Annals of Clinical Microbiology and Antimicrobials

RESEARCH

Open Access

Mortality and exacerbations in bronchiectasis patients with carbapenem-resistant *Pseudomonas aeruginosa* isolation: a long-term retrospective cohort study

Jibo Sun[1,2], Qingqing Jia[1,2], Wenting Lv[1,2], Shijie Zhang[1,2], Sitong Liu[1,2], Dongguang Wang[1,2], Lian Wang[1,2], Xiang Tong[1,2], Jiehao Chen[3], Xiaoting Chen[3], Yongjiang Tang[1,2*] and Hong Fan[1,2*]

Abstract

Background Few studies have investigated the impact of carbapenem-resistant Pseudomonas aeruginosa (CRPA) on long-term outcomes in bronchiectasis. This study aimed to analyze acute exacerbations and mortality in bronchiectasis patients with CRPA isolation.

Methods This retrospective study included bronchiectasis patients with PA-positive cultures from January 1, 2014, to July 31, 2023, at West China Hospital of Sichuan University. PA was isolated from sputum or bronchoalveolar lavage fluid (BALF) and classified into CRPA and non-CRPA groups based on antimicrobial susceptibility testing. Multivariate logistic regression was used to assess risk factors for acute exacerbations, while multivariate Cox regression identified independent risk factors for all-cause and cause-specific mortality.

Results Among 564 patients with PA-positive isolates, 143 (25.36%) harbored CRPA strains. CRPA isolation was associated with an increased risk of acute exacerbations (adjusted odds ratio [aOR] 2.072, p = 0.001), while antibiotic treatment reduced the risk of exacerbations (aOR 0.439, p = 0.011). CRPA isolation was an independent risk factor for all-cause (adjusted hazard ratio [aHR] 1.488, p = 0.031) and cause-specific mortality (aHR 1.882, p = 0.010). The 1-, 3-, 5-, and 7-year cause-specific survival rates in the CRPA group were 88.6%, 79.8%, 73.2%, and 68.0%, respectively, versus 95.4%, 91.0%, 85.6%, and 81.8% in the non-CRPA group (p = 0.001).

Conclusion CRPA isolation was significantly associated with an increasing risk of acute exacerbations, overall and cause-specific mortality. These findings underscored the urgent need to strengthen antibiotic stewardship to reduce the emergence of CRPA and to implement early detection and targeted management strategies to improve outcomes for patients with CRPA.

Keywords Bronchiectasis, CRPA, Exacerbations, Mortality

*Correspondence:
Yongjiang Tang
lauler@163.com
Hong Fan
fanhong@scu.edu.cn
Full list of author information is available at the end of the article

Introduction

Bronchiectasis is a common respiratory disease characterized by chronic cough, purulent sputum, and hemoptysis [1]. The prevalence of bronchiectasis in Europe in 2013 was 566 cases per 100,000 residents [2], while in China it can be as high as 1200 per 100,000 [3], making it a significant and increasingly serious economic health burden [4, 5]. The main causes of bronchiectasis include congenital, idiopathic, post-infectious, immune deficiency, chronic obstructive pulmonary disease (COPD), connective tissue diseases, ciliary dysfunction, and allergic bronchopulmonary aspergillosis (ABPA) [6, 7]. A large study in Europe showed that 38.1% were classified as idiopathic [1], while idiopathic was most common etiology in China [8, 9].

Exacerbation was a risk factor for repeated hospitalizations, decreased lung function, and increased mortality [10, 11], and it was also a major contributor to the socioeconomic burden of bronchiectasis [12].

Pseudomonas aeruginosa (PA) is an important pathogen in bronchiectasis and associated with worse outcomes [13]. The prevalence of PA in bronchiectasis ranges from 15 to 25% [14–16]. Previous studies have shown that PA isolation is an independent risk factor for acute exacerbations, deteriorating lung function, frequent hospitalizations, and increased mortality in bronchiectasis [13, 17]. Although PA eradication is considered first-line treatment, the rising resistance of PA, particularly the emergence of CRPA, poses significant challenges to these eradication efforts [18, 19]. CRPA is a global threat, complicating treatment and markedly increasing the mortality risk due to its robust biofilm formation [20, 21]. A recent systematic review reported that the mortality for CRPA bloodstream infections approached 35% [22]. WHO has therefore designated CRPA as a Critical Priority [23].

However, there are currently few studies on the long-term outcomes of CRPA isolation in bronchiectasis. Hence, this study aimed to assess acute exacerbations and mortality in bronchiectasis patients with CRPA isolation.

Methods

Study design and population

This retrospective cohort study was conducted at West China Hospital of Sichuan University from January 1, 2014, to July 31, 2023. The study included hospitalized patients diagnosed with bronchiectasis and PA isolated from sputum or bronchoalveolar lavage fluid (BALF). Bronchiectasis was defined according to Hill et al. [7]. Inclusion criteria: a) Age 18 years or older; b) Qualified sputum and BALF samples; c) Isolation of PA from sputum or BALF. The following exclusion criteria were applied: a) Lost to follow-up; b) Patients with concomitant tuberculosis, lung cancer or invasive pulmonary Aspergillosis; c) Acute asthma attack; d) COPD with FEV1 percentage of predicted (FEV1% predicted) < 50; e) absence of chest high-resolution computed tomography (HRCT).

Pathogens isolation

Either deep sputum or BALF was collected. Sputum with < 10 epithelial cells/low-power field [lpf] and > 25 white blood cells/lpf was considered qualified [24]. The samples were inoculated onto blood agar plates and chocolate agar plates containing vancomycin (Autobio, China) and incubated at 35 ℃ in a 5% CO_2 environment for 24–48 h. For bacterial identification, the VITEK-2 automated system (bioMérieux, France) was used with GN67 and XN04 cards. In cases requiring further confirmation, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS, Bruker, Germany) was applied. Antimicrobial susceptibility testing (AST) was initially performed using the VITEK-2 system. For validation, additional methods including broth microdilution (using Kangtai reagents), E-test (Autobio or Kangtai reagents), and disk diffusion (Oxoid, UK) were used. CRPA was defined based on resistance to carbapenem antibiotics according to CLSI (Clinical and Laboratory Standards Institute) guidelines [25]. PA-R is defined as resistance to any of the following antimicrobial agents: antipseudomonal quinolones, cephalosporins, penicillin plusβ-lactamase inhibitors, carbapenems, aminoglycosides, monobactams, and polymyxins [26]. Multidrug resistant (MDR) and extensively drug-resistant (XDR) were defined by Magiorakos et al. [27]. The identified pathogens included PA, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Escherichia coli*, Aspergillus, and others. Mixed isolated pathogens referred to the isolation of PA combined with any of the above microorganisms. Patients were divided into CRPA group and the non-CRPA group based on drug susceptibility testing.

