Clinical Interventions in Aging

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ORIGINAL RESEARCH

Risk Factors, Pathogen Distribution, and Treatment Strategies for Mortality in Elderly Patients with Pulmonary Bacterial Infections

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Background: Elderly patients are particularly vulnerable to pulmonary infections due to immune system decline and comorbidities. This study aims to evaluate the distribution of bacterial pathogens, patterns of antimicrobial resistance, medication strategies, and risk factors associated with mortality in elderly patients with pulmonary infections.

Methods: Data were collected from electronic medical records, encompassing demographic information, clinical characteristics, laboratory results, treatment strategies, and outcomes. Risk factors associated with mortality were identified using the Least Absolute Shrinkage and Selection Operator regression model and were subsequently validated through multivariable logistic regression. Differences between groups were assessed using the independent *t*-test or Mann–Whitney *U*-test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables.

Results: 201 patients were included with 70.6% being male. Clinical improvement was observed in 124 patients, while 77 patients died. Gram-negative bacteria were identified as the most common pathogens, with *Acinetobacter baumannii* (27.5%), *Klebsiella pneumoniae* (23.5%), and *Pseudomonas aeruginosa* (13.2%) being the most frequently isolated species. Notably, 66.0% of the bacterial strains were classified as multidrug-resistant. Furthermore, 65.7% of the patients received combination therapy. Seven risk factors associated with mortality were identified. Body mass index emerged as a protective factor, whereas length of duration, gastrointestinal bleeding, respiratory failure, bacteremia, myocardial infarction, and mechanical ventilation significantly increased the risk of death.

Conclusion: Respiratory failure, mechanical ventilation, gastrointestinal bleeding, extended hospitalization, bacteremia, myocardial infarction, and malnutrition were key risk factors related to mortality in elderly patients with pulmonary infections. Early identification and intervention targeting these risk factors are crucial for improving clinical outcomes.

Keywords: elderly patients, pulmonary infection, multidrug-resistant bacteria, MDRB, risk factors

Introduction

Lower respiratory tract infections have consistently ranked among the leading global causes of mortality over the past two decades, presenting a significant public health challenge. In 2021, these infections were the fifth leading cause of death worldwide, resulting in 2.5 million fatalities, according to the World Health Organization (WHO).[1] Among these infections, bacterial lung infections, particularly pneumonia, are of major concern. The increasing prevalence of antimicrobial resistance (AMR), especially among Gram-negative bacteria (GNB), significantly limits treatment options and contributes to elevated morbidity and mortality, particularly in elderly patients who are already vulnerable due to physiological and comorbidity-related factors.[2,3]

Elderly populations are particularly vulnerable to respiratory infections due to immunosenescence and the high prevalence of comorbidities such as diabetes, COPD, cardiovascular diseases, and chronic kidney disease.[4–7] These factors,

https://doi.org/10.2147/CIA.S571155
Received: 29 September 2025
Accepted: 19 January 2026
Published: 4 February 2026

combined with inadequate nutrition, reduced mobility, and weakened functional capacity, significantly increase susceptibility to infection, leading to prolonged hospitalization and poorer clinical outcomes.[8] The presence of multidrug-resistant (MDR) pathogens, including *Klebsiella pneumoniae* (Kp), *Pseudomonas aeruginosa* (Pa), and *Acinetobacter baumannii* (Ab), is frequently observed in elderly patients, presenting significant challenges for effective antimicrobial therapy.[9,10] Despite the known convergence of these risk factors, quantitative assessments in elderly patients remain scarce.

The global demographic shift towards an aging population exacerbates these concerns. By 2050, the proportion of individuals aged 65 years and older is expected to double, thereby intensifying the burden of respiratory infections.[11] This situation is further complicated by age-related alterations in pharmacokinetics and pharmacodynamics, which heighten the risk of adverse drug reactions and diminish treatment efficacy in elderly patients.[12,13] Notably, deaths attributed to AMR have increased by over 80% among adults aged 70 and older, highlighting the intersection of aging and drug-resistant infections as a critical public health challenge.[14]

In light of the challenges posed by MDR pathogens in elderly patients with pulmonary infections, there is limited integration of AMR profiles with mortality predictors in this population. Most existing risk models focus primarily on clinical factors, but do not adequately account for the impact of AMR on patient outcomes. This study aims to address this gap by constructing a mortality risk model that integrates both clinical factors and AMR profiles of key bacterial pathogens. This study was conducted at a tertiary care hospital in Beijing. The institution serves a large and diverse elderly patient population, many of whom have multiple comorbidities, providing a unique perspective for understanding the impact of MDR pathogens in this high-risk group. Given the significant burden of AMR in this region and the diversity of pathogens present, the findings of this study are particularly relevant for healthcare settings that deal with similar challenges in elderly care. The Least Absolute Shrinkage and Selection Operator (LASSO) regression model was chosen to manage collinearity and effectively select key mortality predictors, ensuring a robust and interpretable model. Unlike traditional tools such as CURB-65 and PSI, which mainly focus on clinical variables, our approach incorporates microbial resistance patterns, offering a more comprehensive risk assessment and potential for more personalized treatment strategies for elderly patients with pulmonary infections.

Methods

Study Design

This retrospective observational study was conducted at the Chinese PLA General Hospital in Beijing, China, through a review of electronic medical records, in accordance with the standards of ICD-10 (International Statistical Classification of Diseases and Related Health Problems, Tenth Revision). The study adhered to the principles outlined in the World Medical Assembly Declaration of Helsinki and received approval from the Ethics Committee of the Chinese PLA General Hospital (No. S2024-394-01).

Inclusion and Exclusion Criteria

Patients who met the following criteria were included in the study: (a) aged ≥65 years; (b) diagnosed with pulmonary infection based on clinical presentation, imaging findings, and positive sputum culture for bacterial pathogens; (c) antimicrobial susceptibility data were available for the identified pathogens; (d) received antimicrobial treatment for more than 24 hours; and (e) patients discharged between March and September 2023.

