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Impact of carbapenem-resistant *Acinetobacter baumannii* infections on acute pancreatitis patients

Di Wu [a], Yilin Huang [a], Junjie Ding [a], Yan Jia [a], Huanmiao Liu [b], Jie Xiao [b], Jie Peng [a, *]

[a] Department of Gastroenterology, Xiangya Hospital, Central South University, Changsha, China
[b] Emergency Department, Third Xiangya Hospital, Central South University, Changsha, China

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ABSTRACT

Background: Carbapenem-resistant *Acinetobacter baumannii* (CRAB) infections present great challenges in clinical practices with high mortality. The aim of this study is to identify the impact of CRAB infections on acute pancreatitis (AP).

Methods: A case-control study was performed via collecting data from March 1st, 2016 to August 1st, 2020 in two comprehensive teaching hospital. Clinical data of the CRAB-positive AP patients were analyzed and compared to a matched control group (case-control ratio of 1:1). Comparisons were performed between with/without CRAB infections and multiple organ failure (MOF), respectively. Independent risk factors of overall mortality were determined via univariate and multivariate analyses.

Results: CRAB infections were associated with higher mortality (49.2% vs. 23.0%, $P < 0.01$). CRAB combined with MOF increased a mortality up to 90% ($P < 0.01$). MOF (Odds ratio (OR) = 21.49, 95% confidence interval (CI) = 5.26–87.80, $P < 0.01$), CRAB infections (OR = 3.58, 95%CI = 1.24–10.37, $P = 0.02$) and hemorrhage (OR = 3.70, 95%CI = 1.21–11.28, $P = 0.02$) were independent risk factors of overall mortality. Lung was the most common site of strains (37 of 82). CRAB strains were highly resistant (>60%) to ten of eleven common antibiotics, except for tigecycline (28%).

Conclusion: High mortality rate in AP patients was associated with CRAB infections and further increased when CRAB infections combined with MOF.

1. Introduction

Acute pancreatitis (AP), one of the most common gastrointestinal diseases, is characterized by a local and systemic inflammatory response with varying clinical courses [1]. Approximately 20% of moderately severe or severe AP complicated with the infections have a substantial mortality rate ranging from 20% to 40% [2]. Severe AP patients are critically ill, hypercatabolic and vulnerable due to systemic and metabolic disturbances. The death cases of AP, especially severe AP, happen in two peak time points, an early inflammatory peak (lasts 2 weeks from the onset) and a late infectious peak (after the first 2 weeks). Although therapeutic improvements have been implemented, severe infections and multiple organ failure (MOF) are still of great concern, leading to worse prognosis in AP patients [3,4]. Gut barrier permeability is increased, followed by bacterial translocations and subsequent bacterial infections [5,6]. Overuse of antibiotics, longer hospitalizations, bacteria translocations and frequent invasive procedures predispose AP patients to infections, especially antimicrobial resistant bacterial infections [7,8]. *Acinetobacter baumannii*, a Gram-negative bacillus with strong ability to acquire drug resistance owing to the plasticity of its genome, is widely distributed in nature. In recent years, *A. baumannii* becomes one of life-threatening bacteria in clinical settings, causing aspiration pneumonia, soft tissue infections and bacteremia which is difficult to treat due to its endless capacity to acquire more serious resistance from overuse of antibiotics [9]. The propensity of *A. baumannii* to be carbapenem-resistant *A. baumannii* (CRAB) presents a great therapeutic challenge, and the treatments with overuse of antibiotics for AP patients in China which ranked 1st in the world may be the main cause of reason for CRAB infections [10]. In 2017, the World Health Organization global priority list of pathogens ranked CRAB into the highest priority category [11]. The features of CRAB threat

* Corresponding author. Department of Gastroenterology, Xiangya Hospital, Central South University, Xiangya road, 410008, Changsha, China
E-mail addresses: wudikdfz@qq.com (D. Wu), 3234996544@qq.com (Y. Huang), 1037702710@qq.com (J. Ding), jiayan1992@outlook.com (Y. Jia), lhmxz@126.com (H. Liu), xiaojiexj@163.com (J. Xiao), pengjie2014@csu.edu.cn (J. Peng).

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include (1) increasing worldwide spread of CRAB in the past decade, (2) limitation of safe and effective antibiotics, and (3) high infection-related mortality rates [12–14]. Carbapenem used to be the most effective antibiotic to treat *A. baumannii* infections, but increasing resistance rates to carbapenem leaves colistin and tigecycline as the last therapeutic options. In China, polymyxin was uncommon and costly, and drug-resistance rate of tigecycline against CRAB infections was significantly rising in recent years [14].