Data collection

Clinical data was extracted from the electronic medical records of hospitalized patients. The data included demographic characteristics (age, sex), comorbidities (e.g., hypertension, diabetes, COPD, asthma), hemoptysis, bronchial artery embolization (BAE), antibiotic treatment, length of hospital stay, laboratory values, and microbiology. We gathered patient information via telephone and outpatient visits until July 31, 2024, or until lost to follow-up or death.

Outcomes and definitions

The primary outcomes were all-cause and cause-specific mortality. Secondary outcome was acute exacerbations

(≥ 2 times within the first-year post-discharge). Acute exacerbations were defined as described by Hill et al. [28]. All-cause mortality included deaths from any cause during the follow-up period. Cause-specific mortality was defined as death resulting from bronchiectasis and its complications, including massive hemoptysis, severe pneumonia, and respiratory failure. The definitions of COPD and asthma were based on previous studies [29, 30].

Statistical analysis

Statistical analyses were performed using R (version 4.2.3) and Stata software (version 17.0). The Shapiro–Wilk test assessed normality of continuous variables. Data with a normal distribution were presented as mean ± standard deviation, while non-normally distributed data were presented as median and interquartile range (IQR). Continuous variables following a normal distribution were analyzed using the t-test; otherwise, the Wilcoxon rank-sum test was applied. Categorical variables were analyzed using the chi-square test. Multivariate logistic regression was used to identify risk factors for acute exacerbations. Kaplan–Meier survival curves were performed to compare the overall and cause-specific survival rates between the CRPA and non-CRPA. Cox proportional hazards regression was employed to determine the risk factors for all-cause mortality and cause-specific mortality. A p-value <0.05 was considered statistically significant.

Results

Patient characteristics

A total of 564 hospitalized PA-positive patients were included in the study, with 143 in the CRPA group and 421 in the non-CRPA group (Supplementary Fig. 1). Median age of patients was 62.55 years, with 41.31% being male. Comorbidities, including hypertension, diabetes, COPD, malignancies, asthma, and others, showed no significant differences between two groups. Hemoptysis, BAE, and antibiotic treatments were also comparable. However, the CRPA group had higher white blood cell (WBC) (7.44 vs. 6.75 $\times 10^9$/L, $p= 0.007$) and absolute neutrophil count (ANC) (5.60 vs. 4.44 $\times 10^9$/L, $p< 0.001$), but lower absolute eosinophil count (AEC) (0.09 vs. 0.11 $\times 10^9$/L, $p= 0.020$) and hemoglobin ($p <0.001$). The median length of hospital stay was longer for CRPA isolation (14 vs. 11 days, $p< 0.001$), and acute exacerbations were more frequent (55.94% vs. 39.67%, $p= 0.001$) (Table 1).

Microbiology

Pathogens were isolated from sputum in 411 patients (72.87%), with a CRPA incidence of 25.36%. PA-R was identified in 333 patients (59.04%). MDR-PA was present in 121 (21.45%), significantly higher in the CRPA group (59.44% vs. 8.55%, $p< 0.001$). *Klebsiella pneumoniae* was isolated in 27 patients (4.79%), with a significantly higher prevalence in the CRPA group (8.39% vs. 3.56%, $p= 0.019$).

Acinetobacter baumannii was found in 30 patients (5.32%), with a higher rate in the CRPA group (13.99% vs. 2.38%, $p< 0.001$). Aspergillus was present in 25 patients (4.43%) without significant group differences ($p =0.873$). Mixed isolated pathogens occurred in 89 patients (15.78%), more frequently in the CRPA group (23.78% vs. 13.06%, $p= 0.002$). Detailed characteristics are presented in Table 2.

Risk factors for acute exacerbations

A multivariate logistic regression analysis was conducted, including variables such as sex, age, body mass index (BMI), diabetes, hypertension, COPD, malignant tumors, hemoptysis, BAE, antibiotic treatment, CRPA isolation, mixed isolated pathogens, lengths of hospital stay, WBC, ANC, AEC, PLT, and HB. The results showed that CRPA isolation was associated with approximately double the risk of acute exacerbations compared to non-CRPA (adjusted odds ratio [aOR] 2.072, 95% confidence interval [CI] [1.366–3.144], $p= 0.001$). Conversely, antibiotic treatment was associated with a significantly reduced risk of exacerbations (aOR 0.439, 95% CI[0.233–0.829], $p= 0.011$) (Fig. 1).

Overall and cause-specific survival probability

During a median follow-up of 39 months (IQR 16–68), 152 patients (26.96%) died, with detailed characteristics provided in Supplementary Table 1. Kaplan–Meier curves indicated that the overall survival rate in the CRPA group was significantly lower than that in the non-CRPA group ($p <0.0001$) (Supplementary Fig. 2). Specifically, the 1-year, 3-year, 5-year, and 7-year survival rates for the CRPA group were 81.8%, 67.9%, 58.8%, and 53.1%, respectively, compared to 91.7%, 81.9%, 75.8%, and 68.6% for the non-CRPA group. A total of 82 patients (14.56%) experienced cause-specific mortality, with characteristics detailed in Supplementary Table 2. The CRPA group also demonstrated significantly lower survival rates ($p =0.001$) (Supplementary Fig. 3). The 1-year, 3-year, 5-year, and 7-year survival rates for the CRPA group were 88.6%, 79.8%, 73.2%, and 68.0%, respectively, while the non-CRPA group had survival rates of 95.4%, 91.0%, 85.6%, and 81.8%.