Patients were excluded if: (f) the primary site of infection was not pulmonary; (g) the patient was discharged mid-treatment for personal reasons and incapable to evaluate treatment outcomes. More screening details are provided in Figure 1.

Data Collection

Data were collected from the hospital's electronic medical records and encompassed the following variables. Demographic Information: Age, sex, and body mass index (BMI); Clinical Characteristics: Length of hospital stay, ICU admission, mechanical ventilation usage, and the presence of comorbidities (eg, hypertension, diabetes, COPD, coronary artery disease); Laboratory Results: White blood cell count (WBC), C-reactive protein (CRP), interleukin-6 (IL-

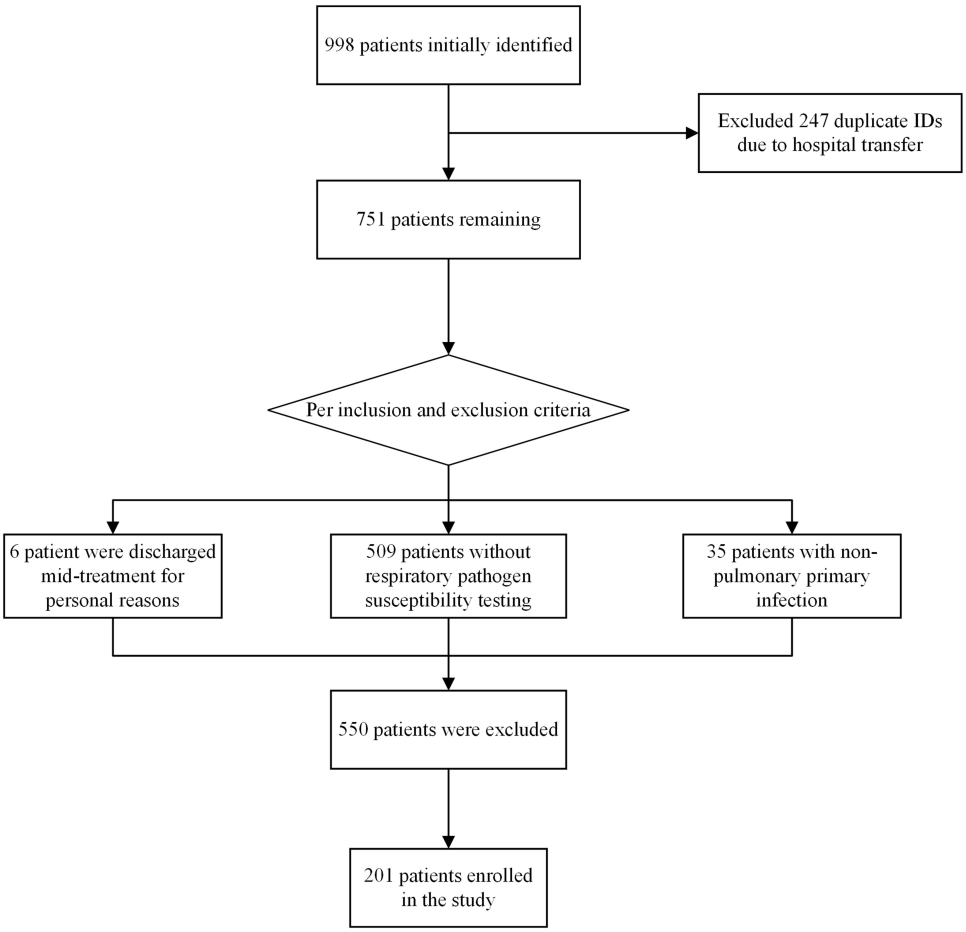

Figure 1 Flowchart of patient inclusion and exclusion.

6), platelet count (PLT), hemoglobin (Hb), serum albumin (Alb), total bilirubin (TBIL), serum creatinine (Cr), and respiratory antimicrobial susceptibility testing (AST) results; Treatment Data: Antibiotics used, duration of therapy, and the application of mechanical ventilation. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score was used to assess the severity of illness in ICU patients. For pathogens, only the first isolate from each source in the same patient was included in the analysis.

Definitions

This study incorporated two primary outcomes: mortality and clinical improvement. Clinical improvement was defined as either a reduction in or the complete resolution of clinical signs and symptoms, as assessed by the attending clinician. Multidrug-resistant bacteria (MDRB) were defined as bacteria resistant to more than two classes of antibacterial agents. AST (Broth microdilution method) was conducted according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI) or relevant published literature that identifies breakpoints.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on the data distribution. Categorical variables were presented as frequencies and percentages. Differences between groups were assessed using the independent *t*-test or Mann–Whitney *U*-test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables.

To identify variables associated with mortality, the LASSO regression model was utilized to address collinearity and overfitting. Variables with more than 20% missing data were excluded from the analysis, while those with less than 20%

missing data were imputed using multiple imputation. The LASSO model was validated through 10-fold cross-validation, with the regression coefficients penalized based on the λ value, which was chosen at the minimum λ (λ min) for optimal model performance.

Following the LASSO selection, variables with a $P < 0.05$ in univariate analysis were incorporated into the multivariate logistic regression analysis. The odds ratio (OR) and 95% confidence interval (95% CI) were calculated for each variable to evaluate their association with mortality. The multivariate logistic regression analyses were two-tailed, and statistical significance was defined as a $P < 0.05$. LASSO regression was performed using Anaconda version 3.0.2, while other statistical analyses were conducted using SPSS version 27.0. The detailed code implementation of the LASSO regression is provided in the Supplementary Materials.

Results

Population Characteristics

A total of 201 patients were included in the study, with a median age of 83 years (IQR: 76 to 90). Among the patients, 124 experienced clinical improvements, while 77 died. The cohort comprised 142 males (70.6%) and 59 females (29.4%). The median length of hospitalization was 36 days (IQR: 19 to 70), with 39.8% of patients requiring admission to the ICU. Additionally, 147 patients were infected with MDRB, and 132 patients received combination therapy. The most common comorbidities included hypertension (63.7%), renal insufficiency (38.9%), cerebrovascular diseases (37.8%), and diabetes (37.3%). The characteristics of the patients are summarized in Table 1.

