within 30 days, EM and LM were defined as death within 3 and more than 5 calendar days from the first positive blood culture, respectively.

RESULTS

A total of 212 CRAB bacteremia cases were included in the analysis. Of 122 (57.5%) patients with 30-day mortality, EM was observed in 75 (61.5%) patients and LM in 39 (32.0%) patients. The proportion of severe sepsis or septic shock, Pitt score, and Sequential Organ Failure Assessment (SOFA) score was significantly higher in patients with EM than those with LM. While urinary tract infection as the factor of site of infection and the severity of illness were independent predictors of LM, only factors representing the severity of illness were independent risk factors for EM.

CONCLUSION

Our data suggest that a large proportion of CRAB bacteremia with high severity progress to a rapidly fatal course, regardless of the underlying diseases or source of infection. Further studies might be needed to investigate the microbiological factors associated with CRAB and pathogen-host interaction in patients with EM.

Background

- High proportion of mortality in CRAB bacteremia occurs rapidly.
- No clinical studies investigating
  - → the predictive factors for early mortality (EM)
  - → the difference between EM and late mortality (LM)

► **The risk factors associated with EM and the difference between risk factors associated with EM and LM in CRAB bacteremia should be evaluated.**

Methods

Patient population and clinical data

- Prospective observational study between September 2017 to August 2018 at 10 hospitals
- All patients whose blood cultures were positive for CRAB
  - collected microbiological and demographic data, underlying comorbidities, origin of bacteremia, severity of illness, antibiotic therapy, and mortality

Definitions

- In the cases with 30-day mortality
  - → EM: death within three calendar days after first positive blood culture
  - → LM: death more than five calendar days after first positive blood culture

- Empirical therapy
  - → Appropriate if the isolate was susceptible to the antibiotics in vitro and the duration of use was over 48 h
  - → Inappropriate otherwise
- Active empirical therapy at least once
  - → the empirical use of colistin at least once after collection of the first positive blood culture

- Hospital-acquired infection: the bacteremia occurring after 48 hours of hospitalization
- Healthcare-associated infection: the fulfilment of any one of the criteria
  - (i) Hospitalization for more than 2 days within the last 1 year
  - (ii) Living in a nursing home within the last 1 year
  - (iii) Parenteral therapy within 30 days
  - (iv) renal replacement therapy within 30 days

- Immunosuppressant use: any chemotherapy, use of more than 20mg of prednisolone or equivalent of corticosteroids over 1 week, or the use of other immunosuppressive agents within 30 days
- The clinical severity of illness: assessed by the Pitt bacteremia score and the SOFA score

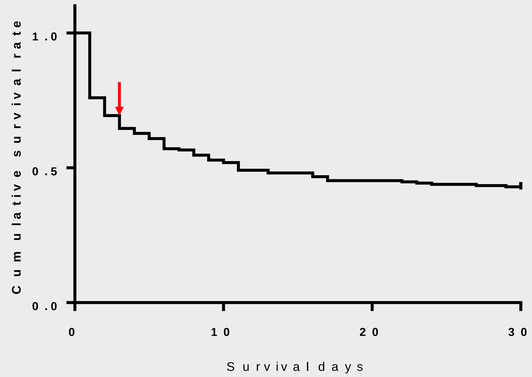
Results

Factors associated with EM compared to 30-day survivors

Risk factors	EM (*n* = 75)	30-day survivors (*n* = 90)	Univariate		Multivariate	
			OR (95% CI)	*P*	aOR (95% CI)	*P*
Age, mean (±SD)	66.3 (±15.4)	64.5 (±18.8)	1.01 (0.99-1.02)	0.508	–	–
Male	51 (68.0)	55 (61.1)	1.35 (0.71-2.58)	0.359	–	–
ICU stay at bacteremia onset	42 (56.0)	48 (53.3)	1.11 (0.60-2.06)	0.732	–	–
Hospital-acquired infection	65 (86.7)	75 (83.3)	1.30 (0.55-3.09)	0.553	–	–
Healthcare-associated infection	74 (98.7)	86 (85.6)	3.44 (0.38-31.48)	0.274	–	–
Mixed bacteremia	3 (4.0)	10 (11.1)	0.33 (0.09-1.26)	0.105	–	–
Site of infection						
Primary bacteremia	23 (30.7)	26 (28.9)	1.09 (0.56-2.13)	0.803	–	–
CRBSI	30 (40.0)	35 (38.9)	1.05 (0.56-1.96)	0.884	–	–
Pneumonia	29 (38.7)	25 (27.8)	1.64 (0.85-3.16)	0.139	–	–
Urinary tract infection	13 (17.3)	17 (18.9)	0.90 (0.41-2.00)	0.796	–	–
Intra-abdominal infection	3 (4.0)	7 (7.8)	0.49 (0.12-1.98)	0.320	–	–
Underlying medical condition						
CCI ≥ 3	65 (86.7)	67 (74.4)	2.23 (0.99-5.05)	0.054	2.87 (0.86-9.54)	0.085
Heart disease	10 (13.3)	9 (10.0)	1.39 (0.53-3.61)	0.505	–	–
Liver disease	19 (25.3)	16 (17.8)	1.57 (0.74-3.32)	0.239	–	–
Diabetes mellitus	22 (29.3)	34 (38.9)	0.68 (0.36-1.32)	0.255	–	–
Malignancy	18 (24.0)	21 (23.3)	1.04 (0.51-2.13)	0.920	–	–
Cerebrovascular disease	12 (16.0)	20 (22.2)	0.67 (0.30-1.47)	0.315	–	–
Transplantation	7 (9.3)	2 (2.2)	4.53 (0.91-22.50)	0.065	4.77 (0.59-38.49)	0.143
Immunosuppressant use	12 (16.0)	7 (7.8)	2.26 (0.84-6.07)	0.106	–	–
Clinical severity						
Severe sepsis or septic shock	66 (88.0)	21 (23.3)	24.10 (10.29-56.41)	**<0.001**	35.29 (13.43-92.76)	**<0.001**
Pitt score, median (IQR)	7.00 (6.00-11.00)	2.00 (1.00-4.00)	1.69 (1.44-1.98)	**<0.001**	1.83 (1.50-2.22)	**<0.001**
SOFA score, median (IQR)	13.00 (10.00-17.00)	5.00 (3.00-8.25)	1.49 (1.33-1.67)	**<0.001**	1.54 (1.35-1.76)	**<0.001**
Appropriate empirical antibiotics	1 (1.3)	24 (26.7)	0.04 (0.01-0.28)	**0.001**	0.02 (0.01-0.14)	**<0.001**
Empirical colistin at least once	8 (10.7)	22 (24.4)	0.37 (0.15-0.89)	**0.026**	0.12 (0.04-0.38)	**<0.001**

- Appropriate empirical antibiotic therapy and active empirical therapy at least once were significantly associated with a decreased risk of EM.
- The risk factors for EM were severe sepsis or septic shock, Pitt score, and SOFA score.

Kaplan-Meier survival curve of patients with CRAB bacteremia



- Of the 122 cases with 30-day mortality
  - → 75 (61.5%) were classified as EM
  - → 39 (32.0%) were classified as LM

Conclusion

- **In conclusion, we found that a high proportion of death with CRAB bacteremia were classified as EM.**
- **The only independent risk factor for EM was the severity of illness.**
- **LM was associated with both the severity of illness and specific sites of infection.**
- **Further studies are needed to clarify the microbiological characteristics associated with EM.**

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