Risk factors for mortality

A multivariate Cox proportional hazards regression analysis was performed to identify risk factors for

Table 1 The characteristics of included patients

Variables	All patients (N = 564)	Non-CRPA (N = 421)	CRPA (N = 143)	p-value
Demographics				
Age (years), median (IQR)	62.55 (52.50–70.95)	61.50 (52.40–70.20)	64.30 (52.80–73.60)	0.117
Male	233 (41.31%)	168 (39.90%)	65 (45.45%)	0.244
BMI (kg/m^2)	21.49 (19.20–23.79)	21.50 (19.11–23.83)	21.48 (19.32–23.30)	0.932
Comorbidities				
Hypertension	104 (18.44%)	73 (17.34%)	31 (21.68%)	0.248
Diabetes	70 (12.41%)	46 (10.93%)	24 (16.78%)	0.066
COPD	116 (20.57%)	79 (18.76%)	37 (25.87%)	0.069
Malignant tumors	36 (6.38%)	24 (5.70%)	12 (8.39%)	0.255
Asthma	32 (5.67%)	20 (4.75%)	12 (8.39%)	0.104
Connected tissue disease	23 (4.08%)	16 (3.80%)	7 (4.90%)	0.567
Gastro-oesophageal reflux disease	22 (3.90%)	18 (4.28%)	4 (2.80%)	0.430
Hemoptysis	139 (24.65%)	106 (25.18%)	33 (23.08%)	0.614
BAE	58 (10.28%)	47 (11.16%)	11 (7.69%)	0.238
Antibiotic treatment	515 (91.31%)	389 (92.40%)	126 (88.11%)	0.116
Laboratory Values				
WBC (× 10^9/L), median (IQR)	6.92 (5.31–8.99)	6.75 (5.17–8.74)	7.44 (5.84–9.90)	0.007
ANC (× 10^9/L), median (IQR)	4.73 (3.28–6.52)	4.44 (3.11–6.12)	5.60 (4.04–8.13)	< 0.001
AEC (× 10^9/L), median (IQR)	0.11 (0.05–0.21)	0.11 (0.06–0.22)	0.09 (0.02–0.18)	0.020
PLT (× 10^9/L), median (IQR)	201 (149.5- 263)	199 (149–259)	213 (154–288)	0.152
Hemoglobin (g/L), median (IQR)	118 (106–132)	120 (109–133)	113 (99–127)	< 0.001
Lengths of hospital stay, median (IQR)	12 (9- 15.5)	11 (9–14)	14 (10–20)	< 0.001
Acute exacerbations*	247 (43.79%)	167 (39.67%)	80 (55.94%)	0.001

IQR: interquartile range; BMI: body mass index; COPD: chronic obstructive pulmonary disease; BAE: bronchial artery embolization; WBC: white blood cell; ANC: absolute neutrophil count; AEC: absolute eosinophil count; PLT: platelet count; * ≥ 2 times within the first year post-discharge

Table 2 Microbiological characteristics

Variables	All patients (N = 564)	Non-CRPA (N = 421)	CRPA (N = 143)	p-value
Culture specimen				0.543
Sputum	411 (72.87%)	304 (72.21%)	107 (74.83%)	
Bronchoalveolar lavage fluid	153 (27.13%)	117 (27.79%)	36 (25.17%)	
Bacteria				
PA-R	333 (59.04%)	190 (45.13%)	143 (100.00%)	–
MDR-PA	121 (21.45%)	36 (8.55%)	85 (59.44%)	< 0.001
XDR-PA	7 (1.24%)	0 (0.00%)	7 (4.90%)	–
Klebsiella pneumoniae	27 (4.79%)	15 (3.56%)	12 (8.39%)	0.019
Acinetobacter baumannii	30 (5.32%)	10 (2.38%)	20 (13.99%)	< 0.001
Escherichia coli	14 (2.48%)	9 (2.14%)	5 (3.50%)	0.367
Other	9 (1.60%)	8 (1.90%)	1 (0.70%)	0.322
Aspergillus	25 (4.43%)	19 (4.51%)	6 (4.20%)	0.873
Mixed isolated pathogens	89 (15.78%)	55 (13.06%)	34 (23.78%)	0.002

PA, *Pseudomonas aeruginosa*; CRPA: carbapenem-resistant *Pseudomonas aeruginosa*; R: resistant; MDR: multi-drug resistant; XDR: extensive-drug resistant; ESBL: extended-spectrumβ-lactam; CRAB: carbapenem-resistant *Acinetobacter baumannii*; MRSA: methicillin-resistant *Staphylococcus aureus*

all-cause and cause-specific mortality. Each additional year of age increased the risk of all-cause mortality by 3.3% (adjusted hazard ratio [aHR] 1.033, 95% CI [1.018–1.048], p < 0.001). CRPA isolation raised all-cause mortality risk by 46.7% (aHR 1.488, 95% CI [1.037–2.136], p = 0.031), and higher ANC was also