Table 1 Characters of Patients

Characters	Improvement (n=124)	Death (n=77)	*P*-value
Male	83 (67)	59 (77)	0.143
Age (years)	82 (74, 87)	88 (77, 92)	**0.003**
Length of hospital stay (days)	30 (18, 57.5)	45 (20, 120)	**0.010**
Apache II score	17.85 ± 4.68	23.86 ± 5.9	**<0.001**
BMI (kg/m^2)	22.71 ± 3.97	21.09 ± 3.24	**0.019**
WBC ($\times 10^9/L$)	8.25 (5.98, 11.31)	9.04 (6.32, 13.41)	0.095
N ($\times 10^9/L$)	0.75 (0.68, 0.84)	0.81 (0.74, 0.87)	**0.005**
CRP (mg/dL)	2.27 (0.76, 5.78)	3.79 (1.56, 8.34)	**0.022**
IL6 (pg/mL)	22.06 (8.48, 48.35)	30.10 (11.41, 86.56)	**0.044**
PLT ($\times 10^9/L$)	196 (153.75, 241.25)	191 (120, 252)	0.363
HB (g/L)	108.08 ± 22.75	104.91 ± 22.2	0.333
Alb (g/L)	33.4 (29.7, 36.23)	31.7 (28.6, 34.9)	**0.049**
TBIL (μmol/L)	7.3 (4.88, 12.05)	8.4 (5, 12.9)	0.347
Cr (μmol/L)	78 (60.6, 122.55)	81.6 (59.2, 124.7)	0.890
Diabetes	45 (36)	30 (39)	0.704
ICU admission	52 (42)	28 (36)	0.433
Arrhythmia	20 (16)	8 (10)	0.253
Myocardial infarction	10 (8)	14 (18)	**0.032**
Bacteremia	9 (7)	16 (21)	**0.005**
Alzheimer	11 (9)	13 (17)	0.089
COPD	3 (2)	7 (9)	**0.046**
Atrial fibrillation	10 (8)	10 (13)	0.257
Liver insufficiency	29 (23)	27 (35)	0.073
Renal insufficiency	39 (32)	39 (51)	**0.007**
Cardiac insufficiency	26 (21)	30 (39)	**0.006**
Hypertension	78 (63)	50 (65)	0.771
Coronary artery disease	58 (47)	34 (44)	0.717

(*Continued*)

Table 1 (Continued).

Characters	Improvement (n=124)	Death (n=77)	*P*-value
Gastrointestinal bleeding	17 (14)	31 (40)	**<0.001**
Malignant tumor	27 (22)	17 (22)	0.960
Cerebrovascular diseases	49 (40)	27 (35)	0.527
Pleural effusion	23 (19)	23 (30)	0.063
Respiratory failure	25 (20)	44 (57)	**<0.001**
Stomach catheter	71 (57)	70 (91)	**<0.001**
MDRB	40 (32)	50 (65)	**<0.001**
Co-infected with			
None	44 (36)	12 (16)	**0.003**
Fungi	58 (47)	47 (61)	**0.049**
SARS-Cov-2	9 (7.3)	8 (10)	0.438
Both	16 (13)	10 (13)	0.986
Combination therapy	70 (57)	62 (81)	**<0.001**
Mechanical Ventilation	7 (5.6)	24 (31)	**<0.001**

Notes: Mean ± SD, median (IQR) or n (%); statistical significance is defined as $P < 0.05$, which is bolded in the table.
Abbreviations: IQR, interquartile range; SD, standard deviation; APACHE II, acute physiology and chronic health evaluation II; BMI, body mass index; WBC, white blood cell; N, neutrophils; CRP, C-reaction protein; IL6, interleukin 6; PLT, platelet; HB, hemoglobin; Alb, albumin lac lactate; TBIL, total bilirubin; Cr, creatinine; ICU, intensive care unit; COPD, chronic obstructive pulmonary disease; MDRB, multi-drug-resistant bacteria; SARS-Cov-2, severe acute respiratory syndrome coronavirus 2.

Pathogen Identification and Distribution

A total of 371 bacterial strains were isolated from these patients, with 245 (66.0%) classified as MDRB. In bacteremia cases, MDRB accounted for 88% of the infections. The most common GNB identified were Ab (27.5%), Kp (23.5%), and Pa (13.2%). Gram-positive bacteria (GPB) accounted for a smaller proportion, with *Staphylococcus aureus* (Sa) (3.5%) being the most frequently isolated pathogen.

In addition to bacterial pathogens, 164 fungal strains, primarily from the *Candida species* (87.8%). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in 43 patients. The distribution of these pathogens is presented in Figure 2.

The AMR profiles of common pathogens are detailed in Figure 3, which covers 35 antimicrobial agents or β-lactamase inhibitors. This figure highlights the elevated resistance rates to various antibiotics, particularly among Ab and Kp, which demonstrate significant resistance to carbapenems, cephalosporins, fluoroquinolones, and penicillins/beta-lactamase inhibitors.

Antimicrobial Therapy Strategies

The treatment regimens for the study are detailed in Table 2. A total of 29 antimicrobial agents or β-lactamase inhibitors were utilized throughout the treatment course. Cefoperazone/sulbactam emerged as the most frequently administered antibacterial agent, followed by meropenem, highlighting the necessity for broad-spectrum coverage due to the high prevalence of MDRB infections within this population. Combination therapy regimens predominantly involved the use of meropenem, cefoperazone/sulbactam, and levofloxacin. Notably, there were no significant differences in outcomes between combination and monotherapy for each antimicrobial agent. Furthermore, fluconazole was identified as the most commonly used antifungal agent, aligning with the elevated incidence of *Candida* infections. In terms of antiviral therapy, nirmatrelvir/ritonavir was the sole agent employed for the treatment of SARS-CoV-2.