Most studies have only focused on the pancreatic infections and not extrapancreatic infections which are possibly as a result of bacterial translocation from the gut, and occur frequently in the course of acute pancreatitis [15–17]. In developing countries, such as China and India, multidrug-resistant *A. baumannii* causes a much higher proportion of nosocomial infections in AP patients [6,7,16,18–20]. However, the clinical outcomes and associated risk factors of mortality remains unclear in AP patients complicated with CRAB infections, especially in China.

Hence better methods for the prevention and treatment of CRAB infections are essential, which could improve the outcomes of AP patients. Herein, our innovative study focused on AP patients complicated with CRAB infections aims to: 1) assess the impact of CRAB infections on AP patients; 2) evaluate the role of MOF in CRAB infected AP patients; 3) determine the independent risk factors of overall mortality among AP patients; 4) calculate drug-resistance rates of CRAB strains which may shed light on the anti-infective therapy.

2. Method

2.1. Study design and setting

Our retrospective study was carried out at Xiangya Hospital, a 3500-bed tertiary-care teaching hospital, and Third Xiangya Hospital, an 1800-bed tertiary-care teaching hospital, both affiliated to Central South University, in Changsha, Hunan, China. Clinical and microbiological data of AP patients with and without CRAB, from March 1st, 2016 to August 1st, 2020, were collected from the electronic patient record system. A retrospective case-control study with a case-control ratio of 1:1 was performed. Controls were matched to the cases according to: 1) gender, 2) age and 3) bedside index for severity in AP (BISAP) score at admission. If multiple control patients fitted the inclusion criteria, the one who had been admitted closest to the case patient, was retained. Controls with missing data were excluded. Clinical characteristics included classification as well as etiology of AP, age, sex, referral timing from other hospitals, length of hospitalization, initial antibiotic therapy for CRAB infections. As Fig. S1 shows, mortality rates, risk factors of overall mortality and drug resistance rates of CRAB strains were evaluated.

2.2. Ethics

Informed consents were waived for all enrolled patients due to the retrospective nature. Ethical approval of this retrospective study was granted by the Institutional Review Board of Xiangya Hospital (no.202107130) and Third Xiangya Hospital (no.21087).

2.3. Patients and managements

At the admission, all patients were assessed and managed via the multi-disciplinary team according to the latest international guidelines [21]. The diagnosis and classification of AP were in accordance with the Revised Atlanta Classification [22]. Fine-needle aspiration was never used for diagnosis of 'suspect' infected pancreatic necrosis among AP patients in either hospital. The antibiotic regimen we recorded was the initial therapy (3–5 days) after obtaining the identification and drug-resistant test of CRAB strains. If the patient conditions worsened, we changed or combined new antibiotics as soon as possible. Carbapenem (extended infusion and high-dose) were regarded as an appropriate choice.

2.4. Definitions

Criteria of etiology were as follows: (1) hypertriglyceridemia: triglycerides more than 5.6 mmol/l without other clear pathogeny; (2) gallstone: based on radiological evidence of abdominal ultrasonography and increased serum alanine aminotransferase levels; (3) alcoholism: regular drink of alcohol (>50 g/day) [23]. Sites of infections were diagnosed based on the clinical manifestations and positive results of specimens according to the criteria of the Centers for Disease Control [14]. BISAP score was calculated to evaluate the patients' conditions at the admission [24]. Organ failure was defined for the three organ systems (respiratory, renal, or cardiovascular) according to modified Marshall score [25]. MOF was defined as at least two organs experiencing failure.

2.5. Microbiology

Identification of CRAB was performed via the Vitek-2 system (bioMe'rieux, Marcy L'etoile, France). Minimum inhibitory concentration was performed via micro broth dilution method. Carbapenem-resistance was defined as resistant to either meropenem or imipenem (minimal inhibitory concentration >2 μg/ml) [14]. Drug resistance of polymyxin was not analyzed, as our hospitals did not perform the drug resistance tests of polymyxin until 2020 and only 5 of 61 patients in our study took this test. Intermediate susceptibility in vitro was considered resistance.