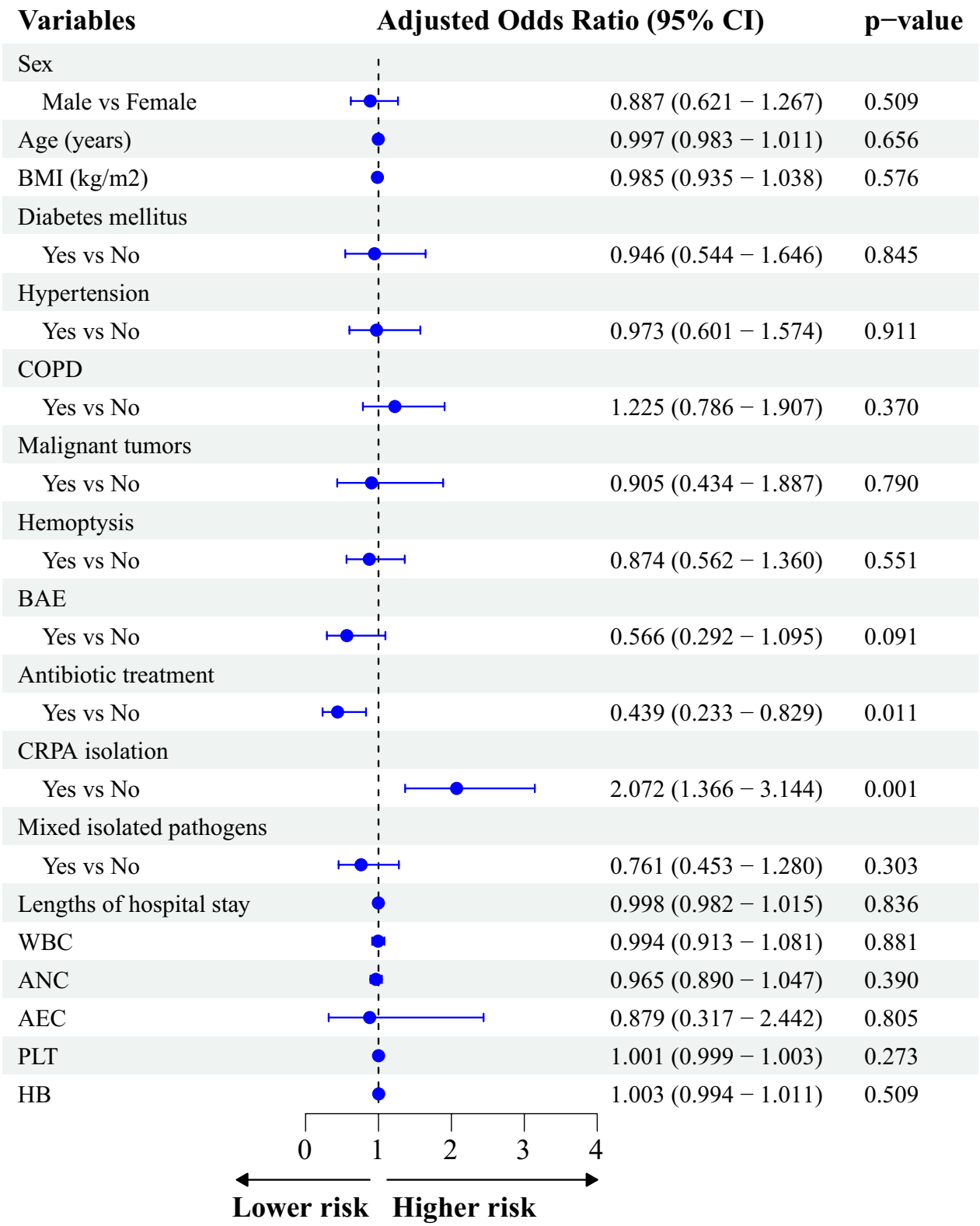

Fig. 1 Multivariate logistic regression of risk factors for acute exacerbations

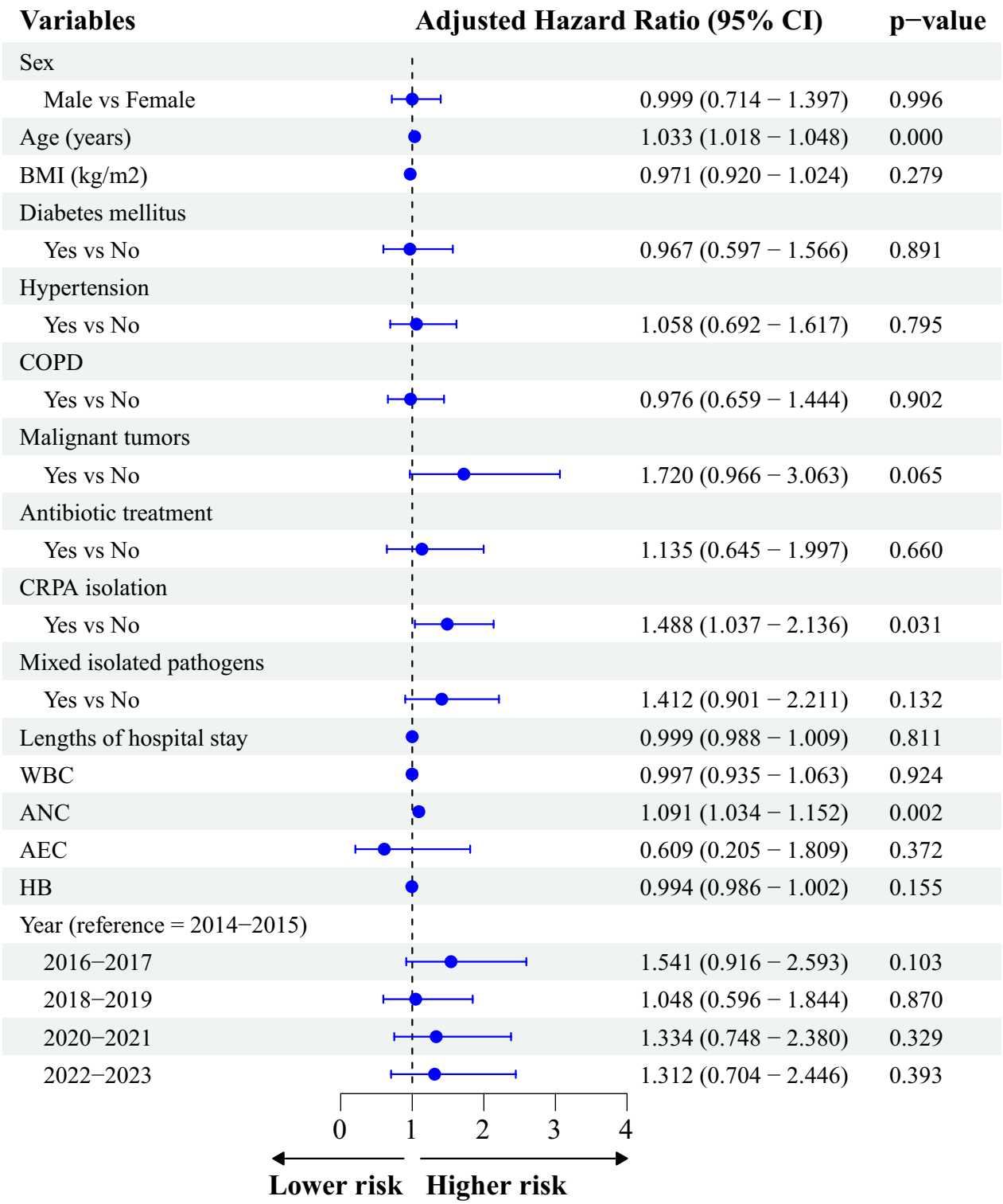

Fig. 2 Multivariate Cox proportional hazards regression of risk factors for all-cause mortality