Variables Screening and Risk Factors Analysis

After screening 38 variables using LASSO regression, 19 variables were identified (Figure 4). Figure 5 presents the performance and detailed computational process of the LASSO model. These 19 variables were subsequently included in a logistic regression analysis to evaluate risk factors associated with mortality. This analysis revealed seven variables

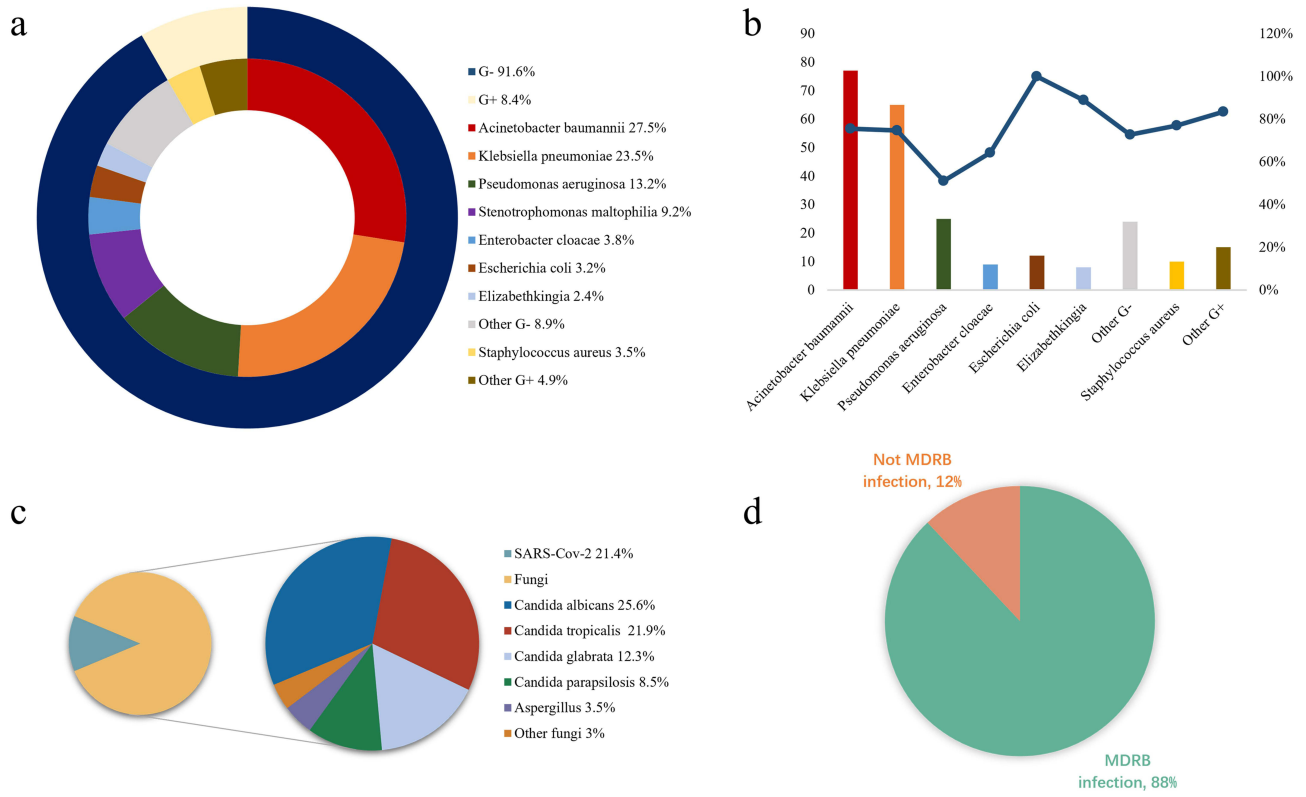

Figure 2 Distribution and characteristics of pathogens. (**a**) Distribution of bacterial isolates. (**b**) Number and proportion of MDRB. (**c**) Distribution of other pathogens, including viruses and fungi. (**d**) Proportion of MDRB among patients with bacteremia.

significantly related to death: length of hospital stay ($P < 0.001$, OR = 1.01, 95% CI = 1.01–1.02), myocardial infarction ($P = 0.042$, OR = 3.70, 95% CI = 1.05–13.12), bacteremia ($P < 0.001$, OR = 8.89, 95% CI = 2.53–31.88), gastrointestinal bleeding ($P = 0.003$, OR = 4.49, 95% CI = 1.68–11.99), respiratory failure ($P < 0.001$, OR =7.16, 95% CI = 2.87–17.85), mechanical ventilation ($P < 0.001$, OR = 7.98, 95% CI = 2.47–25.77), and BMI ($P = 0.002$, OR = 0.77, 95% CI = 0.65–0.91). The results of the data analysis indicate that, except BMI which serves as a protective factor, all other variables identified are associated with an increased risk of patient mortality (Table 3).

Discussion

Elderly patients are at an increased risk of infection due to the decline of their immune systems and the prevalence of comorbidities. In this study, we systematically assessed the distribution of pathogens, patterns of AMR, medication strategies, and risk factors associated with mortality in elderly patients with pulmonary infections. The results revealed MDR-GNB are main pathogens and clinical factors including respiratory failure, mechanical ventilation, the length of duration, gastrointestinal bleeding, and BMI significantly influenced the prognosis of elderly patients. These factors not only reflect the overall health status of the patients but also emphasize the importance of individualized management during treatment.