2.6. Statistical analysis

Continuous variables, expressed using medians with standard deviations, and categorical variables, described in absolute numbers and in percentages, were compared with Student's t-test or Mann–Whitney *U* test and the $\chi 2$ test or Fisher exact tests, respectively. The binary logistic regression analysis was used to determine independent risk factors of mortality. Odds ratio (OR) and 95% confidence interval (CI) were calculated to evaluate the associations. *P*-value < 0.05 (two-tailed) was considered statistically significant. Statistical analyses were performed using SPSS 24.0 (IBM SPSS Statistics, IBM Corp., Armonk, NY, US).

3. Results

3.1. Patient characteristics

Approximately 3565 AP patients were admitted to our hospitals during the 5-year study period, including 2423 mild AP, 952 moderately severe AP and 190 severe AP patients. 61 AP patients with CRAB infections, and a matched number (n = 61) of without CRAB infections served as control (Table 1). Seventy-eight patients (63.9%) were male with a mean age of 48.9 + 12.6 years. Hypertriglyceridemia (n = 46, 37.7%) was the leading etiology, followed by gallstone (n = 42, 34.4%), alcoholism (n = 8, 6.6%) and others (n = 26, 21.3%). There were 104 patients (85.2%) referred from other hospitals with 2 days delay since the onset of AP. Hemorrhage, intestinal leakage and pancreatic fistula, as major complications, occurred in 30 (24.6%), 12 (9.8%) and 12 (9.8%) patients, respectively. There were 17 patients with positive CRAB cultures from multiple sites. Lung was the most common site of infections (n = 37), followed by pancreas (peri) (n = 36), bloodstream (n = 6)

Table 1
Clinical characteristics and comparison between with and without CRAB infections.

Characteristics	Total	Without CRAB (n = 61)	With CRAB (n = 61)	*P*-value
Age, years (mean ± SD)	48.9 ± 12.6	47.8 ± 13.3	48.9 ± 12.6	0.61
Sex, n (%)				0.06
Male	78 (63.9)	34 (55.7)	44 (72.1)	
Female	44 (36.1)	27 (44.3)	17 (27.9)	
Etiology, n (%)				0.50
Hypertriglyceridemia	46 (37.7)	19 (31.1)	27 (44.3)	
Gallstone	42 (34.4)	23 (37.7)	19 (31.1)	
Alcoholism	8 (6.6)	4 (6.6)	4 (6.6)	
Others	26 (21.3)	15 (24.6)	11 (18.0)	
Classification of AP, n (%)				0.59
Moderately severe AP	59 (48.4)	28 (45.9)	31 (50.8)	
Severe AP	63 (51.6)	33 (54.1)	30 (49.2)	
Therapeutic treatments, n (%)				0.09
Conservative treatment	19 (15.6)	10 (16.4)	9 (14.8)	
Interventional treatment	42 (34.4)	27 (44.3)	15 (24.6)	
Surgical treatment	61 (50.0)	24 (39.3)	37 (60.7)	
Referred patient, n (%)	104 (85.2)	51 (83.6)	53 (86.9)	0.61
BISAP score at admission (mean ± SD)	2.0 ± 0.8	1.8 ± 0.7	2.1 ± 0.8	0.20
MOF, n (%)	27 (22.1)	7 (11.5)	20 (32.8)	0.01*
ICU stays, days (mean ± SD)	14.5 ± 18.1	5.3 ± 8.5	23.7 ± 20.3	<0.01*
Hospitalization, days (mean ± SD)	37.3 ± 23.9	27.4 ± 16.4	47.2 ± 26.1	<0.01*
Major complications, n (%)				
Hemorrhage	30 (24.6)	8 (13.1)	22 (36.1)	0.01*
Intestinal leakage	12 (9.8)	3 (4.9)	9 (14.8)	0.13
Pancreatic fistula	12 (9.8)	4 (6.6)	8 (13.1)	0.36
Mortality	44 (36.1)	14 (23.0)	30 (49.2)	<0.01*

**P* values are statistically significant between with and without CRAB infections group.

and biliary tract (n = 3). CRAB patients showed significantly longer hospitalization and intensive care unit (ICU) stays (47.2 vs. 27.4 days, $P < 0.01$; 23.7 vs. 5.3 days, $P < 0.01$, respectively). MOF (32.8% vs. 11.5%, $P = 0.01$) and hemorrhage (36.1% vs. 13.1%, $P = 0.01$) were more frequently occurred in the CRAB group than without CRAB group. The mortality rate was significantly higher among patients with CRAB than without CRAB infections (49.2% vs. 23.0%, $P < 0.01$).