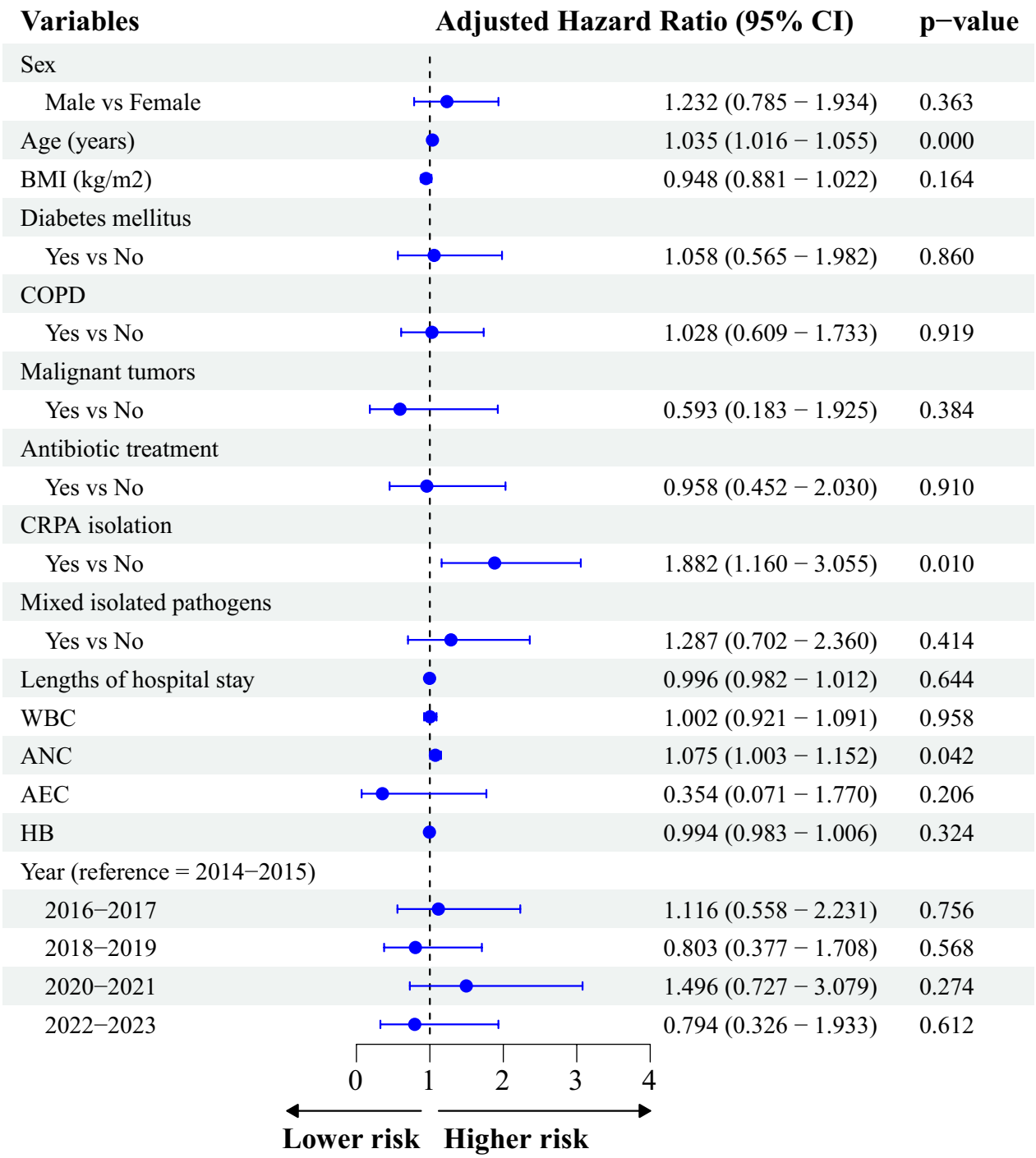

Fig. 3 Multivariate Cox proportional hazards regression of risk factors for cause-specific mortality

associated with increased risk (aHR 1.091, 95% CI [1.034–1.152], p = 0.002) (Fig. 2). For cause-specific mortality, age increased risk (aHR 1.035, 95% CI [1.016–1.055], p < 0.001).CRPA isolation nearly doubled the risk (aHR 1.882, 95% CI [1.160–3.055], p =

0.010), and higher ANC also significantly elevated risk (aHR 1.075, 95% CI [1.003–1.152], p = 0.042) (Fig. 3).

Discussion

In this study, we analyzed acute exacerbations and mortality in bronchiectasis patients with CRPA isolation. The key findings are as follows. First, isolation of CRPA emerged as a significant risk factor for acute exacerbations in patients with bronchiectasis. Second, patients with CRPA isolation exhibited markedly lower survival rates compared to those without CRPA. Finally, CRPA isolation was associated with a notable increase in the risk of both all-cause and cause-specific mortality.

To our knowledge, this is the first study to investigate both all-cause and cause-specific mortality in bronchiectasis patients with CRPA isolation. The long-term follow-up and large sample size contribute to the robustness of the findings, providing valuable insights for clinical decision-making. Our results indicate that CRPA isolation is an independent risk factor for acute exacerbations, all-cause mortality, and cause-specific mortality in patients with bronchiectasis compared to non-CRPA. These findings suggest that CRPA can complicate and exacerbate the condition of bronchiectasis patients, with survival analysis further supporting this conclusion. Previous studies have already confirmed that PA is closely associated with repeated hospitalizations, frequent exacerbations, declining lung function, and poorer quality of life in patients with bronchiectasis [13, 14, 16]. Our study confirmed that patients with CRPA isolation face approximately double the risk of acute exacerbations compared to those with non-CRPA, underscoring the significant impact of CRPA on disease progression. This highlights the urgency of early detection and aggressive management of CRPA to prevent frequent exacerbations and related complications.