The distribution and characteristics of drug resistance among bacterial strains in elderly patients present significant challenges for infection management. In this study, the most frequently isolated GNB were Ab, Kp, and Pa, while Sa emerged as the predominant GPB. A separate study conducted at a different hospital in Beijing during the same period investigated elderly patients with COVID-19, many of whom experienced secondary lung infections and mixed infections. The strain distribution reported in that study was consistent with our findings.[15] Another ten-year (2007–2016) multi-center study in China focusing on elderly patients with hospital-associated pneumonia (HAP) also yield the similar distribution of pathogens with our study.[16] In contrast, an 11-year (2009–2020) national surveillance study on community-acquired pneumonia (CAP) in China revealed that among patients over 60, the most prevalent pathogens were Kp

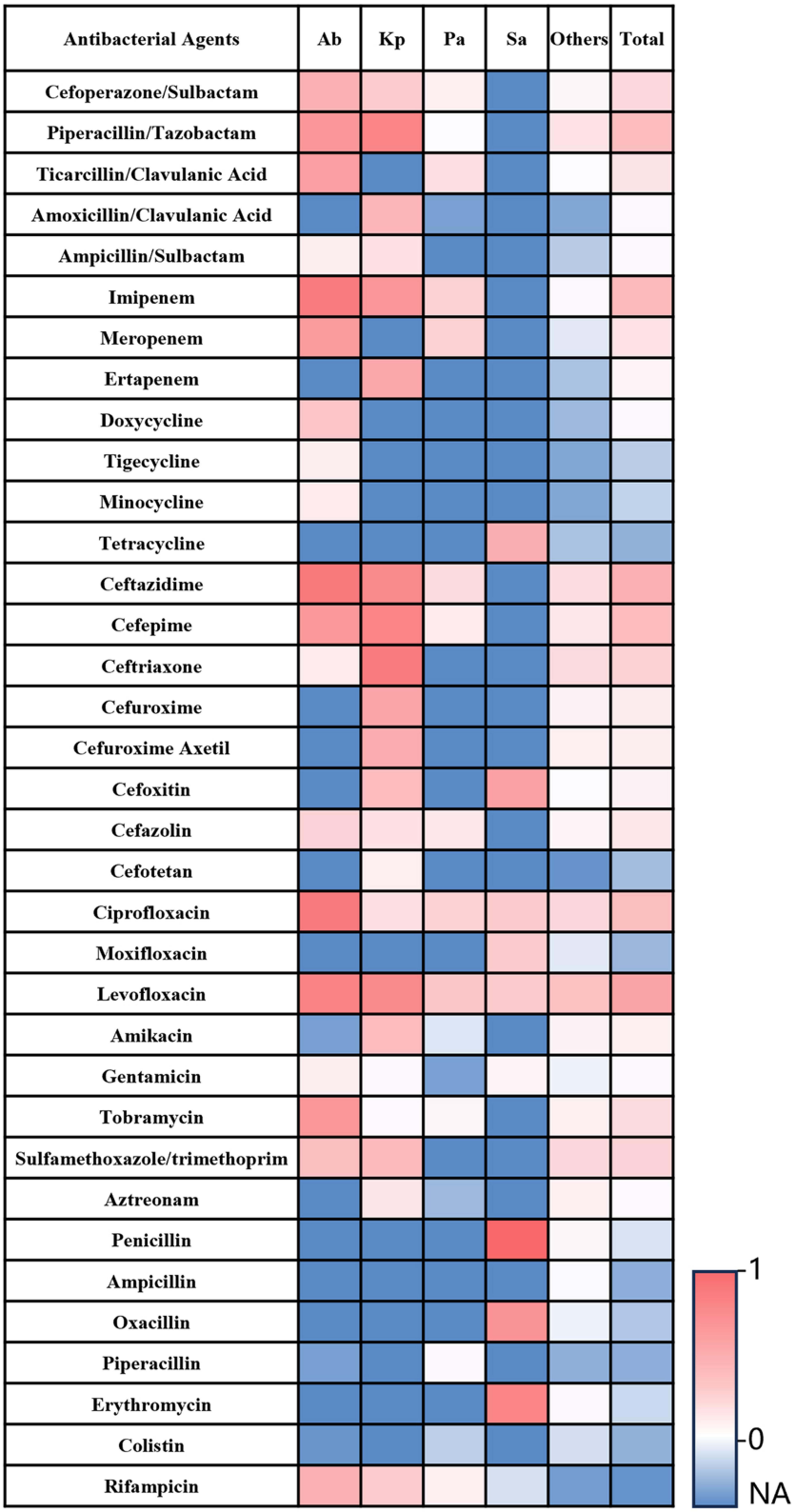

Figure 3 Heatmap of antimicrobial resistance profiles of common pathogens.

https://doi.org/10.2147/CIA.S571155

Table 2 Summary of the Usage of Antimicrobial Agents

Total Antimicrobial Agents	n	Comb-Imp	Mono-Imp	*P*-value
Antibacterial agents				
Meropenem	122	33	21	0.20
Biapenem	38	17	9	1.00
Imipenem/Cilastatin	20	2	5	0.20
Cefoperazone/Sulbactam	125	29	40	0.09
Ceftazidime/Avibactam	24	6	2	1.00
Moxifloxacin	15	5	2	1.00
Levofloxacin	86	31	17	0.24
Cefuroxime	5	1	3	1.00
Cefuroxime Axetil	12	3	6	0.51
Ceftriaxone	26	4	12	1.00
Ceftazidime	34	5	13	0.54
Cefaclor	3	1	2	–
Cefmetazole	17	2	6	1.00
Cefdinir	11	0	6	0.06
Teicoplanin	47	16	3	0.64
Vancomycin	47	14	3	1.00
Tigecycline	66	21	9	0.06
Minocycline	28	12	0	0.24
Piperacillin/Tazobactam	85	22	30	0.78
Linezolid	49	18	5	0.67
Colistin Sulfate	34	11	1	0.79
Amikacin	31	8	0	0.55
Trimethoprim/Sulfamethoxazole	8	7	0	–
Antifungal agents				
Voriconazole	19	–	–	–
Posaconazole	4	–	–	–
Fluconazole	68	–	–	–
Caspofungin	33	–	–	–
Amphotericin B	7	–	–	–
Antiviral agent				
Nirmatrelvir/Ritonavir	32	–	–	–

Note: Statistical significance is defined as $P < 0.05$.
Abbreviation: Comb/Mono-Imp, Combination/Monotherapy-Improvement.

and Pa, followed by *Streptococcus pneumoniae* (Sp) and Sa.[17] For both HAP and CAP, the overall infection rate of GNB is the highest, with Kp being a pathogen that requires close attention. For elderly patients who are hospitalized for a long duration, particular attention should be given to infections caused by Ab.