3.2. Comparison between CRAB infected AP patients with and without MOF

In Table 2, MOF only occurred in the severe AP patients ($P < 0.01$) with significant longer ICU stays compared to the contrast group (33.1 vs. 19.1 days, $P = 0.01$). Patients in the MOF group had higher rates of pancreatic fistula (30.0% vs. 4.9%, $P = 0.02$) compared with patients without MOF. Overall mortality rate was significantly higher in patients with MOF (90.0% vs. 29.3%, $P < 0.01$). There was no significant difference between the two groups in the antibiotic therapy ($P = 0.33$).

3.3. Risk factors of mortality

In Table 3, variables that had statistical significance ($P < 0.05$) for association with mortality included age >50 years old ($P = 0.01$), MOF ($P < 0.01$), CRAB infections ($P < 0.01$) and hemorrhage ($P < 0.01$) in the univariate analysis. In the multivariate analysis, MOF (OR = 21.49, 95%CI = 5.26–87.80, $P < 0.01$), CRAB infections (OR = 3.58, 95%CI = 1.24–10.37, $P = 0.02$) and hemorrhage (OR = 3.70, 95%CI = 1.21–11.28, $P = 0.02$) were independent risk factors of overall mortality.

3.4. Drug-resistance of CRAB strains

Drug-resistance rates of all the 82 CRAB strains to 10 of 11 antibiotics were more than 60% except for tigecycline (28%). The antibiotic resistance rates and distributions of CRAB isolates *were* shown in Table 4.

4. Discussion

A. baumannii has a strong ability to remain activated for several months, which presents us a great challenge to eliminate transmission after nosocomial colonization. With rising rates of resistances, CRAB infections have progressively become more lethal resulting in longer hospitalizations, greater health care costs, and higher mortality rates in recent years [26]. The predisposing factors of CRAB infections were reported as previous *A. baumannii* colonization, exposure to antimicrobial drugs as well as invasive procedures such as ventilator-assisted respiration and central venous catheterization, and prognosis was worse in critically ill patients [27]. According to a previous preliminary study, *A. baumannii* infections were significantly associated with mortality among severe AP patients [18]. To our knowledge, this is the first case-control study for specifically investigating the impact of CRAB on AP patients. We firstly found that CRAB infections were associated with higher mortality, longer hospitalization and ICU stays, MOF as well as hemorrhage.

According to Zhu et al., hypertriglyceridemia (37.7%) and gallstone (34.4%) were two leading etiologies in our study which may be attributed to unhealthy lifestyle, such as spicy food and high-fat diet in China [6,28]. In line with Tian et al., our study proved that CRAB was an emerging cause of pneumonia and pancreatic infections, influencing clinical outcomes of AP patients with overall mortality up to 49.2% [18]. In our research, we also found that MOF was strongly related to the occurrence of CRAB infections which indicated MOF, especially respiratory failure, and might induce ventilator-associated CRAB pneumonia. According to Grag et al., MOF, as a fatal co-morbidity, was associated with CRAB infections which significantly increased the mortality from 29.3% to 90.0% among CRAB infected AP patients (with and without MOF) [29]. On the one hand, all the MOF patients, among CRAB group, were categorized into severe AP which may need longer ICU stays with larger amount of antibiotics that subsequently enhance the risk of drug-resistance. On the other hand, severe infections could result in multiple organs injuries leading to MOF. Unsurprisingly,

Table 2
Clinical characteristics and comparison between with and without MOF among 61 CRAB infected AP patients.