Inflammation and infection are important factors in worsening the condition of patients [31]. Chronic bacterial infections and persistent airway inflammation form a vicious cycle that impairs bronchial mucociliary clearance and leads to structural lung damage. This cycle exacerbates bronchiectasis, potentially resulting in further deterioration and even death[32].PA-induced chronic infections and increased inflammation are key contributors to the poor prognosis in bronchiectasis patients [17]. The ability of PA to form biofilms is a critical factor in its persistence and pathogenicity in bronchiectasis. Biofilms shield bacteria from immune attacks and enhance antibiotic resistance, complicating treatment efforts and contributing to disease and mortality [33, 34]. The rapid global rise of CRPA, with resistance rates of 10% to 50%, poses a major public health threat [35]. It was likely that the biofilm formation by PA associated with carbapenem resistance may contribute to enhanced virulence and increased mortality [21].

There was still a controversy regarding the association between PA isolation and mortality in bronchiectasis [13–16]. However, our study demonstrated that CRPA significantly increased the risk of both all-cause and cause-specific mortality. This discrepancy with earlier studies may stem from their failure to differentiate between CRPA and non-CRPA, potentially underestimating the contribution of CRPA to mortality. In contrast, by specifically classifying PA into CRPA and non-CRPA groups, our study more clearly highlighted the strong association between CRPA and increased mortality. This finding aligns with other studies indicating that CRPA is associated with higher mortality rates, particularly in critically ill patients [36]. A multicenter study reported a 30-day mortality rate of 32.8% for CRPA bloodstream infections, with an attributable mortality of 19%, demonstrating that the risk of death was nearly three times higher than in the non-CRPA group [37]. Furthermore, our study identified age and ANC as significant predictors of both all-cause and cause-specific mortality. Advanced age is linked to a decline in immune function and an increase in comorbidities, while ANC reflects the patients'immune status and their ability to respond to infections. Previous studies have demonstrated that peripheral neutrophils play a fundamental role in chronic airway inflammation and are key predictors of acute exacerbations in bronchiectasis patients [38–40]. Additionally, neutrophil elastase levels in sputum are critical indicators of lung function decline and exacerbations in these patients [41, 42].

This study has several limitations. First, despite including a large sample size, the retrospective nature of the study resulted in a 10.8% loss to follow-up, which may impact the study results. Therefore, prospective investigations are crucial for further validation. Second, we used two or more acute exacerbations within the first year post-discharge as a surrogate endpoint rather than specific counts of exacerbations to minimize recall bias. Third, antibiotic treatment was only recorded during hospitalization, which means that antibiotic use during follow-up was not included in the analysis, potentially underestimating the impact of antibiotic therapy. Fourth, due to the isolation of multiple pathogens, specifying the antibiotic treatment regimens proved challenging; therefore, we only recorded whether antibiotic treatment was administered. Consequently, ongoing research remains essential. Fifth, a notable percentage of patients exhibit both bronchiectasis and COPD. Although patients with severe COPD were excluded from the study, the progression of COPD over time may have exaggerated the mortality attributed to bronchiectasis. Therefore, future

research should prioritize prospective multicenter cohort studies to validate the long-term outcomes of CRPA in bronchiectasis. Additionally, it is essential to explore effective treatment strategies and preventive measures to enhance clinical outcomes for patients with CRPA.

Conclusions

The prevalence of CRPA isolation was high in hospitalized patients with bronchiectasis. CRPA isolation significantly increased the risk of acute exacerbations, all-cause and cause-specific mortality. Additionally, advanced age and elevated ANC were identified as important predictors of mortality. The CRPA group had lower all-cause and cause-specific survival rates. The study emphasizes the urgent need to enhance antibiotic management to reduce the emergence of CRPA and to implement early detection and targeted management strategies to improve outcomes for patients.

Further prospective, multi-center research is warranted to validate these findings and develop effective treatment strategies that could improve the clinical outcomes in bronchiectasis patients with CRPA isolation.

Abbreviations

ABPA	Allergic bronchopulmonary aspergillosis
AEC	Absolute eosinophil count
aHR	Adjusted hazard ratio
ANC	Absolute neutrophil count
aOR	Adjusted odds ratio
BAE	Bronchial artery embolization
BALF	Bronchoalveolar lavage fluid
BMI	Body mass index
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
CRPA	Carbapenem-resistant Pseudomonas aeruginosa
FEV1	Forced expiratory volume in 1 s
HB	Hemoglobin
HRCT	High-resolution computed tomography
IQR	Interquartile ranges
MDR	Multi-drug resistant
PA	Pseudomonas aeruginosa
PLT	Platelet count
WBC	White blood cell
XDR	Extensively drug-resistant

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12941-025-00798-4.

Supplementary material 1: Table 1. The characteristics of all-cause mortality patients.

Supplementary material 2: Table 2. The characteristics of cause-specific mortality patients.

Supplementary material 3: Fig. 1. Flow chart of the selected population.

Supplementary material 4: Fig. 2. Kaplan–Meier curves revealed overall survival probability.

Supplementary material 5: Fig. 3. Kaplan–Meier curves showed cause-specific survival probability.

Acknowledgements

None.

Author contributions

Jibo Sun, Qingqing Jia, Wenting Lv, Jiehao Chen, Xiaoting Chen, Shijie Zhang, Xiang Tong and Sitong Liu collected the clinical data. Jibo Sun, Qingqing Jia, Yongjiang Tang and Hong Fan contributed to interpretation of results and revision of the manuscript. Jibo Sun, Qingqing Jia, Wenting Lv, Dongguang Wang, Lian Wang and Yongjiang Tang wrote the manuscript. Yongjiang Tang and Hong Fan supervised the conceptualization, writing, and review process of the article. All authors read and approved the final manuscript.