The resistance characteristics of bacteria also pose a significant concern. Although MDRB was not identified as a risk factor in this study, the pathogens demonstrated high levels of resistance to multiple antibiotic classes, with MDRB strains accounting for 64.7% of the total isolates. This finding aligns with the 64.9% observed in the study conducted by Yin et al.[16] Bacteremia, a recognized independent risk factor for mortality in elderly patients, is often complicated by the development of septic shock, organ failure, and other life-threatening conditions.[18–21] In our study, bacteremia was identified as a significant risk factor for mortality, with MDRB playing a pivotal role in exacerbating the infection. Notably, 88% of the pathogens isolated from bacteremia patients were MDRB, which suggests that the presence of MDR pathogens may aggravate bacteremia, contributing to higher mortality rates. MDR pathogens in elderly patients are associated with prolonged hospital stays, increased rates of respiratory failure, and significantly higher mortality compared to infections caused by non-resistant strains.[22] Furthermore, the prevalence of resistance to critical antibiotics, such as carbapenems, cephalosporins, and fluoroquinolones, which are frequently employed for severe infections,

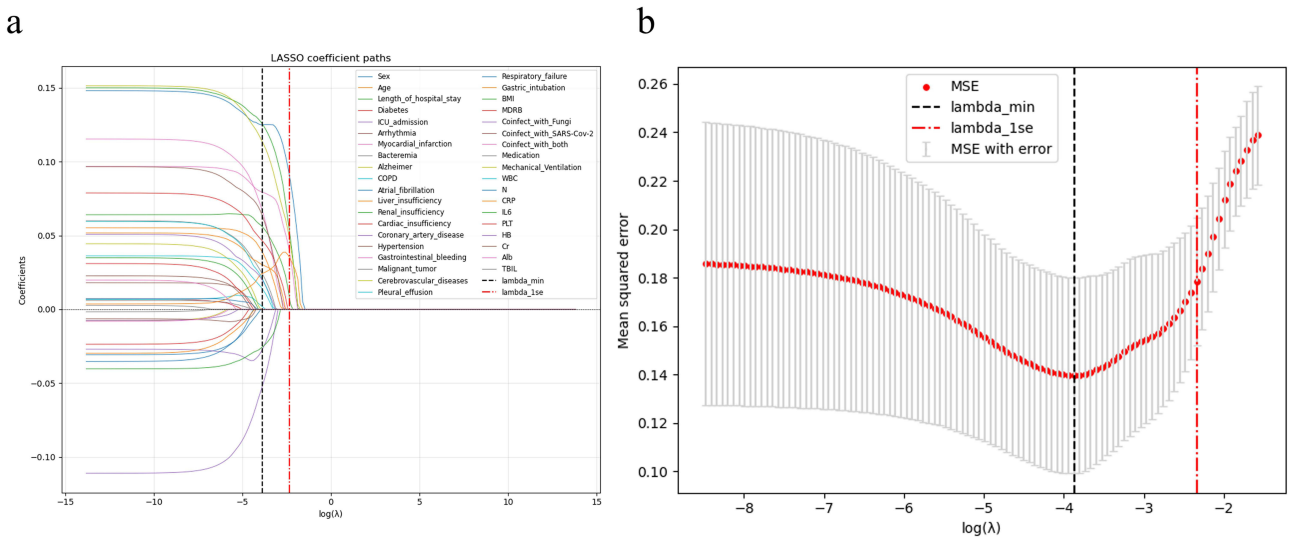

Figure 4 Variable selection using the LASSO binary logistic regression model. A coefficient profile plot was generated against the log (lambda). (**a**) LASSO coefficient profiles for the 38 variables. (**b**) The tuning parameter (λ) selection in the LASSO model was conducted using 10-fold cross-validation based on the minimum criteria.

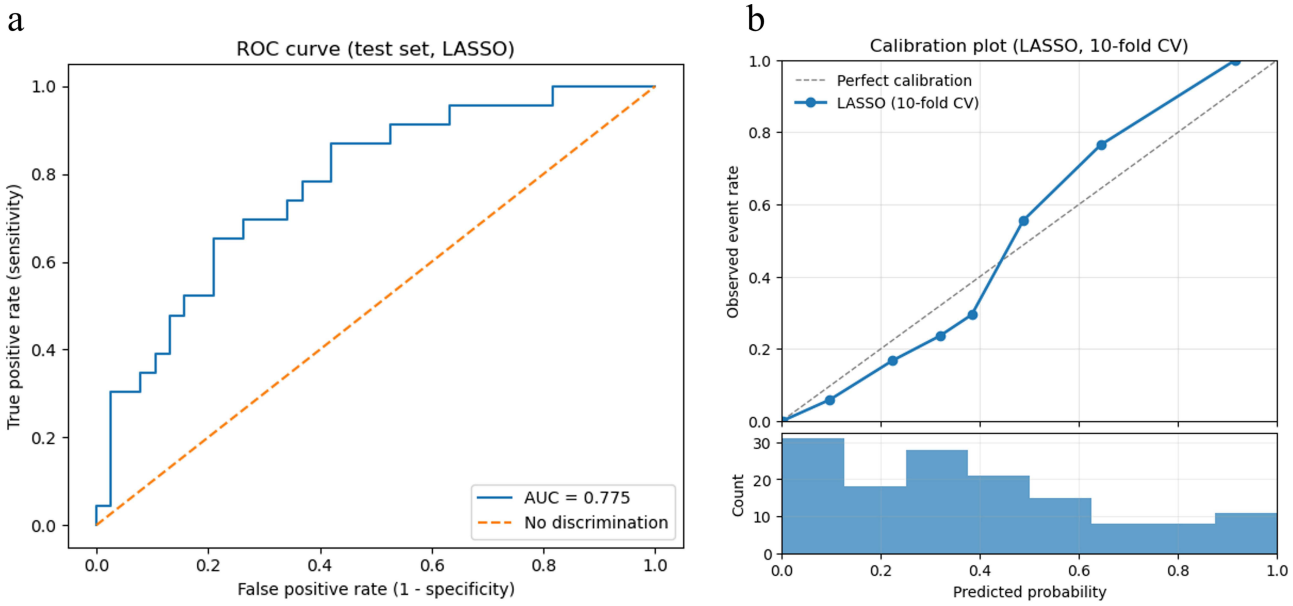

Figure 5 Discrimination and calibration performance of the LASSO model. (**a**) ROC curve and AUC. (**b**) Calibration plot showing the agreement between predicted and observed probabilities.