Characteristics	Without MOF (n = 41)	With MOF (n = 20)	*P*
Age, years (mean ± standard deviation)	48.4 ± 13.5	50.1 ± 10.8	0.65
Sex, n (%)			0.14
Male	27 (65.9)	17 (85.0)	
Female	14 (34.1)	3 (15.0)	
Etiology, n (%)			0.92
Hypertriglyceridemia	17 (41.5)	10 (50.0)	
Gallstone	13 (31.7)	6 (30.0)	
Alcoholism	3 (7.3)	1 (5.0)	
Others	8 (19.5)	3 (15.0)	
Classification of AP, n (%)			<0.01*
Moderately severe AP	31 (75.6)	0	
Severe AP	10 (24.4)	20 (100.0)	
CRAB bloodstream infection, n (%)	2 (4.9)	4 (20.0)	0.08
Referred patient, n (%)	35 (85.4)	18 (90.0)	0.92
BISAP score at admission (mean ± SD)	2.0 ± 0.8	2.2 ± 0.8	0.57
Antibiotic therapy, n (%)			0.33
Carbapenem (high dose, extended infusion)	11 (26.8)	6 (30.0)	
Cefoperazone-sulbactam	11 (26.8)	3 (15.0)	
Tigecycline	3 (7.3)	2 (10.0)	
Quinolone	0	1 (5.0)	
Carbapenem and tigecycline	10 (24.4)	7 (35.0)	
Cefoperazone-sulbactam and tigecycline	3 (7.3)	0	
Polymyxins and fosfomycin	2 (4.9)	0	
Carbapenem and sulphonamides	1 (2.4)	1 (5.0)	
Intervention for pancreatic necrosis, n (%)			0.15
Conservative therapy	6 (14.6)	3 (15.0)	
Only percutaneous catheter drainage	3 (7.3)	3 (15.0)	
Only endoscopic transluminal drainage	5 (12.2)	4 (20.0)	
Percutaneous catheter drainage step-up to minimal access retroperitoneal necrosectomy	17 (41.5)	3 (15.0)	
Percutaneous catheter drainage step-up to video-assisted retroperitoneal debridement	5 (12.2)	3 (15.0)	
Endoscopic transluminal drainage step-up to endoscopic transluminal necrosectomy	0	2 (10.0)	
Step-up to open necrosectomy	2 (4.9)	0	
Open necrosectomy	3 (7.3)	2 (10.0)	
ICU stays, days (mean ± SD)	19.1 ± 19.3	33.1 ± 19.6	0.01*
Hospitalization, days (mean ± SD)	48.4 ± 24.6	45.0 ± 29.6	0.66
Major complications, n (%)			
Hemorrhage	11 (26.8)	11 (55.0)	0.05
Intestinal leakage	4 (9.8)	5 (25.0)	0.23
Pancreatic fistula	2 (4.9)	6 (30.0)	0.02*
Mortality	12 (29.3)	18 (90.0)	<0.01*

**P* values are statistically significant between survival and mortality group.

Table 3
Univariate and multivariate analysis of risk factors for mortality in AP patients.

Variable	Survival (n = 78)	Mortality (n = 44)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	*P*	OR (95% CI)	*P*
Age ≥50 years old, n (%)	27 (34.6)	26 (59.1)	2.73 (1.28–5.84)	0.01*	2.17 (0.78–6.04)	0.14
Male, n (%)	51 (65.4)	27 (61.4)	0.84 (0.39–1.81)	0.66	–	–
Referral from other hospitals, n (%)	67 (85.9)	37 (84.1)	0.87 (0.31–2.43)	0.79	–	–
MOF, n (%)	4 (5.1)	23 (52.3)	20.26 (6.31–65.10)	<0.01*	21.49 (5.26–87.80)	<0.01*
CRAB infections, n (%)	31 (39.7)	30 (68.2)	3.25 (1.49–7.09)	<0.01*	3.58 (1.24–10.37)	0.02*
Hemorrhage, n (%)	9 (11.5)	21 (47.7)	7.00 (2.81–17.43)	<0.01*	3.70 (1.21–11.28)	0.02*

**P* values are statistically significant.

multivariate analysis revealed that both CRAB infections and MOF were independent risk factors of overall mortality. MOF outperformed CRAB infections as the strongest prognostic factor of mortality which may be more focused in the further study. Similarly with Ning et al., we also demonstrated that hemorrhage was an independent risk factor of mortality [16].

In our study, lung was the most common site of CRAB infections which enhanced the importance to strengthen the management of extra-pancreatic infections in the course of AP [30]. Some researches, of extra-pancreatic infections developing before pancreatic infections, supported the hypothesis that extra-pancreatic infections may be the origin of pancreatic infections, but this was still not verified in our study for the lacking of precise chronological records [15]. The relationship between pancreatic and extra-pancreatic infections is of great interest to be investigated in the future.

We found that drug-resistance rates of all CRAB strains to 10 of 11 common antibiotics were more than 60% except for tigecycline (28%) among AP patients. Our findings were similar with earlier studies in developing country reporting that the drug resistance situation was worst with CRAB [7,16,18]. Tigecycline, the most active in vitro measurements, is active against CRAB with long half-life as well as post-antibiotic effects and a high volume of distribution except for bloodstream. Unfortunately, increased use of tigecycline as ultimate choice was associated with the emergence of tigecycline-resistance which indicated tigecycline may be used

Table 4
Resistance rates of 82 CRAB strains to 11 antibiotics according to the different sites of infections.