Funding

This work was supported by 1.3.5 project for disciplines of excellence-Clinical Research Incubation Project, West China Hospital, Sichuan University (2019HXFH008).

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee on Biomedical Research at the West China Hospital of Sichuan University (No. 2022455). Informed consent was also waived by the ethics committee of the West China Hospital.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Pulmonary and Critical Care Medicine, West China Hospital, Sichuan University, Chengdu 610041, China. [2]State Key Laboratory of Respiratory Health and Multimorbidity, Chengdu 610041, China. [3]Animal Laboratory Center, West China Hospital, Sichuan University, Chengdu 610041, China.

Received: 19 January 2025 Accepted: 23 April 2025
Published online: 06 May 2025

References

1. Chalmers JD, Polverino E, Crichton ML, Ringshausen FC, De Soyza A, Vendrell M, Burgel PR, Haworth CS, Loebinger MR, Dimakou K, et al. Bronchiectasis in Europe: data on disease characteristics from the European Bronchiectasis registry (EMBARC). Lancet Respir Med. 2023;11(7):637–49.
2. Quint JK, Millett ER, Joshi M, Navaratnam V, Thomas SL, Hurst JR, Smeeth L, Brown JS. Changes in the incidence, prevalence and mortality of bronchiectasis in the UK from 2004 to 2013: a population-based cohort study. Eur Respir J. 2016;47(1):186–93.
3. Lin JL, Xu JF, Qu JM. Bronchiectasis in China. Ann Am Thorac Soc. 2016;13(5):609–16.
4. Feng J, Sun L, Sun X, Xu L, Liu L, Liu G, Wang J, Gao P, Zhan S, Chen Y, et al. Increasing prevalence and burden of bronchiectasis in urban Chinese adults, 2013–2017: a nationwide population-based cohort study. Respir Res. 2022;23(1):111.
5. Roberts JM, Goyal V, Kularatna S, Chang AB, Kapur N, Chalmers JD, Goeminne PC, Hernandez F, Marchant JM, McPhail SM. The economic burden of bronchiectasis: a systematic review. Chest. 2023;164(6):1396–421.
6. Gao YH, Guan WJ, Liu SX, Wang L, Cui JJ, Chen RC, Zhang GJ. Aetiology of bronchiectasis in adults: a systematic literature review. Respirology (Carlton, Vic). 2016;21(8):1376–83.