underscores the necessity for treatment strategies that are tailored to the specific resistance profiles of the implicated pathogens.[23,24] The management of infections in elderly patients requires more careful consideration than in younger populations due to altered pharmacokinetics, polypharmacy, and the presence of multiple comorbidities.[25–27] Additionally, the situation is further complicated by the occurrence of atypical symptoms in elderly individuals.[28] Therefore, the careful selection of antibiotics, appropriate dose adjustments, modifications in usage patterns, and diligent monitoring based on both AST and pharmacokinetic factors are critical for minimizing adverse outcomes and improving clinical management.[29–32]

In response to the rising incidence of MDR infections, combination therapy has become a widely adopted strategy for managing these complex cases, with 65.7% of patients in this study receiving combination regimens. We find that the mortality rate of patients receiving combination therapy is significantly higher than that of those receiving monotherapy

https://doi.org/10.2147/CIA.S571155

Table 3 Analysis of Risk Factors

Variables	Univariate Analysis		Multivariate Analysis	
	P	OR (95% CI)	*P*	OR (95% CI)
Age	**0.004**	1.05 (1.02 ~ 1.09)		
Length of hospital stay	**<0.001**	1.01 (1.01 ~ 1.01)	**<0.001**	1.01 (1.01 ~ 1.02)
ICU admission	0.433	0.79 (0.44 ~ 1.42)		
Myocardial infarction	**0.036**	2.53 (1.06 ~ 6.03)	**0.042**	3.70 (1.05 ~ 13.12)
Bacteremia	**0.007**	3.35 (1.40 ~ 8.03)	**<0.001**	8.98 (2.53 ~ 31.88)
COPD	**0.048**	4.03 (1.01 ~ 16.10)		
Liver insufficiency	0.074	1.77 (0.95 ~ 3.31)		
Renal insufficiency	**0.007**	2.24 (1.25 ~ 4.02)	0.064	2.23 (0.96 ~ 5.18)
Cardiac insufficiency	**0.006**	2.41 (1.28 ~ 4.52)	0.100	2.15 (0.86 ~ 5.36)
Coronary artery disease	0.588	0.85 (0.48 ~ 1.51)		
Gastrointestinal bleeding	**<0.001**	4.24 (2.14 ~ 8.41)	**0.003**	4.49 (1.68 ~ 11.99)
Pleural effusion	0.065	1.87 (0.96 ~ 3.64)		
Respiratory failure	**<0.001**	5.28 (2.81 ~ 9.91)	**<0.001**	7.16 (2.87 ~ 17.85)
Gastric intubation	**<0.001**	7.46 (3.18 ~ 17.54)	0.068	2.72 (0.93 ~ 7.96)
BMI	**0.025**	0.89 (0.81 ~ 0.99)	**0.002**	0.77 (0.65 ~ 0.91)
Coinfect with Fungi	0.050	1.78 (1.01 ~ 3.18)		
Coinfect with SARS-Cov-2	0.440	1.48 (0.55 ~ 4.02)		
Mechanical Ventilation	**<0.001**	7.57 (3.07 ~ 18.66)	**<0.001**	7.98 (2.47 ~ 25.77)
WBC	0.051	1.06 (1.00 ~ 1.12)		

Notes: Statistical significance is defined as $P < 0.05$, which is bolded in the table.
Abbreviations: OR, odds ratio; CI, confidence interval; ICU, intensive care unit; COPD, chronic obstructive pulmonary disease; BMI, body mass index; SARS-Cov-2, severe acute respiratory syndrome coronavirus 2; WBC, white blood cell.

(81% vs 19%, $P < 0.001$). However, after applying the LASSO model for variable selection, this factor was penalized, indicating that it was not a major determinant of mortality compared to other variables, or that it was linearly correlated with other factors. It is possible that the observed higher mortality rate in the combination therapy group is confounded by other variables, such as the severity of the patients' underlying conditions, comorbidities, and the presence of more resistant pathogens, rather than being directly attributable to the type of therapy. Further analysis of the outcomes of various antimicrobial agents revealed no significant difference in mortality between combination and monotherapy. Previous research investigating the effects of combination versus monotherapy on outcomes in ICU elderly patients, has also reported no significant differences in treatment outcomes.[33,34] The primary objective of combination therapy is to enhance therapeutic efficacy and mitigate the development of AMR.[35] A meta-analysis found that a reduction in resistance development was only observed for specific bacterial strains under combination therapy. Nonetheless, they posited that combination therapy remains a viable strategy to decelerate bacterial resistance, despite the potential for it to also expedite resistance development.[36] Another meta-analysis suggested that combination therapy involving at least two agents with demonstrated in vitro activity led to lower mortality rates in patients with bloodstream infections and infections caused by carbapenemase-producing *Enterobacteriaceae*. In cases where the combination included only one in vitro active agent, no difference in mortality was observed.[37] These findings underscore the necessity for combination therapy to be guided by continuous monitoring of bacterial resistance patterns, using of antimicrobial agents with good in vitro activity and synergistic effects against resistant pathogens. While combination therapy may not always demonstrate superior clinical efficacy, it remains a potentially valuable component of treatment strategies for elderly population, particularly in light of the escalating challenge of AMR.[14,38]