Antimicrobial	Lung (n = 37)	Pancreas (peri) (n = 36)	Bloodstream (n = 6)	Biliary tract (n = 3)	Total strains (n = 82)
Amoxicillin-clavulanate	37 (100)	36 (100)	6 (100)	3 (100)	82 (100)
Amikacin	35 (95)	35 (97)	5 (83)	3 (100)	78 (95)
Ciprofloxacin	37 (100)	36 (100)	6 (100)	3 (100)	82 (100)
Gentamicin	35 (95)	34 (94)	6 (100)	3 (100)	78 (95)
Levofloxacin	36 (97)	36 (100)	6 (100)	3 (100)	81 (99)
Sulfamethoxazole	24 (65)	28 (78)	5 (83)	1 (33)	58 (71)
Tobramycin	34 (92)	32 (89)	5 (83)	3 (100)	74 (90)
Piperacillin-tazobactam	37 (100)	36 (100)	6 (100)	3 (100)	82 (100)
Cefoperazone-sulbactam	23 (62)	25 (69)	5 (83)	3 (100)	56 (68)
Ceftriaxone	37 (100)	36 (100)	6 (100)	3 (100)	82 (100)
Tigecycline	10 (27)	10 (28)	3 (50)	0 (0)	23 (28)

Notes: Values are no. (%) of resistant strains, except as indicated.

under rigorous management [14]. Based on this finding, enhancing administration of antibiotics should be advocated to reduce the overuse of broad-spectrum antibiotics, especially carbapenem on the emergency. Prophylactic antibiotic therapy which may be the most possible reason for high drug-resistance rates, was not recommended for the prevention of infectious complication in AP according to the latest guideline [5]. Due to high referral rates and deficiency of pre-admission data, we could not analyze risk factors associated with occurrence of CRAB infections among AP patients. Only 5 patients in our study did the drug-resistance test of polymyxin with all susceptible results. Polymyxin is less frequently used (favorable against bacteremia) and known to have the activity against CRAB. It was proven effective even in critical situations, but showed nephrotoxicity, so it may be used with caution among AP patients with renal failure [31].

Extended infusion and high dose of carbapenems can maximize time and concentration above minimum inhibitory concentration, resulted in prosperity outcomes [14,17]. For its part, leveraging this nature can result in a well treatment efficacy in low-minimum inhibitory concentration CRAB strains. These data are of particular importance to make up the lack of therapeutic options for CRAB infections among AP patients. In the era of carbapenem-resistance, clinicians may explore novel combination therapies in their local medical centers instead of creating 'new' antibiotics.

Preventions are better and more important than treatments for CRAB infections among AP patients. CRAB screening at admission of ICU is considered to be an effective method for surveillance of CRAB colonization which is recommended in institutions with high prevalence rates of CRAB, thus to guide clinicians to avoid overuse of antibiotics in AP patients complicated with 'suspected' infections when microbiologic results are pending [14,32,33].

There are some limitations in our study. Firstly, our study is limited to unincluded variables, potential deficient data and selection biases by its retrospective nature. We tried to use the latest precise definition to decrease the selection biases. However, there was a borderline different distribution of sex between case and control group which was one of selection biases with no significance impact on the results via univariate analyses. Most patients have no details of prophylactic use of antibiotics before admission. Prospective studies, which focus on surveillance of CRAB, are required to verify our findings with larger sample size. Secondly, the percentage of MOF was significantly higher in the CRAB group. The MOF caused by the severity of AP itself could not be ignored. Patients with more severe category of AP could suffer from more exposure to antibiotics, which would possibly result in drug-resistance. There may be a mutual cause and effect relationship between MOF and CRAB infections which may be difficult to correct in multivariable analysis. Thirdly, we chose the AP patients without CRAB infections as control group, so our study could only assess the hazard of CRAB infections on the AP patients instead of patients suffered from other bacterial infections which need to be further verified. Finally, we hope to encourage other institutions to design novel researches to identify the phenotypic and genotypic characteristics of CRAB, underlying mechanisms of resistances and appropriate combination therapies on their local areas.

5. Conclusion

Given significantly higher mortality and possibility of MOF observed in patients with CRAB infections, further efforts and effective strategies to prevent against CRAB infections are urgently required. CRAB infections combined with MOF could significantly increase the mortality. MOF, CRAB infections and hemorrhage were independent risk factors of mortality in AP patients. CRAB strains were most frequently found in lung with high resistance rates to common antibiotics except for tigecycline. Antibiotic therapy should be prescribed based on the drug-susceptibility results.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pan.2021.12.004.

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