7. Hill AT, Sullivan AL, Chalmers JD, De Soyza A, Elborn SJ, Floto AR, Grillo L, Gruffydd-Jones K, Harvey A, Haworth CS, et al. British thoracic society guideline for bronchiectasis in adults. Thorax. 2019;74(Suppl 1):1–69.
8. Guan WJ, Gao YH, Xu G, Lin ZY, Tang Y, Li HM, Lin ZM, Zheng JP, Chen RC, Zhong NS. Aetiology of bronchiectasis in Guangzhou, southern China. Respirology. 2015;20(5):739–48.
9. Qi Q, Wang W, Li T, Zhang Y, Li Y. Aetiology and clinical characteristics of patients with bronchiectasis in a Chinese Han population: a prospective study. Respirology (Carlton, Vic). 2015;20(6):917–24.
10. Chalmers JD, Aliberti S, Filonenko A, Shteinberg M, Goeminne PC, Hill AT, Fardon TC, Obradovic D, Gerlinger C, Sotgiu G, et al. Characterization of the "Frequent Exacerbator Phenotype" in bronchiectasis. Am J Respir Crit Care Med. 2018;197(11):1410–20.
11. De Angelis A, Johnson ED, Sutharsan S, Aliberti S. Exacerbations of bronchiectasis. Eur Respir Rev. 2024;33(173): 240085.
12. Chalmers JD, Mall MA, McShane PJ, Nielsen KG, Shteinberg M, Sullivan SD, Chotirmall SH. A systematic literature review of the clinical and socioeconomic burden of bronchiectasis. Eur Respir Rev. 2024;33(173): 240049.
13. Dicker AJ, Lonergan M, Keir HR, Smith AH, Pollock J, Finch S, Cassidy AJ, Huang JTJ, Chalmers JD. The sputum microbiome and clinical outcomes in patients with bronchiectasis: a prospective observational study. Lancet Respir Med. 2021;9(8):885–96.
14. Araújo D, Shteinberg M, Aliberti S, Goeminne PC, Hill AT, Fardon TC, Obradovic D, Stone G, Trautmann M, Davis A, et al. The independent contribution of Pseudomonas aeruginosa infection to long-term clinical outcomes in bronchiectasis. Eur Respir J. 2018;51(2):1701953.
15. Wang R, Ding S, Lei C, Yang D, Luo H. The contribution of *Pseudomonas aeruginosa* infection to clinical outcomes in bronchiectasis: a prospective cohort study. Ann Med. 2021;53(1):459–69.
16. Pieters A, Bakker M, Hoek RAS, Altenburg J, van Westreenen M, Aerts J, van der Eerden MM. Predicting factors for chronic colonization of *Pseudomonas aeruginosa* in bronchiectasis. Eur J Clin Microbiol Infect Dis. 2019;38(12):2299–304.
17. Finch S, McDonnell MJ, Abo-Leyah H, Aliberti S, Chalmers JD. A Comprehensive analysis of the impact of *Pseudomonas aeruginosa* colonization on prognosis in adult bronchiectasis. Ann Am Thorac Soc. 2015;12(11):1602–11.
18. Polverino E, Goeminne PC, McDonnell MJ, Aliberti S, Marshall SE, Loebinger MR, Murris M, Cantón R, Torres A, Dimakou K, et al. European Respiratory Society guidelines for the management of adult bronchiectasis. Eur Respir J. 2017;50(3):1700629.
19. Conceicao M, Shteinberg M, Goeminne P, Altenburg J, Chalmers JD. Eradication treatment for *Pseudomonas aeruginosa* infection in adults with bronchiectasis: a systematic review and meta-analysis. Eur Respir Rev. 2024;33(171): 230178.
20. Reyes J, Komarow L, Chen L, Ge L, Hanson BM, Cober E, Herc E, Alenazi T, Kaye KS, Garcia-Diaz J, et al. Global epidemiology and clinical outcomes of carbapenem-resistant *Pseudomonas aeruginosa* and associated carbapenemases (POP): a prospective cohort study. The Lancet Microbe. 2023;4(3):e159–70.
21. Ma Y, Aung TT, Lakshminarayanan R, Chua SL. Biofilm formation and virulence potential of carbapenem-resistant *Pseudomonas aeruginosa*. Lancet Microbe. 2023;4(7): e489.
22. Hassoun-Kheir N, Guedes M, Ngo Nsoga MT, Argante L, Arieti F, Gladstone BP, Kingston R, Naylor NR, Pezzani MD, Pouwels KB, et al. A systematic review on the excess health risk of antibiotic-resistant bloodstream infections for six key pathogens in Europe. Clin Microbiol Infect. 2023. https://doi.org/10.1016/j.cmi.2023.09.001.
23. WHO. Media Center. WHO publishes list of bacteria for which new antibiotics are urgently needed. World Health Organization: Feb 27, 2017. https://www.who.int/news/item/27-02-2017who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed. Accessed 24 Aug 2024.
24. Wolff BJ, Bramley AM, Thurman KA, Whitney CG, Whitaker B, Self WH, Arnold SR, Trabue C, Wunderink RG, McCullers J, et al. Improved detection of respiratory pathogens by use of high-quality sputum with TaqMan array card technology. J Clin Microbiol. 2017;55(1):110–21.
25. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. 35th ed. Wayne: CLSI; 2025.
26. Gao YH, Guan WJ, Zhu YN, Chen RC, Zhang GJ. Antibiotic-resistant *Pseudomonas aeruginosa* infection in patients with bronchiectasis: prevalence, risk factors and prognostic implications. Int J Chron Obstruct Pulmon Dis. 2018;13:237–46.
27. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, Harbarth S, Hindler JF, Kahlmeter G, Olsson-Liljequist B, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect. 2012;18(3):268–81.
28. Hill AT, Haworth CS, Aliberti S, Barker A, Blasi F, Boersma W, Chalmers JD, De Soyza A, Dimakou K, Elborn JS, et al. Pulmonary exacerbation in adults with bronchiectasis: a consensus definition for clinical research. Eur Respir J. 2017;49(6):1700051.
29. Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, Bourbeau J, Han MK, Martinez FJ, Montes de Oca M, et al. Global initiative for chronic obstructive lung disease 2023 report: GOLD executive summary. Eur Respir J. 2023;61(4):2300239.
30. Reddel HK, Bateman ED, Becker A, Boulet LP, Cruz AA, Drazen JM, Haahtela T, Hurd SS, Inoue H, de Jongste JC, et al. A summary of the new GINA strategy: a roadmap to asthma control. Eur Respir J. 2015;46(3):622–39.
31. Choi H, Ryu S, Keir HR, Giam YH, Dicker AJ, Perea L, Richardson H, Huang JTJ, Cant E, Blasi F, et al. Inflammatory molecular endotypes in bronchiectasis: a european multicenter cohort study. Am J Respir Crit Care Med. 2023;208(11):1166–76.
32. Cole PJ. Inflammation: a two-edged sword–the model of bronchiectasis. Eur J Respir Dis. 1986;147:6–15.
33. Ghosh M, Raghav S, Ghosh P, Maity S, Mohela K, Jain D. Structural analysis of novel drug targets for mitigation of *Pseudomonas aeruginosa* biofilms. FEMS Microbiol Rev. 2023. https://doi.org/10.1093/femsre/fuad054.
34. Mejía-Manzano LA, Vázquez-Villegas P, Prado-Cervantes LV, Franco-Gómez KX, Carbajal-Ocaña S, Sotelo-Cortés DL, Atehortúa-Benítez V, Delgado-Rodríguez M, Membrillo-Hernández J. Advances in material modification with smart functional polymers for combating biofilms in biomedical applications. Polymers. 2023;15(14):3021.
35. Karampatakis T, Antachopoulos C, Tsakris A, Roilides E. Molecular epidemiology of carbapenem-resistant *Pseudomonas aeruginosa* in an endemic area: comparison with global data. Eur J Clin Microbiol Infect Dis. 2018;37(7):1211–20.
36. Saravanan M, Belete MA, Arockiaraj J. Carbapenem-resistant *Pseudomonas aeruginosa* in intensive care units increase mortality as an emerging global threat. Int J Surg. 2023;109(4):1034–6.
37. Falcone M, Tiseo G, Carbonara S, Marino A, Di Caprio G, Carretta A, Mularoni A, Mariani MF, Maraolo AE, Scotto R, et al. 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(12):2059–69.
38. Boyton RJ, Altmann DM. Bronchiectasis: current concepts in pathogenesis, immunology, and microbiology. Annu Rev Pathol. 2016;11:523–54.
39. Fuschillo S, De Felice A, Balzano G. Mucosal inflammation in idiopathic bronchiectasis: cellular and molecular mechanisms. Eur Respir J. 2008;31(2):396–406.
40. Martinez-García M, Olveira C, Girón R, García-Clemente M, Máiz-Carro L, Sibila O, Golpe R, Méndez R, Rodríguez Hermosa JL, Barreiro E, et al. Peripheral neutrophil-to-lymphocyte ratio in bronchiectasis: a marker of disease severity. Biomolecules. 2022;12(10):1399.
41. Shoemark A, Cant E, Carreto L, Smith A, Oriano M, Keir HR, Perea L, Canto E, Terranova L, Vidal S, et al. A point-of-care neutrophil elastase activity assay identifies bronchiectasis severity, airway infection and risk of exacerbation. Eur Respir J. 2019;53(6):1900303.
42. Chalmers JD, Moffitt KL, Suarez-Cuartin G, Sibila O, Finch S, Furrie E, Dicker A, Wrobel K, Elborn JS, Walker B, et al. Neutrophil elastase activity is associated with exacerbations and lung function decline in bronchiectasis. Am J Respir Crit Care Med. 2017;195(10):1384–93.

Publisher's Note