In our study, both respiratory failure and mechanical ventilation were strongly associated with increased mortality. A multicenter study in Italy demonstrated that elderly patients with respiratory failure had a significantly higher mortality rate compared to those without it (16.6% vs 8.2%, $P < 0.001$), suggesting that respiratory failure reflects the severity of the underlying condition.[39] Mechanical ventilation, the primary therapeutic modality for patients with respiratory failure,

has also been shown to contribute to increased mortality.[40] Similar findings were reported in studies conducted in Israel and Spain, where mechanical ventilation was found to reduce survival rates in elderly patients with pneumonia.[41,42] Furthermore, mechanical ventilation is associated with various complications, particularly ventilator-associated pneumonia (VAP), which can worsen the underlying infection and lead to worse outcomes.[43] Elderly patients generally exhibit lower physiological resilience compared to younger individuals, and their prognosis often worsens following mechanical ventilation. A European multicenter study on VAP reported that the mortality rate was higher in elderly patients than in middle-aged patients (51% vs 35%, $P = 0.036$).[44] Given these considerations, non-invasive ventilation should be considered as the initial treatment for patients whenever feasible to reduce the need for invasive mechanical ventilation and its associated risks. If non-invasive oxygenation support fails to achieve oxygen saturation > 90%, mechanical ventilation should likely be considered. The management approach should be tailored to the specific underlying condition.[45] Furthermore, preventing VAP is crucial for improving patient outcomes. A detailed prevention strategy recommends several measures, such as maintaining proper hygiene, elevating the head of the bed, and minimizing sedation, which can significantly reduce the incidence of ventilator-associated complications. Whenever possible, early extubation and weaning from mechanical ventilation should be prioritized to minimize ventilation duration and reduce associated risks.[46]

Myocardial infarction, as a mortality risk factor, may aggravate heart failure and respiratory dysfunction in elderly patients through vascular remodeling and circulatory impairment.[47–49] The vascular remodeling that occurs after myocardial infarction leads to reduced oxygen supply to vital tissues, including the lungs.[50,51] This is particularly problematic in elderly patients, whose immune and circulatory systems are often weakened due to aging. Reduced blood flow increases the likelihood of tissue hypoxia and immune dysfunction, creating a conducive environment for the development of severe pulmonary infections.[52–54] Additionally, the presence of MDRB presents a significant challenge in the management of infections in these patients. The combination of impaired cardiac function, vascular remodeling, and compromised pulmonary health can create a vicious cycle, where worsening heart failure exacerbates pulmonary infections, and the infection in turn places additional strain on the heart.[55,56] This intricate multi-system interaction underscores the urgent need for comprehensive interventions targeting vascular protection, immune modulation, and precise oxygen therapy. Early detection and tailored treatments remain key to improving clinical outcomes and reducing mortality in this high-risk population.[57]

Our study identified prolonged hospital stays as a significant risk factor for mortality. Extended hospitalization is a well-established predictor of mortality in elderly patients with pneumonia, as it may signify more severe disease or complications, along with a reduced response to treatment.[58,59] Additionally, longer hospital stays enhances the susceptibility of elderly patients to nosocomial MDR pathogens. As our research findings demonstrate, the strains affecting elderly patients are predominantly MDRB, which further complicates disease treatment.

Moreover, gastrointestinal bleeding is significantly increasing the risk of death in our study. This finding corroborates existing research that highlights its impact on prognosis in patients with infections.[60,61] In elderly patients, the occurrence of gastrointestinal bleeding may be linked to several factors, including long-term use of anticoagulants, malnutrition, and adverse drug reactions.[62] Additionally, proton pump inhibitors (PPIs), which are commonly used to manage gastrointestinal bleeding, may further increase the risk of infections. PPIs can elevate gastric pH levels and alter the normal oropharyngeal microbiota, potentially heightening susceptibility to respiratory infections by enabling pathogens to survive more effectively.[63] This risk is particularly relevant for elderly patients, who may already have compromised immune systems and heightened vulnerability to infections. Consequently, when managing pulmonary infections in elderly patients, it is essential to carefully consider the risks associated with gastrointestinal bleeding and the use of PPIs, implementing appropriate preventive and therapeutic measures to enhance their outcomes.

Many studies have shown that a low BMI in elderly populations is frequently associated with malnutrition and frailty, both of which would critically impair immune function, hinder recovery, and increase susceptibility to complications. Consequently, this exacerbates the severity of pulmonary infections.[64–66] Our study further highlights that a lower BMI is strongly linked to poorer outcomes in elderly patients with pneumonia. Since elderly patients often have unique dietary needs and may encounter barriers to adequate nutrition, such as difficulty swallowing or reduced appetite, nutritional support and rehabilitation programs should be integrated into the comprehensive management.[67,68] A randomized

controlled trial demonstrates that nutrition interventions can significantly improve the nutritional status and overall health of elderly patients with pneumonia, thereby reducing readmission rates.[69]

The present study has several limitations that should be considered when interpreting the results. First, the retrospective design constrains our ability to establish causal relationships between the identified risk factors and mortality. While we identify certain factors associated with increased mortality, it is important to note that these findings are associative markers rather than indicators of causality. The statistical results do not imply direct cause-and-effect relationships. Second, as this study was conducted at a single center, the generalizability of the findings may be limited to other settings with different patient populations or treatment protocols. Furthermore, variability in clinical management practices among different healthcare providers, particularly regarding the use of antibiotics and supportive care, may contribute to differences in patient outcomes that are not adequately addressed in this analysis.

Conclusion

This study demonstrates the complexity of pulmonary infections in elderly patients and underscores the need for comprehensive management strategies. Key factors requiring attention include gastrointestinal bleeding, mechanical ventilation, nutritional status, myocardial infarction, and MDR pathogens. Notably, a higher BMI, indicating better nutritional reserve, was identified as a significant protective factor associated with improved prognosis. While the retrospective, single-center design limits generalizability, the use of LASSO regression enhanced model robustness in identifying these risk factors. Future research should focus on validating these findings and developing tailored treatment protocols for this vulnerable population.

Ethical Approval and Consent to Participate

As patient consent for the review of medical records was waived by the Ethics Committee of the Chinese PLA General Hospital (Approval No. S2024-394-01), we ensured that all patient data used in this study were anonymized and handled with strict confidentiality. All personal identifiers have been removed to protect patient privacy, and the data were analyzed in accordance with ethical standards for research involving human subjects.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study was funded by the New Medicine Clinical Research Fund (4246Z512).

Disclosure

The authors declare that there are no commercial or financial relationships that could be perceived as potential conflicts of interest in relation to this research.

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